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Colonization by *Streptococcus agalactiae* in a cohort of unselected 1003 pregnant women in Porto Alegre, Brazil

Abstract

Objective: To determine the frequency of *Streptococcus agalactiae (*GBS) colonization in pregnant women in Porto Alegre, Brazil, and to evaluate obstetric, perinatal outcomes and antimicrobial resistance.

Methods: This prospective cohort study enrolled 1003 pregnant women and vaginal and rectal swabs were collected between the 35th and 37th gestational weeks and cultured in selective medium. In case of GBS, the patients received chemoprophylactic treatment during labor. This study was approved by the Ethics Research Committee of the institution. The level of significance was set at $p<0.05$.

Results: The prevalence of GBS infection was 9.27% (95%CI: 7.5%-11.1%). There was an association between premature membrane rupture (PROM) and GBS maternal colonization. The antibiotic used was penicillin G in 86.4% of the cases. Neonates of mothers with GBS infection had lower gestational age at birth ($p<0.05$) and fetal length ($p<0.05$) than those of mothers without GBS colonization, but there were no higher rates of neonatal ICU admission or birth weight differences Resistance to antimicrobial agent was found in 7.6% of the cases.

Conclusion: Prenatal screening and labor management have been adequate to avoid invasive neonatal disease due to GBS infection. Randomized studies should be conducted to confirm whether GBS treatment during prenatal follow-up may reduce PROM rates and preterm deliveries.

Keywords: maternal infection, intrapartum prophylaxis, neonatal septicemia, group B *Streptococcus*, premature rupture of membranes, preterm delivery

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Abbreviations: PROM, premature rupture of membranes; GBS, group B beta-hemolytic *streptococcus,* CDC, centers for disease control and prevention

Synopsis: Neonates of mothers with GBS infection had lower gestational age at birthday than those of mothers without GBS colonization.

Introduction

In the last decades, group B beta-hemolytic *Streptococcus* of Lancefield (GBS), or *Streptococcus agalactiae,* has been the etiologic agent most often identified in early onset neonatal infection.[1] With the adoption of screening strategies and appropriate antibiotic treatment, 86% of the cases of early-onset neonatal disease may be prevented. Therefore, the cost-benefit ratio seems favorable for the implementation of prenatal screening and appropriate management measures.[2,3] During gestation, GBS seems to raise the risk of miscarriage, premature rupture of membranes (PROM) and preterm labor, and some studies suggest that it may be associated with low birth weight, although findings vary widely.[3,4] Moreover, GBS antimicrobial susceptibility has not been uniformly demonstrated in several studies about antimicrobial agents used routinely in obstetrics.[5,6] This study aimed to evaluate the frequency of vaginal-rectal GBS colonization in unselected pregnant women in Porto Alegre, Brazil, and obstetric and perinatal outcomes associated with GBS colonization in high and low-risk pregnant women and antimicrobial resistance.

Patients and methods

The patients in this study were selected prospectively when seen in the Prenatal Outpatient Service of Complexo Hospitalar Santa Casa de Porto Alegre (ISCMPA). This prospective cohort study enrolled 1003 consecutive pregnant women in an unselected sample, including both, healthy pregnant women according to clinical and laboratory tests and patients with several diseases. The only criterion for selection was acceptance to participate in the study. Women were divided into groups according to the classification of pregnancy, whether low risk, or high risk due to maternal diseases that might affect the rates of GBS infection. Samples for GBS analysis were collected using vaginal-rectal swabs between the 35th and 37th gestational weeks in accordance with the CDC guidelines for cultures, previously described by several authors.[2]

When GBS infection was confirmed, patients received chemoprophylaxis during delivery according to susceptibility results, preferably using penicillin G. Sample size was previously calculated according to estimated mean frequency of GBS infection among pregnant women; an unselected sample of 1000 pregnant women was estimated for a standard error of the proportion lower than 1.5%. The variability of the proportion of positive cases of maternal GBS infection was assessed according to frequency, 95% confidence interval (CI) and the nonparametric chi-square test (X^2) for the analysis of the effect of different diseases on the positive rates of GBS infection. The level of significance was set at $p<0.05$.

Results

Infection was found in 9.27% of the 1003 pregnant women included in the study (95%CI 7.5 to 11.1%). Of the women with infection, 6.7% were white, 1.6%, of mixed racial background, and 1%, black. There were no significant associations between infection rates and skin color of the patients with infection. The analysis of gestational risk factors, such as diabetes, hypertension, thyroid disease and heart disease, revealed no differences in the rates of infection prevalence among pregnant women of high and low obstetric risk (p>0,10). Table 1 shows the significant associations between risk factors, such as preterm delivery (1.1%) and PROM (0.8%) in patients with GBS infection when compared with pregnant women without infection (p=0.04).

Table 1 Association between risk factors during labor and GBS infection rate

Risk factor	No infection		Preterm delivery		PROM	
	N	(%)	n	(%)	n	(%)
No	799	(79.7)	67	(6.7)	35	(3.5)
Yes	72	(7.2)	11**	(1.1)	8*	(0.8)

X^2,16.93; p, 0.01; *Fisher: p, 0.04;**Fisher: p, 0.09.

The antibiotic most often used was penicillin G, in 84.6% of the cases, followed by ampicillin and clindamycin, both in 6.8%. The minimum time of antibiotic use was 4 hours. Antimicrobial resistance was found in 7.6% of the cases. All cases of resistance were to erythromycin, and 40% of them (3%) were also cross-resistant to clindamycin. There were no significant associations between infection rates and type of delivery (P=0.30).

Infants of infected mothers had significantly lower gestational age, 38.6 vs. 38.2 (p=0.04) and fetal length, 49.2 vs. 48.2 (p=0.01) than infants of mothers without infection, with no differences related to birth weight, 3,2 vs. 3,1 Kg (p>0.05). Despite these differences, the rate of admissions to neonatal ICU due to conditions at birth or maternal infection was not significantly higher (X^2=1.9; p=0.17).

Discussion

Our study found a 9.7% prevalence of maternal GBS infection, similar to rates found in the literature.[2,7–10] A study published by Miura et al.,[11] which identified 1.2 case of GBS invasive neonatal disease in 1000 live births, justifies the implementation of GBS screening routines during prenatal follow-up for all pregnant women in our milieu. Since the implementation of screening and antibiotic prophylaxis during delivery of pregnant women with GBS infection, no case of neonatal invasive disease due to this microorganism has been identified, which demonstrates that the implementation of this strategy has a favorable cost-benefit ratio.[4,12] Although aware of the limitations of defining skin color of our population sample due to the heterogeneous ethnic composition of the Brazilian population, our study did not find any significant differences in infection rates according to skin color. These results are similar to those published by other authors.[5] The use of antimicrobial agents during delivery in patients with GBS infection was clearly satisfactory and prevented severe conditions, such as meningitis, pneumonia, septicemia and admission to a neonatal ICU. It also confirmed the importance of implementing this type of screening strategy during prenatal follow-up, which is supported by others.[13] The analysis of antimicrobial resistance revealed that most cases in our study were susceptible to penicillin. International recommendations based on the CDC guidelines suggest the use of penicillin as the first choice for intrapartum prophylaxis, but patients allergic to beta-lactamic antibiotics are a matter of concern. International guidelines recommend the use of erythromycin and clindamycin in these cases. However, several studies found rates of resistance to macrolides and lincosamides greater than 10%.[2,14,15] In our study, all cases of resistance were to erythromycin, and 40% of them (3%) were cross-resistant to clindamycin.

A study conducted in Ribeirão Preto, Brazil, did not confirm uniform resistance to penicillin and other beta-lactamic antibiotics tested in GBS samples isolated from HIV-positive pregnant women. Resistance to clindamycin was found in 80% of the sample; to erythromycin, in 55%; to penicillin, in 45%; and to cephalothin, in 35%.[2] Our study did not find higher rates of cesarean sections among patients with GBS infection. These results are not surprising because GBS infection is not an indication for cesarean delivery[2,3,5,13] One of the important findings of our study with large sample size was the significant difference of maternal GBS infection in preterm deliveries and PROM. Maternal GBS infection is a known risk factor for preterm delivery and PROM,[16] but there is no consensus in international literature to support a conclusive cause and effect association.[13,17,18] Some of the results found in this study raise questions about whether additional treatment during gestation may minimize the outcomes associated with PROM and low birth weight, because the recommended treatment only during delivery does not affect it in any important way. Further prospective randomized studies should be conducted to define this issue.

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Conflicts of interest

Author delares there is no conflict of interest.

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