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Original Article

Evolving a National Preventive Protocol for Vertical Transmission of Group B *Streptococcus* in a Low-Resource Country: The Culture-Based Approach

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Abstract

Objective: The study objective was to determine the role and applicability of the culture-based approach to Group B *Streptococcus* (GBS) screening and the effect on pregnancy outcome. **Materials and Methods:** This is a prospective cross-sectional study involving 166 consenting antenatal clinic attendees at 35–37 weeks' gestation using purposive sampling. All participants had vaginal and rectal swabs collected and cultured with the availability of culture results at the time of presentation in labor. All GBS-colonized mothers received intrapartum prophylaxis with parenteral antibiotics based on antibiotic sensitivity from the onset of labor or the rupture of membrane until delivery. Statistical analysis was conducted using SPSS software version 21.0, while $P < 0.05$ was considered statistically significant. **Results:** The GBS maternal prevalence was 7.8%, and culture-positive women had both vaginal and rectal colonization. Marital status ($P = 0.002$), multiple sexual partners ($P = 0.001$), previous sexually transmitted infections ($P = 0.013$), and low socioeconomic status ($P = 0.012$) were significantly associated with GBS colonization. GBS isolates were 100% sensitive to ampicillin, all participants had a minimum of two doses of intrapartum prophylaxis with parenteral ampicillin, there was no maternal morbidity, and the vertical transmission of GBS was 0%. **Conclusions:** The culture-based approach and the culture-based maternal intrapartum prophylaxis prevented both maternal and neonatal complications from GBS. Establishing regional- and national-level preventive protocols will be a central strategy for the prevention.

Keywords: Group B *Streptococcus*, maternal sepsis, national protocol, neonatal sepsis, screening protocol, vertical transmission of infections

Introduction

Group B *Streptococcus* (GBS) is a vertical transmissible infection and a cause of puerperal infection and neonatal sepsis.[1] Its prevalence in humans varies depending on the geographical location, race, socioeconomic status, and a history of previously affected infants and previous preterm delivery.[2] GBS infection was initially thought to be a disease of developed countries; however, studies showed a similar prevalence in low-resource countries.[3] Reports across the African continent have also revealed that GBS is emerging as an important cause of neonatal sepsis, especially in low-income countries.[4,5]

Globally, GBS carriage among parturient ranges between 10.0% and 40.0%.[1,3,6] In Nigeria, it ranges from 6.6% to 32.0%.[7-10] GBS is associated with significant maternal peripartum disease including bacteremia, endocarditis, chorioamnionitis, and endometritis.[2] Asymptomatic GBS infection is equally deleterious with associated adverse pregnancy outcomes including low birth weight, preterm delivery, and premature rupture of membrane (PROM).[5] In addition, neonatal GBS disease affects 0.1–0.5/1000 live births,

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resulting in up to 50.0% neonatal mortality and significant long-term morbidity.[11]

There are two main approaches, namely the culture- and risk-based approaches, to screening for GBS infection in pregnancy. The culture-based approach is based on the universal antenatal maternal screening at 35–37 weeks' gestation using culture of low vaginal and/or rectal swab. This is the gold standard and standard of care in developed countries, especially in the USA.[5,11] The risk-based approach is based on clinical risk factor evaluation in parturient; thus, it is limited only to symptomatic women although it is cost-effective and time saving and targets women without prior contact with health personnel.[5] Therefore, it is preferred in some countries, especially in low-resource settings. Neonatal GBS infection can be prevented by the administration of prophylactic intravenous antibiotics based on the sensitivity pattern of the GBS strain isolated from the colonized pregnant woman.[12] Although oral administration may cause a transient decrease in the GBS load, bacterial eradication is not achieved except in GBS urinary tract infection; thus, it is not recommended.[12]

Despite the documented maternal morbidity and neonatal morbidity and mortality from GBS disease, many institutions in low-resource countries lack a standardized protocol to prevent its vertical transmission.[13] This study, therefore, aimed to add to the available evidence to stimulate the formation of institutional protocols for GBS management in low-resource countries.

Materials and Methods

This was a cross-sectional study involving 166 antenatal clinic attendees at a tertiary hospital in North-Central Nigeria. The sample size was calculated; purposive sampling was employed while the inclusion criteria were booked status, gestational age of 35–37 weeks, and willingness to participate. Unbooked women, those outside the specified gestational age, and those unwilling to participate were excluded from the study. After obtaining consent, all participants had low vaginal and rectal swabs collected and analyzed with the availability of culture result at the time of presentation in labor. The samples were collected using separate swab sticks for the vagina and rectum; the swab sticks were transferred in Todd Hewitt medium to the laboratory for analysis using an earlier described guideline.[14] The samples were inoculated onto blood and chocolate agars and incubated for 18–24 h at 35°C–37°C in ambient air (blood agar) and carbon dioxide-enriched atmosphere (a candle extinction jar). The culture plates were inspected to identify organisms suggestive of GBS (i.e., narrow zone of β-hemolysin). The isolates were further characterized using a combination of Gram stain and biochemical tests, i.e., catalase test; bacitracin susceptibility test; and Christie–Atkins–Munch–Peterson tests, to distinguish between *Staphylococcus* and *Streptococcus*. Antibiotic sensitivity was done by disc diffusion method. All GBS isolates were first inoculated into sterile normal saline, and the suspension was adjusted to 0.5% McFarland standard. The suspension was used to inoculate Mueller–Hinton agar into which single antibiotic discs were applied and incubated at 37°C aerobically for 18–24 h inside the candle extension jar. *Staphylococcus aureus* (ATCC® 25923) strain was used as the control, and the results were read and interpreted by comparing inhibition zone diameter of test with the control according to laboratory (Clinical and Laboratory Standards Institute) guidelines.

Participants thereafter had routine antenatal follow-ups and were required to present early in labor. All GBS-positive parturient had prophylaxis with intravenous ampicillin 2 g stat, and then 1 g 4 hourly till delivery starting from the time of presentation in labor. Puerperal follow-up was with telephone calls and counseling to re-present if there were fever, foul-smelling lochia, or abnormal vaginal discharge. All neonates were monitored for the first 48 h for the symptoms and signs of early-onset neonatal sepsis which included grunting, poor feeding, lethargy, fever (temperature ≥38°C), tachycardia (heart rate >160/min), or tachypnea (respiratory rate >60 cycles/minute). Neonates without the clinical features of GBS were discharged home at 48 h after educating the mother on the signs of neonatal GBS disease such as grunting, poor feeding, fever, irritability, lethargy (limpness), and immediate presentation, if such was noticed. In addition, the mothers were phoned daily during the 1st week of life to find out the clinical conditions of the neonates. Babies with feature of neonatal infection were admitted at the neonatal intensive care unit and managed appropriately including a GBS culture to ascertain the source of infection. While awaiting the results of investigations, empirical treatment using parenteral penicillin and intramuscular gentamycin was commenced for the babies.

Ethical approval was obtained from the ethical review committee of the tertiary institution before the commencement of the study. Statistical analysis was conducted using SPSS software version 21.0 (IBM, Armonk, NY, USA), and $P < 0.05$ was considered statistically significant.

Results

The age range of the 166 participants was 18–39 years (mean ± standard deviation = 30.3 ± 4.9). Thirteen participants were culture positive for GBS, with a prevalence of 7.8% (78.0/1000). All colonized women had both vaginal and rectal colonization. The maternal biosocial factors that significantly related to GBS carriage included marital status ($P = 0.002$), multiple sexual partners ($P = 0.001$), previous sexually transmitted infection ($P = 0.013$), and low socioeconomic status ($P = 0.012$) [Table 1].

Table 2 shows that the only statistically significant risk factor for GBS carriage was preterm PROM ($P = 0.001$). In addition, GBS carriage was statistically significantly ($P = 0.001$) related to gestational age at delivery as more than half of the GBS carriers (53.8%) had preterm delivery, whereas two (15.4%) had babies with low birth weight. At the end of 24 h,

Table 1: Relationship between parturient biosocial characteristics and Group B *Streptococcus* carriage

Risk factors	GBS, *n* (%)			t/χ^2	*P*
	Positive	Negative	Total		
Age					
Mean±SD	27.92±6.97	30.50±4.70		−1.821	0.070
≤20	3 (23.1)	3 (2.0)	6 (3.6)	10.771	0.029*
21-25	3 (23.1)	21 (13.7)	24 (14.5)		
26-30	3 (23.1)	55 (35.9)	58 (34.9)		
31-35	2 (15.4)	50 (32.7)	52 (31.3)		
>35	2 (15.4)	24 (15.7)	26 (15.7)		
Marital status					
Single	6 (46.2)	4 (2.6)	10 (6.0)	36.541	0.002*
Married	4 (30.8)	140 (91.5)	144 (86.7)		
Divorced	2 (15.4)	7 (4.6)	9 (5.4)		
Widow	1 (7.7)	2 (1.3)	3 (1.8)		
Religion					
Christianity	3 (23.1)	66 (43.1)	69 (41.6)	2.761	0.251
Islam	10 (76.9)	82 (53.6)	92 (55.4)		
Traditional	0 (0.0)	5 (3.3)	5 (3.0)		
Educational status					
None	3 (23.1)	14 (9.2)	17 (10.2)	5.961	0.114
Primary	5 (38.5)	21 (13.7)	26 (15.7)		
Secondary	2 (15.4)	39 (25.5)	41 (24.7)		
Tertiary	3 (23.1)	79 (51.6)	82 (49.4)		
Gravidity					
1	2 (15.4)	35 (22.9)	37 (22.3)	0.68	0.712
2-4	7 (53.8)	92 (60.1)	99 (59.6)		
≥5	4 (30.8)	26 (17.0)	30 (18.1)		
Parity					
0	2 (15.4)	2 (1.3)	4 (1.8)	6.259	0.099
1	7 (53.8)	67 (43.8)	74 (45.8)		
2-4	3 (23.1)	72 (47.1)	75 (44.6)		
≥5	1 (7.7)	12 (7.8)	13 (7.8)		
Sexual partners					
1	3 (23.1)	138 (90.2)	141 (84.9)	42.20	<0.001*
≥2	10 (76.9)	15 (9.8)	25 (15.1)		
History of STI					
Yes	9 (69.2)	50 (32.7)	59 (35.5)	6.987	0.013*
No	4 (30.8)	103 (67.3)	107 (64.5)		
Average income of spouse ($)					
≤90	7 (53.8)	31 (20.3)	38 (22.9)	7.657	0.012
>90	6 (46.2)	122 (79.7)	128 (77.1)		

*Statistically significant (i.e., $P<0.05$). *t*: Independent sample *t*-test, GBS: Group B *Streptococcus*, SD: Standard deviation, STI: Sexually transmitted infection

nine (69.2%) neonates were healthy, whereas four (30.8%) had perinatal asphyxia; on the 7th day of life, all neonates of GBS carrier mothers were healthy with no neonatal sepsis recorded. All GBS carrier mothers received intrapartum intravenous ampicillin; 15.4% received two doses while 53.8% received five doses; there was no maternal puerperal complication.

Table 3 shows that all the 13 (100%) GBS carriers isolated were sensitive to ampicillin, 11 (84.6%) to vancomycin, 9 (69.2%) to erythromycin, and 10 (76.9%) to gentamycin. On logistic regression [Table 4], the significant predictor of GBS carriage was found to be multiple sexual partners, which was an independent predictor of GBS carriage ($P = 0.024$) with an odd that is eight times higher than that of a parturient with a single sexual partner.

Discussion

The incidence of GBS among pregnant women in this study was 7.8%, which is comparable to 6.6%–11.3% in parts of Nigeria,[7-9] 4.0% in Togo,[15] and 9.5% in Korea.[16] Other studies from different regions of Africa reported a prevalence of 16.5%–19.0%,[15,17,18] while an international study[1] reported the prevalence to be 29.0% for Africans, 13.0% for Asians, and 21.0% for Europeans. The wide variation in the reported prevalence may be attributed to differences in the geographical

Table 2: Maternal risk factors associated with Group B *Streptococcus* carriage

Risk factors	GBS, *n* (%)			χ^2	*P*
	Positive	Negative	Total		
Prior history of GBS					
Yes	0 (0.0)	0 (0.0)	0 (0.0)	NA	NA
No	13 (100.0)	153 (100.0)	166 (100.0)		
Preterm SPROM					
Yes	7 (53.8)	18 (11.8)	25 (15.1)	13.460	<0.001*
No	6 (46.2)	135 (88.2)	141 (84.9)		
Prolonged SPROM					
Yes	0 (0.0)	0 (0.0)	0 (0.0)	NA	NA
No	13 (100.0)	153 (100.0)	166 (100.0)		
Chorioaminionitis					
Yes	0 (0.0)	0 (0.0)	0 (0.0)	NA	NA
No	13 (100.0)	153 (100.0)	166 (100.0)		
Gestational age at delivery (weeks)					
<37	7 (53.8)	18 (11.8)	25 (15.1)	13.175	0.001*
37-40	6 (46.2)	117 (76.5)	123 (74.1)		
>40	0 (0.0)	18 (11.8)	18 (10.8)		
Birth weight (kg)					
<2.5	2 (15.4)	7 (4.6)	9 (5.4)	1.004	0.605
2.5-3.9	11 (84.6)	138 (90.2)	149 (89.8)		
≥4.0	0 (0.0)	8 (5.2)	8 (4.8)		
1st min Apgar score					
<7	7 (53.8)	87 (56.9)	94 (56.6)	0.044	1.000
≥7	6 (46.2)	66 (43.1)	72 (43.4)		
5th min Apgar score					
<7	3 (23.1)	9 (5.9)	12 (7.2)	3.029	0.082
≥7	10 (76.9)	144 (94.1)	154 (92.8)		
Neonatal sepsis at day 7					
Yes	0 (0.0)	0 (0.0)	0 (0.0)	NA	NA
No	13 (100.0)	153 (100.0)	166 (100.0)		
Maternal puerperal outcome					
No puerperal sepsis	13 (100.0)	145 (94.8)	158 (95.2)	0.714	1.000
Puerperal sepsis	0 (0.0)	8 (5.2)	8 (4.8)		

*Statistically significant (i.e., $P<0.05$). GBS: Group B *Streptococcus*, NA: Not available, SPROM: Spontaneous premature rupture of membranes

Table 3: Antibiotic sensitivity pattern of Group B *Streptococcus*-positive carriers

Antibiotic sensitivity pattern	Sensitive, *n* (%)	Resistant, *n* (%)
Ampicillin	13 (100.0)	0 (0.0)
Clindamycin	2 (15.4)	11 (84.6)
Vancomycin	11 (84.6)	2 (15.4)
Erythromycin	9 (69.2)	4 (30.8)
Gentamycin	10 (76.9)	3 (23.1)

location and other demographic variables such as maternal age, gestational age, obstetric history, study population, as well as the culture and the isolation techniques. Studies have also shown that racial and genetic factors are known contributing factors to variations in GBS carriage.[1]

Although a majority of participants in this study were aged 26–35 years, the highest GBS colonization was among single mothers aged 18–30 years. The young women were more sexually active; this corroborates a previously reported association of GBS with sexually active young women having multiple sexual partners and poor socioeconomic status.[18] The observed association of GBS colonization with primiparity appears similar to other reports from Nigeria,[17] which may be linked to the expected higher sexual activity among them. The effect of GBS colonization in preterm delivery was documented in this study to corroborate earlier reports.[4,18] In this study, there was culture-based screening, adequate intrapartum parenteral prophylaxis, and no vertical transmission of GBS infection. In a study on risk-based approach to GBS management among women with risk factors for GBS conducted in the same city as the index study, 20.8% of the participants had risk factors for vertical transmission of GBS and despite parenteral intrapartum prophylaxis, the incidence of early-onset neonatal GBS disease among women with risk factors was 12.9/1000.[4] This finding contrasts with the index study which reported no vertical transmission, thereby suggesting better outcome with the culture-based approach. Another challenge with the risk-based approach is the cases

Table 4: Multiple logistic regression of predictors of Group B *Streptococcus* carriage

Variable	OR	95% CI	*P*
Age group (years)			
≤20 (Ref)			
21-25	0.557	0.019-16.543	0.735
26-30	0.687	0.024-20.014	0.827
31-35	0.768	0.047-12.650	0.854
>35	0.362	0.017-7.563	0.513
Marital status			
Single			
Married	2.940	0.072-119.338	0.568
Divorced	3.892	0.221-68.447	0.353
Widow	12.375	0.930-164.704	0.057
Sexual partners			
Single (Ref)			
Multiple	8.438	1.332-53.473	0.024*
History of STI			
Yes (Ref)			
No	1.615	0.314-8.306	0.566

*Statistically significant (P<0.05). Ref: Refers to reference category for logistic regression analysis, OR: Odds ratio, STI: Sexually transmitted infection, CI: Confidence interval

of inadequate prophylaxis due to late presentation. In Ilorin, Nigeria, a risk-based evaluation for GBS transmission reported that neonatal GBS disease occurred in babies of mothers who had inadequate antibiotics (less than two doses) due to late presentation in labor.[4] This remains a major challenge on the effectiveness of the risk-based approach as some parturient are unable to attain adequate prophylaxis unlike the culture-based approach. However, proponents of the risk-based approach have emphasized their particular benefit for unbooked patients, which is common in low-resource settings and also because it is less expensive.[5] In addition, this study reported no maternal complication unlike 17.5% in another study using the risk-based approach.[5] Therefore, the culture-based approach for GBS prevention is shown to be superior to the risk-based approach.

This study reported no resistance to ampicillin, thereby supporting ampicillin as the drug of choice for intrapartum antibiotics prophylaxis for GBS colonization in pregnant women.[18] However, the observed resistance to erythromycin compares to reports by other researchers.[19] This further supports the recommendation that antibiotic susceptibility testing for erythromycin therapy is desirable to prevent neonatal GBS infection.[20] However, erythromycin remains the drug of choice for women with serious penicillin allergy although Tazi *et al*. reported GBS susceptibility to all other antimicrobial and low-level resistance against aminoglycosides.[21] The opinion is that differences in antimicrobial use, prophylaxis protocol, and serotype frequency may account for these differences.[22]

While antibiotic resistance is global, physicians have been encouraged to join public health authorities, the infection-control community, and the pharmaceutical industry to curb the inappropriate use of antibiotics and promote responsible prescribing.[23]

Conclusions

Nigeria requires effective institutional as well as national policies on the prevention of neonatal GBS as the disease is not uncommon in our country as well as in other low-income countries. The culture-based approach offers better maternal and neonatal outcome which in effect may eradicate vertical GBS transmission. Parturient in Nigeria also deserve the maximal effort to treat the infection and prevent the eventual complications.

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Conflicts of interest

There are no conflicts of interest.

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ملخص المقال باللغة العربية

تطوير بروتوكول وقائي وطني للانتقال العمودي للمجموعة البكتيرية العقدية نوع (ب) في بلد منخفض الموارد: النهج القائم على الاستنبات.

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الهدف: الهدف من هذه الدراسة هو تحديد دور وإمكانية تطبيق النهج القائم على الاستنبات (زرع البكتيريا) لفحص المجموعة البكتيرية العقدية نوع (ب) وتأثيرها على نتائج الحمل.

المرضي والطرق: هذه دراسة مستعرضة اِستِبَاقِيَّة تشمل 166 امرأة حامل في الأسبوع 35-37 من الحمل وذلك عبر أخذ عينات من المستقيم والمهبل لكل امرأة للفحص عن احتمالية العدوي بالمجموعة البكتيرية العقدية نوع (ب)، مع توفر نتائج التحاليل عند الولادة. تلقت جميع الأمهات الاتي تم تشخيص أصابتهم بالمجموعة البكتيرية العقدية نوع (ب) العلاج الوقائي باستخدام المضادات الحيوية عن طريق الحقن بناءً على حساسية المضادات الحيوية من بداية المخاض أو تمزق الغشاء حتى الولادة. أجريت التحليل الإحصائية باستخدام برنامج SPSS، الإصدار 21.0، في حين اعتبر (P <0.05) ذا دلالة إحصائية.

النتائج: أثبتت النتائج أن 7.8% من الحوامل كن مصابات بعدوي المجموعة البكتيرية العقدية نوع (ب)، وكانت العدوي تشمل كل من المهبل والمستقيم. وارتبطت هذ العدوي ارتباطا وثيقا وذا دلالة إحصائية بعدة عوامل منها الحالة الاجتماعية، وتعدد الشركاء الجنسيين، الالتهابات السابقة المنقولة جنسياً، والحالة الاجتماعية والاقتصادية المنخفضة (P<0.05). ومن ناحية أخري كانت جميع عينات البكتيريا العقدية نوع (ب) المعزولة من الحوامل حساسة بنسبة 100٪ للمضاد الحيوي أمبسلين، ولذا تم علاج جميع الأمهات المصابات بحقن جرعتين من الأمبسلين على الأقل كعلاج وقائي قبل الولادة. بعد الولادة لم نلاحظ أي اعتلال للأمهات، كما أن نقل العدوي الرأسي من الأم إلى الجنين كان صفراً.

الاستنتاج: إن النهج القائم على الاستنبات (زرع البكتيريا)، وقاعدة العلاج الوقائي بالمضادات الحيوية المعتمدة على نتائج زرع البكتيريا منعت كل من المضاعفات الأمومية والوليدية التي قد تنتج نتيجة عدوي الأم بالبكتيريا العقدية نوع (ب). وعليه سيكون إنشاء بروتوكولات وقائية على الصعيدين الإقليمي والوطني استراتيجية مهمة للوقاية من العدوي للأم والطفل.

الكلمات المفتاحية: البكتيريا العقدية نوع (ب)، تعفن الدم الأم، البروتوكول الوطني، الإنتان الوليدي، بروتوكول الفرز، الانتقال الرأسي للعدوى.