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Group B *Streptococcus* rectovaginal colonization screening on term pregnancies: culture or polymerase chain reaction?

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ABSTRACT

Objectives: The aim of this study was to evaluate if screening Group B *Streptococcus* colonization by intrapartum polymerase chain reaction could improve intrapartum administration of antibiotic prophylaxis, compared with antepartum culture screening and analyze the sensitivity and specificity of polymerase chain reaction test.

Methods: 198 pregnant women with Group B *Streptococcus* colonization antepartum culture screening were included. When they arrived at hospital for delivery, two rectovaginal swabs were collected: for culture and polymerase chain reaction method.

Results: The rate of Group B *Streptococcus* colonization antepartum detected by culture was 16.7%; at delivery was 17.2% when detected by culture and 19.7% using polymerase chain reaction method. The rate of inconclusive polymerase chain reaction tests was 0.5%. Considering intrapartum culture screening as gold standard, sensitivity and specificity of polymerase chain reaction test for intrapartum Group B *Streptococcus* colonization was 97.1% and 95.7%, respectively. The global rate of discordance between antepartum and intrapartum Group B *Streptococcus* colonization was 6.6%. The rate of women not treated with intrapartum antibiotic prophylaxis in the setting of positive intrapartum culture was significantly lower using intrapartum polymerase chain reaction test (0.5%) than with antepartum culture method (3.5%, $p = 0.035$).

Conclusion: The use of intrapartum antibiotic prophylaxis can be more efficient when screening Group B *Streptococcus* colonization intrapartum by polymerase chain reaction test. Polymerase chain reaction method had a good performance in our study, with high sensitivity and specificity.

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Introduction

Group B *Streptococcus* (GBS) is the most frequent cause of severe early-onset infection (<7 days of age) in newborn infants and is responsible for pneumonia, septicemia, and meningitis in neonates [1,2]. Colonization of maternal genitourinary and gastrointestinal tract occurs in 20-40% and is one of the most important risk factors for early onset neonatal group B streptococcal (EOGBS) disease, which occurs in 1% of children exposed to GBS [3–5].

In order to prevent the EOGBS disease, in 2002, Centers for Disease Control and Prevention (CDC) advised all pregnant women to be screened for GBS colonization at 35–37 weeks of pregnancy and, for those colonized with GBS, intrapartum administration of antibiotic prophylaxis (IAP). In addition, women with a previous infant with GBS infection, women with GBS bacteriuria during the present pregnancy and women with unknown colonization status and intrapartum risk factors (rupture of membranes (ROM) ≥18h, maternal fever or preterm labor (<37 weeks of pregnancy)) should also be treated [6]. A significant reduction in the incidence of EOGBS disease has been reported since the implementation of IAP policies.

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In the United States, there was a decline from 1.7/1000 live births in 1990s to 0.22/1000 in 2015 [7]. The reasons for the remaining cases of GBS infections are:

- 15% of pregnant women are not tested for GBS vaginal colonization [8,9];
- There is a poor correlation between antenatal screening results and intrapartum maternal GBS colonization as a result of an intermittent vaginal colonization. A French study concluded that 7.0% of women with negative culture test at 35–37 weeks had a positive test at delivery and 5.1% of women with positive culture test at 35–37 weeks had a negative test at delivery [1,2,4,10];
- Besides the success of universal screening and IAP, 80% of EOGBS disease cases that still occur are in neonates born to mothers with unknown or negative antenatal GBS screening and 65% do not have any risk factor for EOGBS disease [1,10–12];
- Antepartum screening at 35–37 weeks of gestation excludes the 7–11% of women who have a preterm delivery before 35 weeks of gestation, and this group has the highest risk for serious neonatal GBS infection [10].

IAP carries some risks for the mother and baby, including anaphylaxis, increased medicalization of labor and neonatal period, increased antibiotic resistance, intestinal complaints, nausea, changes in neonatal bowel microbiome, higher risk of necrotizing enterocolitis and Candida spp. colonization which are theoretically linked to a number of late effects in the child such as allergy, obesity and diabetes [1,13–17].

In order to optimize the use of IAP and to increase the diagnostic sensitivity and specificity of GBS colonization, molecular tests as polymerase chain reaction (PCR) that allow a rapid screening of genital colonization have been developed. One of the main advantages of PCR over traditional culture approach is time elapsed between sampling and test result: PCR results are available 1–2h after sampling and bacterial culture is known after 24–72h, which allows us to perform a PCR test when women are admitted at the hospital for delivery [1].

The primary objective of the present study is to evaluate if the use of PCR assay at delivery to detect GBS colonization, instead of antepartum traditional culture tests, can improve the use of IAP. The secondary aim is to analyze the sensitivity and specificity of PCR assay.

Methodology

Inclusion and exclusion criteria

Pregnant women admitted to labor ward at the Department of Gynecology and Obstetrics of Centro Hospitalar Universitário São João (CHUSJ) were included.

Exclusion criteria were women less than 18 years, indication for scheduled cesarean section, women presenting with signs of imminent delivery, pregnancies less than 35 weeks and pregnant women without GBS antepartum screening after 35 weeks of pregnancy.

Design of study

When pregnant women arrived at hospital for delivery, they were asked to participate in the study after oral and written information was given and written informed consent was signed. Each woman became her own control and there were no refusal. At time of admission, two rectovaginal swabs were collected: for culture and molecular (PCR) method.

These results were blinded, obstetricians and midwives were not informed of the intrapartum results and the decision for intrapartum antibiotic prophylaxis was based on the current GBS antepartum screening by culture. IAP was initiated according to protocol of the obstetrics department (2 g of ampicillin intravenously followed by 1 g every 4 h until delivery or clindamycin 900 mg intravenously every 8 h if an allergy to penicillin was known). If chorioamnionitis was suspected during labor (persistent intrapartum fever with fetal tachycardia or leukocytosis ($>$15000 cells/mm^3) or purulent amniotic fluid), antibiotic treatment was initiated: 2 g of ampicillin intravenously every 6 h and gentamycin intravenously 5 mg/kg every 24 h.

The recruitment to this study was made in two phases according to financial support. Phase I occurred between June and October of 2019 and phase II between August and October of 2020.

The parameters systematically collected for each woman were: patient's age; parity; gestational age; GBS bacteriuria during current pregnancy; previous infant with EOGBS disease; result of GBS screening at 35-37 weeks (negative or positive); duration of rupture of membranes; duration of labor; mode of delivery; result of PCR assay (negative, positive or inconclusive); antimicrobial treatments received by the mother and the baby and presence of EOGBS disease on newborn. The protocol was approved by the ethics committee of the CHUSJ.

This study was supported by a grant of The Portuguese Society of Obstetrics and Maternal-Fetal Medicine.

Microbiological procedure

Specimen collection

A rectovaginal swab with transport medium Amies (deltalab®) was taken from each parturient at 35-37 weeks of gestation. At admission to labor ward, another two rectovaginal swabs were collected: one with transport medium Amies (deltalab®) and one with liquid transport medium (Cepheid® Collection Device).

To collect the samples, a rectovaginal swab was inserted in the lower one-third part of the pregnant woman's vagina and rotated several times to sample secretions from the mucosa. Then, the same swab was inserted into the anal sphincter (approximately 2.5 cm) and rotated to sample anal crypts.

The swabs were transported immediately, at ambient temperature, to the microbiology laboratory (available 24 h a day, 7 days a week) to be processed.

Sample culture

The swabs were streaked on plates of Granada® selective medium (Chromogen Biomerieux®), incubated 18 to 24 h at 37° under 5% CO_2 and evaluated for growth in orange colonies. If the first observation was negative, the incubation period was prolonged for another 18 to 24 h. GBS colonization was defined as positive in the presence of at least one orange colony and is defined as negative in the absence of any orange colonies after two overnight incubations.

Molecular detection

GeneXpert® system (Cepheid®) was used for the molecular detection, which is a rapid real-time PCR which integrates DNA extraction, amplification and detection in the same automated process. The collected swab was transferred to a chamber of the Xpert® GBS cartridge, and loaded into a Cepheid GeneXpert® device. The overall process takes approximately 50 min. The positive or negative result was based on the detection of a target gene sequence.

Statistical analysis

The statistical analyses were performed using SPSS, version 27.0 [IBM Corp. Released 2020. IBM SPSS Statistics for Macintosh, Version 27.0. Armonk, NY: IBM Corp]. The diagnostic performance of the PCR test (sensitivity, specificity, predictive values) was calculated using the culture intrapartum test as gold-standard. Outcomes were compared using chi-squared test. A p value of <0.05 was considered significant.

Results

During the two phases of the study, 205 pregnant women were recruited, 7 of them were excluded because GBS antepartum screening was not available. The study group included 198 pregnant women, all of them with three GBS test results available: antepartum culture, intrapartum culture and intrapartum PCR.

The participants demographic characteristics, pregnancy surveillance and labor details are shown in Table 1. Almost two thirds were admitted in labor, 18.7% had fever during labor and 26.8% received

Table 1. Demographic, pregnancy and labor characteristics of the studied sample.

Pregnant women's age (median; 1st quartile, 3rd quartile)		33 years old (28; 36)
Gestational age at delivery (median; 1st quartile, 3rd quartile)		39^{+3} weeks(38^{+4}; 40^{+0})
Parity	Nuliparous (n,%)	110 (53.7%)
	Multiparous (n, %)	95 (46.3%)
Time from rupture of membranes to delivery (median; 1st quartile, 3rd quartile)		7 h (4;13)
Duration of labor (median; 1st quartile, 3rd quartile)		7 h (4;10)
Antibiotics during pregnancy (n, %)		21 (10.6%)
Lower urinary infection during pregnancy (n,%)		19 (9.6%)
Labor	Spontaneous (n,%)	131 (66.2%)
	Induced (n,%)	67 (33.8%)
Prelabor rupture of membranes (n,%)		65 (32.8%)
Number of cesarean deliveries (n, %)		31 (15.7%)
Intrapartum maternal fever (n,%)		37 (18.7%)
Suspected intrapartum chorioamnionitis (n,%)		13 (6.6%)
Confirmed intrapartum chorioamnionitis (n,%)		10[a] (5.1%)
Antibiotics during labor (n, %)		53 (26.8%)
• IAP for GBS		30 (56.6%)
• Suspected intrapartum chorioamnionitis		10 (18.8%)
• IAP for GBS and suspected intrapartum chorioamnionitis		3 (5.7%)
• Pre-operative cesarean section prophylaxis		7 (13.2%)
• Third-degree perineal tears prophylaxis		3 (5.7%)

[a]Placental histological exam unavailable in the remaining three cases.

intrapartum antibiotics mainly for GBS prophylaxis (33 in 53) and for suspected intrapartum chorioamnionitis (13 in 53).

The rate of GBS colonization antepartum detected by culture was 16.7% (33/198) at a median gestational age of 36 weeks. The rate of GBS colonization at delivery was 17.2% (34/198) when detected by culture and 19.7% (39/198) using PCR method at a median gestational age of 39^{+3} weeks. The rate of inconclusive PCR tests was 0.5% (1/198) (Table 2).

Considering intrapartum culture screening as gold standard, sensitivity, specificity, positive predictive value and negative predictive value of PCR test for intrapartum GBS colonization was 97.1% (33 in 34), 95.7% (157 in 164), 84.6% (33 in 39) and 99.4% (157 in 158), respectively. The antepartum culture screening exhibited lower sensitivity (79.4%, $p = 0.0245$), lower negative predictive value (95.8%, $p = 0.0363$), lower positive predictive value (81.8%, $p = 0.7525$) and higher specificity (96.3%, $p = 0.7819$) (Table 3).

Among women with a negative antepartum culture test, 4.2% percent (7 in 165) had a positive test at delivery and 18.2% (6 in 33) of women with a positive antepartum culture test had a negative test at delivery. This results in a global rate of discordance between antepartum and intrapartum GBS colonization of 6.6% (13 in 198). The time between antepartum GBS screening and labor was not statistically different between cases of antepartum and intrapartum GBS colonization discordance (23.5 ± 10.1 days) and agreement (22.1 ± 8.9 days, $p = 0.739$)

The percentage of women treated with IAP in the setting of negative intrapartum culture result was similar between antepartum culture method and intrapartum PCR test (6 in 198, 3%). However, the rate of women not treated with IAP in the setting of positive intrapartum culture was significantly lower using intrapartum PCR test (1 in 198, 0.5%) than antepartum culture method (7 in 198, 3.5%, $p = 0.035$) (Table 3).

Considering the 6 women treated with IAP in the setting of negative intrapartum culture result, all of them received IAP with ampicillin. However, two of them initiated antibiotics for treatment of a suspected intrapartum chorioamnionitis (ampicillin and gentamicin) which was confirmed on placental histological examination.

In the case of women not treated with IAP in the setting of positive intrapartum culture based on antepartum culture method, 1 in 7 initiated antibiotics for treatment of a suspected intrapartum chorioamnionitis (ampicillin and gentamicin) confirmed on placental histological examination, and the newborn was not admitted to neonatal intensive care unit (NICU). There was one case of EOGBS disease in a pregnant women with negative antepartum culture screening and positive intrapartum screening for GBS (both culture and PCR), with 12 h of rupture of membranes at delivery that the newborn was admitted to NICU. The newborn was treated with gentamycin during 6 days and ampicillin during 10 days and GBS was confirmed on blood culture. There were no complications in the women not treated with IAP in the setting of positive intrapartum PCR test.

Antibiotics were administered to 4 of 198 newborns for different reasons: nosocomial sepsis by *Staphylococcus epidermidis* (admitted to NICU because of suspected cardiac pathology), prophylactic urinary antibiotic on a newborn with hydronephrosis, EOGBS disease and neonatal sepsis with negative blood cultures.

Table 2. Performance of antepartum culture test, culture and PCR test at delivery.

		Culture at delivery		
		Positive	Negative	Total (%)
Culture antepartum	Positive	27	6	33 (16.7%)
	Negative	7	158	165 (83.3%)
PCR at delivery	Positive	33	6	39 (19.7%)
	Negative	1	157	158 (79.8%)
	Inconclusive	–	1	1 (0.5%)
Total		34 (17.2%)	164 (82.8%)	198

Discussion

In our study, we found a difference between antepartum and intrapartum GBS colonization in 6.6% pregnant women as a result of an intermittent vaginal GBS

Table 3. Comparing antepartum culture and intrapartum PCR test for detection for vaginal GBS (intrapartum culture taken as the gold standard).

	Antepartum culture	PCR intrapartum	p value
Sensitivity (n/N, %)	27/34 (79.4%)	33/34 (97.1%)	0.0245
Specificity (n/N, %)	158/164 (96.3%)	157/164 (95.7%)	0.7819
PPV (n/N, %)	27/33 (81.8%)	33/39 (84.6%)	0.7525
NPV (n/N, %)	158/165 (95.8%)	157/158 (99.4%)	0.0363
Women adequately treated with IAP (n/N, %)	27/34 (79.4%)	33/34 (97.1%)	0.0245
Women adequately not treated with IAP (n/N, %)	158/164 (96.3%)	158/164 (96.3%)	1.0000

colonization as described in other published reports [2,10]. The prevalence of rectovaginal GBS colonization during labor was 17.2% (detected by culture method, the gold standard), a percentage similar to other studies realized in France (14.8% and 12.5%), but lower than a study conducted in Finland (29.7%) [2,10,18].

The advantage of PCR over culture method is the time between sampling collection and test result (1-2h versus 24-72h, respectively), making PCR test the only method feasible to detect GBS colonization intrapartum. Furthermore, PCR test using the Xpert GBS test from Cepheid® can be performed by people not trained in molecular biology because nucleic acids are extracted automatically, making PCR test an easy, fast and suitable method for intrapartum screening of GBS rectovaginal colonization.

The median labor duration in our population was 7 h and the results would be available before labor in 89% of pregnant women (11% with labor duration $\leq$ 2 h). However, some studies identify limited and lower effectiveness of IAP when administered less than four hours before birth [19,20]. Accordingly, if we screen GBS colonization with PCR test intrapartum, we need to consider the time it takes to obtain the test result, which means adding a maximum of two hours to the four-hour interval for adequate IAP. Although this may be a disadvantage comparing to cultural method, one must consider that intrapartum GBS screening with PCR allows a more reliable IAP than cultural method (97.1% versus 79.4%).

PCR method had a good performance in our investigation when compared with culture method for intrapartum GBS colonization: sensitivity and specificity were 97.1% and 95.7%, respectively. These values were similar to other studies, which described values between 61.8% and 100% for sensitivity and 75.8% and 99.6% for specificity [2,10,18,21–23].

Furthermore, sensitivity of intrapartum PCR test was higher than antepartum culture method to detect GBS colonization during labor, statistically significant difference, as supported by other authors [2,10,24]. The false positive rate of PCR test could be explained by detection of non-viable organisms by PCR test and not by culture and/or the presence of micro-organisms (enterococci, for example) that interfere and inhibit GBS growth on culture method and/or low bacterial loads not detected by traditional culture methods [1,2,25–27].

Besides a good sensitivity and specificity, we found a rate of inconclusive PCR results of 0.5% which is lower when compared with similar studies, describing a percentage of inconclusive results from 4% to 13% [10,18,23,24,28].

A study using cultural test at 34-38 weeks of gestation and PCR test at delivery concluded that women were inadequately treated with prophylactic antimicrobial treatment in 13.6% and 4.5% of cases, respectively and PCR testing is significantly better in terms of cost and effectiveness [2]. The decrease on antibiotic use and cost-effectiveness of intrapartum PCR was also corroborated by an article which also reported a significant decrease in EOGBS disease rate [29]. Another study found that PCR can reduce the intrapartum use of antibiotic by 63% without missing any GBS colonization and shortening hospital stay significantly compared to cultural method [1].

In our study, PCR method adequately detected pregnant women who were candidates for IAP in 97.1% of the cases and could lead to a more reliable use of IAP (in comparison with antepartum culture method). In the particular cases of premature preterm rupture of membranes or preterm labor without antepartum GBS screening, PCR test could identify the candidates for IAP instead of administering IAP to all pregnant women in these situations of higher risk of EOGBS disease.

The case of EOGBS disease detected among the seven pregnant women who tested negative by antepartum culture method and became positive intrapartum (PCR and culture test) could have been avoided if intrapartum screening was applied and IAP was initiated.

Conclusion

Based on our results, we think we can improve the use of IAP with PCR test, given that 97.1% of pregnant women would be treated correctly using intrapartum PCR test instead of only 79.4% adequately treated if we used antepartum culture method. Besides, PCR method had a good performance in our study, with sensitivity and specificity of 97.1% and 95.7%, respectively, allowing us to rely on its discriminatory power.

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Disclosure statement

No potential conflict of interest was reported by the author(s).

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Data availability statement

Data available on reasonable request.

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