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Is Antenatal Group B Streptococcal Carriage a Predictor of Adverse Obstetric Outcome?

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ABSTRACT

Objectives: While early-onset neonatal GBS sepsis is positively associated with premature birth and prolonged rupture of membranes, there is debate in the literature as to whether maternal GBS colonization is a predictor of adverse obstetric outcome. This is a critical issue to resolve for appropriate management (expectant vs. interventional management) of the patient presenting with premature rupture of membranes, who has no overt signs of sepsis, but who is colonized with GBS.

Methods: Since 1981 it has been hospital policy to screen all public patients antenatally for genital carriage of GBS by collection of a low vaginal swab at 28–32 weeks. All patients colonized with GBS antenatally are given penicillin as intrapartum chemoprophylaxis. Review of all GBS-colonized antenatal patients for a 12-month period (580 of 4,495 patients) and a randomized (every fourth consecutive antenatal patient) number of noncolonized patients (958) was made. Lower vaginal GBS colonization and other risk factors for preterm delivery were assessed using univariate and multivariate generalized linear modeling.

Results: In the study group, the maternal GBS colonization rate was 12.9%. When cofounding variables were controlled in a multivariate analysis, the association between antepartum GBS colonization and preterm labor and preterm rupture of membranes was not significant.

Conclusion: Maternal antenatal carriage of GBS does not predict preterm labor. Therefore it is appropriate that expectant management occur for a GBS-colonized woman who ruptures her membranes, is not in labor, and has no evidence of sepsis. Infect. Dis. Obstet. Gynecol. 8:138–142, 2000. © 2000 Wiley-Liss, Inc.

KEY WORDS

group B streptococcus; preterm labor; preterm rupture of the membranes

Group B streptococcus (GBS) is a major cause of early-onset neonatal sepsis occurring at a rate of 1–4 per 1,000 live births.[1,2] The source of GBS is the maternal genital tract, where it colonizes 15–20% of women.[1,2] Obstetric risk factors associated with early-onset neonatal GBS infections include: premature onset of labor (< 37 weeks gestation), prolonged rupture of the membranes (> 12 hours), heavy maternal genital GBS colonization, multiple births, GBS bacteriuria, presence of maternal sepsis, and lack of or low levels of maternal antibodies to type-specific capsular polysaccharide of GBS serotype infecting the neonate.[1–4] Yet whether maternal GBS genital colonization is a predictor of preterm delivery or preterm rupture of membranes is unclear, with reports from various centers finding a positive correlation,[5–8] while others have not.[9–11] This is an important issue to resolve to ensure appropriate management of the patient presenting with premature rupture of membranes, who has no

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Clinical Study

overt signs of sepsis, but who is colonized with GBS. Consequently, whether the patient should be managed expectantly or otherwise is debatable.[12,13]

In order to prevent early-onset neonatal GBS sepsis, it has been policy since 1981 for all public antenatal patients at the Royal Women's Hospital, Melbourne, Australia to be screened antenatally for GBS.[14] We have shown that intrapartum chemoprophylaxis administered to all colonized women not only reduces neonatal GBS sepsis, but also is cost effective.[14,15] We therefore reviewed the outcome of antenatal patients for a 12-month period, to address the question of whether GBS genital carriage predicts any adverse obstetric outcome and hence assist in formulating management guidelines for patients who are colonized with GBS, but present with premature rupture of the membranes, are clinically not septic, nor in labor.

SUBJECTS AND METHODS

Patient Population

The study population included all public antenatal patients presenting to the Royal Women's Hospital, Melbourne, Australia over a 12-month period. It has been hospital policy to screen all public patients antenatally for genital carriage of GBS by collection of a low vaginal swab. (Rectal cultures have not been included in the screening protocol.) This occurred at week 32 of gestation from 1981 and at week 28 since 1990 to date.[14] Patients found to be colonized with GBS antepartum are given intrapartum chemoprophylaxis (penicillin 600 mg intravenously every 6 hours) for the length of labor (usually 1–3 doses). Those patients with a history of penicillin allergy are treated with erythromycin (500 mg every 6 hours).

The histories of all GBS-colonized patients for a 12-month period were reviewed for the incidence of premature rupture of the membranes [rupture of membranes (ROM) before onset of labor], premature delivery (< 37 weeks of gestation), and for recognized predisposing factors (including renal disease, cardiac disease, pre-eclampsia, hypertension, and multiple births) that may affect obstetric outcome.

The control population represented every fourth consecutive antenatal patient who presented during the same 12-month period and were found to be negative for antenatal GBS carriage.

Microbiology

Antenatal low vaginal swabs were inoculated directly into enrichment broth (Todd-Hewitt containing crystal violet, colistin, and nalidixic acid).[16] After overnight incubation, swabs were subcultured onto Edwards medium (Oxoid Limited, Basingstoke, U.K.). Colonies resembling GBS were identified by coagglutination using Phadebact (Pharmica Diagnostics, Uppsala, Sweden) streptococcal grouping reagents.[14]

Statistics

Three statistical analyses were performed. These included univariate analysis, relative risk (RR) for GBS adjusted for a single confounder, and adjusted RR for both GBS and all possible confounders. The RR for GBS adjusted for a single confounder were calculated using the method of Mantel and Haenszel.[17] The calculation of adjusted RR was attempted via a linear model with log link and binomial family, but convergence was unattainable. A proportional hazards model was then used as suggested by Skov et al.[18]

RESULTS

The total live births for public patients for the 12-month study period was 4,495 infants. Group B streptococcal colonization of pregnant women occurred in 13.0% (583) and these women formed the study group. The control group totaled 958. In the overall population, the projected preterm delivery was 13.5% and with the confounders, multiple births 5.4%, renal disease 0.9%, essential hypertension 0.6%, pre-eclampsia 8.3%, and cardiac disease 0.6%. Tables 1 and 2 show the results for the analyses for the obstetric outcome of premature delivery by ultrasound prediction and by dates, respectively. Table 3 shows the analysis of the obstetric outcome of premature delivery (by ultrasound) together with premature preterm rupture of membranes. It can be seen that there was no positive correlation for development of premature delivery or premature rupture of the membranes when a woman was colonized with GBS.

Preterm delivery occurred in 8% of the study group and 15.2% of the controls. When subdivided into premature delivery with or without premature rupture of membranes, these findings were less common in those GBS-colonized women compared to the control group. These negative associations

TABLE 1. Univariate and multivariate analyses for the obstetric outcome of premature delivery (by ultrasound)

Variable		Premature delivery (%)	n[a]	Crude relative risk	95% CI	Relative risk adjusted for all confounders	95% CI
GBS carriage	−ve	15.2	645	1		1	
	+ve	8.0	475	0.53	0.37–0.75	0.7	0.47–1.04
Renal disease	No	12.1	1109	1		1	
	Yes	18.2	11	1.50	0.43–5.32	1.46	0.35–6.07
Cardiac disease	No	12.2	1112				
	Yes	0	8				
Essential hypertension	No	12.1	1114	1		1	
	Yes	16.7	6	1.38	0.23–8.29	1.3	0.18–9.66
Multiple pregnancies	1	9.7	1076	1		1	
	2	72.73	44	7.52	5.81–9.73	5.34	3.43–8.32
PET	None	10.7	1023	1		1	
	Mild	10.6	66	1.00	0.48–2.05	0.88	0.41–1.90
	Moderate	58.82	17	5.52	3.57–8.53	2.93	1.48–5.81
	Severe	71.43	14	6.70	4.60–9.76	4.41	2.26–8.60

[a]Assessable patients for all variables.

TABLE 2. Univariate and multivariate analyses for the obstetric outcome of premature delivery (by dates)

Variable		Premature delivery (%)	n[a]	Crude relative risk	95% CI	Relative risk adjusted for all confounders	95% CI
GBS carriage	−ve	13.5	764	1		1	
	+ve	6.7	449	0.5	0.34–0.73	0.62	0.41–0.95
Renal disease	No	10.9	1199	1		1	
	Yes	14.29	14	1.31	0.36–4.77	1.43	0.34–5.93
Cardiac disease	No	11.0	1205				
	Yes	0	8				
Essential hypertension	No	11.0	1205				
	Yes	0	9				
Multiple pregnancies	1	8.8	1165	1		1	
	2	62.5	48	7.07	5.31–9.41	5.79	3.72–9.01
PET	None	10.2	1104	1		1	
	Mild	10.4	77	1.02	0.51–2.00	0.81	0.39–1.67
	Moderate	20.0	15	1.95	0.70–5.46	2.67	0.84–8.48
	Severe	52.94	17	5.17	3.20	2.53	1.23–5.19

[a]Assessable patients for all variables.

TABLE 3. Univariate and multivariate analyses for the obstetric outcome of premature delivery (by ultrasound) and preterm premature rupture of membranes

Variable		Premature delivery (%)	n[a]	Crude relative risk	95% CI	Relative risk adjusted	95% CI
GBS carriage	−ve	3.1	923	1		1	
	+ve	1.4	583	0.44	0.20–0.95	0.61	0.27–1.317

[a]Assessable patients for all variables.

with GBS colonization and obstetric outcomes carried through from the univariate to the multivariate analysis when adjustment for all confounders was made. (However the 95% confidence intervals for the relative risk adjustments were not significant as they were on either side of 1.)

There were ten infants with GBS sepsis for this period. One was a late-onset urinary tract infection (infection at day 22 of life of a child born at 27 weeks gestation), and one was stillborn (the infant was 37 weeks gestation at birth and the mother had been recognized antenatally as a GBS carrier; pla-

cental histology showed chorioamnionitis, and placental membranes grew GBS, as did infant tissues of liver, lung, and spleen). Of the eight infants with early-onset sepsis, five were septicaemic with pneumonia (weeks 33, 33, 36, 37 and 40 gestation) and all survived; two had pneumonia alone (weeks 33 and 40 gestation).

Of the eight early-onset neonatal cases, the mothers were not screened for GBS, as they were private patients (not universal policy to screen) or non-booked transfers from other institutions. The one public patient developed maternal sepsis with GBS at 33 weeks gestation. The mother was treated intrapartum because of prolonged rupture of membranes (48 hours) and maternal fever.

DISCUSSION

There is much evidence that intra-amniotic infection (either asymptomatic or clinically apparent) is involved in the pathogenesis of preterm delivery and premature rupture of membranes. More specifically, bacterial products such as phospholipases A_2 and C, endotoxin, and induction of the cytokine cascade, can stimulate the prostaglandin pathway and initiate labor.[19–21] Furthermore, an experimental animal model in rhesus monkeys for intra-amniotic GBS infection and preterm labor supports this concept.[22]

Yet vaginal GBS carriage alone does not necessarily equate with ascending infection, intra-amniotic infection, and prematurity.

We were unable to find a positive correlation with adverse pregnancy outcome for those women colonized antenatally with GBS. These findings concur with those of various other authors.[9–11,23] In particular, Chua et al. reported a similar GBS colonization rate of 14% in their antenatal patients and found no significantly higher incidence for preterm and/or prelabor rupture of membranes in women with GBS carriage, compared with a negative group.[23]

Similarly, Regan et al., in a recent report from the VIP Study Group where they specifically examined cervicovaginal GBS colonization at 23–26 weeks gestation in a multicenter study, found no adverse pregnancy outcome except for the subgroup for those with heavy GBS colonization.[6]

Unfortunately, we were unable to analyze our data with respect to the degree of GBS colonization, as low vaginal swabs were directly inoculated into an enrichment broth and subcultured on to a selective medium, but without making any quantitative assessments. Furthermore, rectal swabs were not part of our screening protocol and therefore the GBS carriage rate may well have been an underestimate. Rectal swabs have had a low acceptance rate by patients and obstetricians. However, swabs collected are low vaginal (almost perineal).

Our findings may be explained in part by the variable nature of genital GBS carriage throughout pregnancy. Many researchers have documented that the sensitivity of antenatal GBS screening for carriage at delivery is in the order of 60–70%.[3,6,24] Furthermore, of those negative at 26–28 weeks gestation, 6–8.5% will be positive at delivery.[3,14] Perhaps those most at risk are women who are persistently colonized with a high bacterial load, yet have not made specific antibody to their colonizing strain of GBS. A more recently recognized risk factor of premature delivery is the presence of bacterial vaginosis and this finding could be a confounder in our data.[9] However, we have not been screening our antenatal population for bacterial vaginosis, and hence cannot analyze our findings of premature delivery findings with respect to this entity.

Therefore, a suitable management plan when finding GBS colonization in the presence of unexplained preterm rupture of the membranes, but with no evidence of sepsis or labor, could be to commence the patient on a five-day course of penicillin, observe carefully for evidence of sepsis, but to not induce labor on these grounds alone.

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