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SHORT REPORT

Accuracy of prenatal culture in predicting intrapartum group B streptococcus colonization status

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Abstract

Objective: To evaluate the positive predictive value (PPV) of group B Streptococcus (GBS) cultures at 35–37 weeks of gestation relative to GBS colonization status at delivery.
Methods: Rectovaginal swabs from 221 women at labor in four Lisbon hospitals were collected for GBS screening according to the CDC guidelines.
Results: The PPV was 24.4%. IAP was administered to 100% of prenatally GBS positive women. There was no case of early onset GBS disease (EOD).
Conclusions: Poor accuracy of prenatal cultures in identifying true candidates for IAP highlights the need for Portuguese clinical and laboratory guidelines to prevent EOD and antibiotic overtreatment of pregnant women.

Keywords

Early onset disease, intrapartum antibiotic prophylaxis, intrapartum screening, *Streptococcus agalactiae*

History

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Introduction

Streptococcus agalactiae, group B Streptococcus (GBS) has multiple serotypes and is an opportunistic human pathogen that can lead to life-threatening infections in newborns and immunocompromized adults [1]. Maternal GBS carriage has been recognized as the major risk factor of early onset disease in newborns (EOD, <7 days of age) [1,2]. Up to 30% of pregnant women are anogenital colonized, although the carrier status is considered dynamic during pregnancy [2,3]. CDC guidelines [2,4] recommend GBS screening at 35–37 weeks of gestation in order to identify women at risk that should undergo intrapartum antibiotic prophylaxis (IAP) to avoid transmission to the newborn during labor; IAP became responsible for the reduction of EOD in developed countries. Nevertheless, strategies to prevent late onset disease (LOD), which occurs after the first week of life, have yet to emerge, as IAP is unable to avoid LOD. The screening-based approach is challenging, as its efficacy relies on its capacity to predict GBS colonization status at the time of labor. Published reports [5,6] showed that both negative (NPV) and positive (PPV) predictive values of prenatal GBS cultures relatively to the GBS status at delivery are suboptimal, especially the PPV. We aimed to evaluate the PPV of GBS positive culture at 35–37 weeks of gestation considering the GBS colonization status at delivery.

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Methods

Patients and study design

Between March 2008 through June 2009, 221 pregnant women presenting a positive result for GBS at 35–37 weeks of gestation from 4 hospitals (Dona Estefânia Hospital, $n = 9$; Maternity Alfredo da Costa, $n = 42$; Fernando Fonseca Hospital, $n = 67$; and CUF Descobertas Hospital, $n = 103$) were selected for this study. It was not possible to determine the laboratories (private and/or public) where pregnant women performed their GBS prenatal nor the methodologies that were used by those laboratories. The unknown colonization status at delivery was also used as an inclusion criterion in order to verify the intrapartum positivity of GBS in this group of women ($n = 88$). Considering the main focus of this study, and due to budget constraints, women with negative GBS cultures at 35–37 weeks of gestation were excluded. All pregnant delivering before 35 weeks of gestation as well as pregnant that had received antibiotic treatment up to 3 weeks before admission were excluded.

This study was approved by the ethics board of the involved institutions, and a written informed consent was obtained from all women prior to their enrolment in the study. Information about age, obstetric risk factors, and type of delivery were collected. Later, information on whether newborns developed EOD during the hospital stay was also acquired.

Collection and culture of specimens

A combined recto-vaginal swab was collected from each parturient on admission for delivery. Swabs were then maintained in a non-nutritive Amies medium (Biomérieux)

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at room temperature until processing at the National Institute of Health in Lisbon, within 24 h, according to the described by the CDC guidelines [4]. Briefly, each swab was inoculated in Todd Hewitt selective media broth at 37°C, 5% CO_2 for 18 h and sub-cultured on Columbia agar supplemented with 5% sheep blood (COS) (Biomérieux) at 37°C in 5% CO_2 for an additional period of 24–48 h.

GBS identification and antibiotic susceptibility testing

S. agalactiae isolates were identified by standard criteria on the basis of colony morphology, Gram staining, non-hydrolysis of aesculin on bile-aesculin agar and group B latex-agglutination test. Antimicrobial susceptibility testing (penicillin G, erythromycin, clindamycin and vancomycin) was performed by Etest according to the Clinical and Laboratory Standards Institute guidelines [7].

Capsular typing and screening of ST-17 hypervirulent lineage

Capsular typing was performed by using specific antisera for serotypes Ia to V (Essum AB) and *cps* genotyping [3]. The detection of ST-17 lineage was achieved by PCR, as described elsewhere [8].

Statistics

Positive predictive value (PPV) of prenatal GBS cultures was calculated through the following formula: [(Number of women GBS+/+) ÷ (number of women GBS+/+ and GBS+/−)] × 100%, where GBS+/+ and GBS+/− correspond to intrapartum positive and negative results, respectively (all samples had been positive positive at prenatal stage) [5].

Results

Vaginal-rectal cultures were obtained from 221 GBS positive women on admission for delivery, 118 (53.4%) and 103 (46.6%) from three public and one private hospitals, respectively. Overall, the average maternal age was 30.4 years (range, 14–45 years) and the average gestational age at labor was 39.0 weeks (range, 35.9–41.4 weeks). The mode of delivery was vaginal or cesarean in 166 (75.1%) and 55 (24.9%) women, respectively. Among 55 women giving birth by cesarean section, 38 (69.1%) were performed electively and 17 (30.9%) were performed after labor, of whom 38 (69.1%) occurred at the private hospital. Of 221 prenatally GBS-positive women, only 54 remained positive at delivery, corresponding to a PPV of 24.4%. All these 54 prenatal GBS-positive women received IAP (ampicillin was the first choice for IAP in the four hospitals). However, on a risk-based screening (e.g. preterm delivery), only 11 (5%) would have justified antibiotic treatment.

None of the 88 parturients without prior GBS screening revealed intrapartum GBS colonization; however, 9/9 attending to the private hospital and 17/79 attending to public hospitals (the ones presenting risk factors: preterm deliveries [$n = 14$]; GBS bacteriuria during the current pregnancy [$n = 2$]; previous child with EOD [$n = 1$]) received IAP.

The serotype distribution showed the predominance of serotype III (25/54 [46.3%]) followed by serotypes Ia (10/54 [18.5%]), II (9/54 [16.7%]), V (7/54 [12.9%]), Ib (2/54 [3.7%]) and IV (1/54 [1.9%]), which was quite similar to that described in Portugal for GBS colonization during the last trimester of pregnancy [3]. The lineage ST17 was identified in 56% (14/25) of the isolates belonging to serotype III; however, no newborn developed EOD during hospital stay.

All clinical isolates were fully susceptible to penicillin G or vancomycin. We observed a resistance rate of 7.4% to erythromycin and 1.8% to clindamycin, which were low when compared to our previous data [3].

Discussion

In the present study, public and private hospitals evidenced differences regarding both the GBS screening during pregnancy and the selection of candidates for IAP. As an example, only nine pregnant cases were presented to the private hospital without GBS screening at 35–37 weeks of gestation, and all received IAP, versus 79 attending to public hospitals, where IAP was provided exclusively to the 17 parturients comprehending risks. The lack of GBS screening during pregnancy suggests unawareness, or indifference regarding the free health care provided under the supervision of low-risk pregnancy in Portugal. Thus, social factors contributing to the exclusion from pregnancy surveillance in Portugal seem to need urgent assessment and adjustment.

Although a great heterogeneity of PPVs has been described [5,6,9] ranging (43–100%), our study revealed a considerably low PPV of 24.4%. This weak concordance between prenatal and intrapartum culture results could be attributed to several variables, namely (1) timing of prenatal GBS screening; (2) laboratory methodologies; and (3) antibiotic usage.

The influence of the timing of prenatal GBS screening in this study would be neglectable; in fact, all enrolled GBS positive women were screened at 35–37 weeks of gestation, which has been considered ideal for correlating with GBS colonization status at delivery, by longitudinal studies [9].

The observed discrepancy could be explained, in part, by methodological heterogeneity (sampling, swab storage and transport, and culturing procedures) that could not be determined in the present study. In fact, in Portugal, the health system allows pregnant women to freely choose the laboratories where antenatal GBS screening is performed (screening at the same hospital of delivery is rare), implicating that a multitude of laboratories were involved, each one using their particular GBS detection protocols. There is neither Portuguese GBS laboratory screening guidelines nor recommendations for following scientific guidelines internationally accepted, such as the provided by the CDC. In this scenario, an heterogeneity of methodologies applied to GBS detection are to be expected, comprehending the proposed by the CDC guidelines but also less expensive and time-consuming procedures, such as direct plating in both Columbia 5% sheep blood agar and chromogenic medium (such as Strepto B ID or Granada). Each procedure has inherent limits and drawbacks that can lead to GBS misidentification.

Another technical explanation could hold on the proliferation of non-GBS isolates during storage and transport, such as Enterococcus and Proteus species, impairing the

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identification and recovery of GBS on blood agar plates. Indeed, and consistent with published data [10], 12.2% of our intrapartum cultures from prenatally GBS-positive women evidenced an overgrowth of Gram negative bacteria in blood agar plates (not supplemented with antibiotics), which might have obscured GBS colonies culminating in false-negative results. This emphasizes the need to improve the subculture system by using selective GBS media (Columbia agar with colistin and nalidixic acid or a commercial chromogenic agar), as is currently recommended by the 2010 CDC guidelines [2]. Indeed, Van Dyke and colleagues [11] revealed that 61.4% of EOD cases occurred in term newborns whose mothers were GBS-negative at 35–37 weeks. Whether those negative cultures were false-negative results or the parturients acquired GBS during the interval between pregnancy screening and delivery is unknown, but it surely evidences major variations in GBS colonization status during pregnancy.

As we excluded pregnant subjected to antibiotic treatment within 3 weeks before delivery, we would expect no influence of this factor for the low PPV; however, we cannot exclude that some pregnant women during their hospital admission questionnaire omitted (by unidentified reasons) taking medication, namely antibiotics. In fact, although in Portugal a medical prescription is required for antibiotic purchase, irregularities to this rule exist, allowing self-medication.

In conclusion, the reasons underlying a low PPV of prenatal culture in predicting GBS colonization during labor in Portugal are hard to determine due to the lack of national clinical and laboratory guidelines for GBS prevention that would contribute to the uniformity and quality of GBS screening. This requisite would surely contribute to a higher PPV that would prevent EOD while avoiding overtreatment of pregnant women.

Also, and until the availability of an effective GBS vaccine, new reliable and fast intrapartum diagnostic tools should be developed to supplement antenatal GBS screening.

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Declaration of interest

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References

1. Edwards MS, Nizet V. Group B streptococcal infections. In: Remington JS, Klein JO, Wilson CB, et al, eds. Diseases of the fetus and newborn infant, 7th ed. Philadelphia, PA: Elsevier; 2011:419–69.
2. Centers for Disease Control and Prevention (CDC). Prevention of perinatal group B streptococcal disease. Revised guidelines from CDC, 2010. MMWR Recomm Rep 2010;59:1–36.
3. Florindo C, Viegas S, Paulino A, et al. Molecular characterization and antimicrobial susceptibility profiles in Streptococcus agalactiae colonizing strains: association of erythromycin resistance with subtype III-1 genetic clone family. Clin Microbiol Infect 2010;16: 1458–63.
4. Centers for Disease Control and Prevention (CDC). Prevention of perinatal group B streptococcal disease. Revised guidelines from CDC. MMWR Recomm Rep 2002;51:1–22.
5. Lin FY, Weisman LE, Azimi P, et al. Assessment of intrapartum antibiotic prophylaxis for the prevention of early-onset group B Streptococcal disease. Pediatr Infect Dis J 2011;30:759–63.
6. El Helali N, Nguyen JC, Ly A, et al. Diagnostic accuracy of a rapid real-time polymerase chain reaction assay for universal intrapartum group B streptococcus screening. Clin Infect Dis 2009;49:417–23.
7. Clinical and Laboratory Standard Institute (CLSI). Performance Standards for Antimicrobial Susceptibility Testing M100-S19; 19th Informational Supplement. Wayne: CLSI; 2009.
8. Lamy MC, Dramsi S, Billoët A, et al. Rapid detection of the highly virulent group B Streptococcus ST-17 clone. Microbes Infect 2006; 8:1714–22.
9. Valkenburg-van den Berg AW, Houtman-Roelofsen RL, Oostvogel PM, et al. Timing of group B streptococcus screening in pregnancy: a systematic review. Gynecol Obstet Invest 2010;69:174–83.
10. Tazi A, Réglier-Poupet H, Dautezac F, et al. Comparative evaluation of Strepto B ID chromogenic medium and Granada media for the detection of Group B streptococcus from vaginal samples of pregnant women. J Microbiol Methods 2008;73:263–65.
11. Van Dyke MK, Phares CR, Lynfield R, et al. Evaluation of universal antenatal screening for group B streptococcus. N Engl J Med 2009;360:2626–36.

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