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CLINICAL ARTICLE

Risk-based approach versus culture-based screening for identification of group B streptococci among women in labor

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Synopsis: Culture-based screening had a higher detection rate than the risk-based approach for the identification of group B streptococci in women in labor.

Keywords: Antibiotic prophylaxis; Culture-screening strategy; Early-onset neonatal infection; Group B streptococci; Intrapartum colonization; Risk-based approach.

ABSTRACT

Objective: To compare a risk-based and culture-based screening approach for identification of group B streptococci (GBS) vaginal colonization using an intrapartum rectovaginal culture as the reference standard.

Methods: Pregnant women attending the prenatal clinic at Lillebaelt Hospital, Kolding, Denmark, between April 1, 2013, and June 30, 2014, were invited to participate in a prospective observational study. For prepartum culture-based screening, vaginal and rectal culture samples were obtained, and for reference, standard, paired vaginal and rectal culture samples were collected during labor. Risk factors for risk-based screening were previous early-onset GBS, GBS bacteriuria during pregnancy, maternal temperature ≥38.0℃ intrapartum, and rupture of membranes for more than 18 hours.
Results: The intrapartum rectovaginal GBS colonization rate was 30% (32/108) among participants with risk factors, and 15% (123/794) among participants without risk factors. Culture-based screening demonstrated a sensitivity, specificity, positive predictive value, negative predictive value, and positive likelihood ratio in predicting intrapartum GBS carriage of 78% (95% confidence interval [CI] 71–84), 95% (95%CI 94–97), 78% (95%CI 70–84), 95% (95%CI 94–97), and 17 (95%CI 12–23), respectively; for risk-based screening, these values were 21% (95%CI 15–28), 90% (95%CI 87–92), 30% (95%CI 22–38), 85% (95%CI 83–86), and 2 (95%CI 1–3), respectively.
Conclusions: Culture-based screening performed considerably better than the risk-based screening in identifying intrapartum GBS colonization.

1. Introduction

Early-onset neonatal sepsis is a leading cause of mortality and morbidity in neonates [1, 2]. Group B streptococcus (GBS, *Streptococcus agalactiae* or Lancefield group B streptococcus) is the major cause of severe early-onset group B streptococcal infection (EOGBS) in neonates, defined as GBS acquired before seven days of age [3, 4]. EOGBS is associated with manifestations of severe disease such as respiratory distress, pneumonia, sepsis, and meningitis within the first 24 to 48 hours of life [5]. The most important risk factor for EOGBS is vaginal colonization, causing vertical transmission of bacteria to the fetus during labor and delivery [6]. Therefore, identification of pregnant women colonized with GBS is essential in the prevention of EOGBS. The incidence of EOGBS ranges from 0.5 to 3.0 per 1000 live births with a mortality rate of 4%–10% [7, 8]. It has been estimated that in the absence of any

intervention, approximately 50% of neonates born to colonized mothers become colonized and 1%–2% of them progress to develop invasive disease [9, 10].

Guidelines outline two strategies for the identification of women in labor who should be offered intrapartum antibiotic prophylaxis (IAP): the risk-based approach and the culture-based screening approach [1]. The Royal College of Obstetricians and Gynaecologists (RCOG) recommend IAP only to women in labor with a risk factor (previous neonate with EOGBS, GBS bacteriuria during the current pregnancy, temperature >38 ℃, rupture of membranes (ROM) for more than 18 hours, or delivery at less than 37 weeks of pregnancy) claiming that 66% of EOGBS neonates are born to mothers with one or more of these risk factors [2, 3]. The Centers for Disease Control and Prevention, USA, (CDC), on the other hand, recommend screening at 35 to 37 weeks of pregnancy for GBS rectovaginal colonization as they found that the culture-screening approach was more than 50% more effective than the risk-based approach in preventing EOGBS disease [4]. In the USA, the introduction of this strategy was associated with a decrease in EOGBS incidence from 1.7 to 0.26 cases per 1000 births [5]. In Denmark the EOGBS incidence is as low as 0.2 per 1000 births, even though prevention is based on the risk-based approach alone [6].

To our knowledge, the risk-based approach and the culture-based screening approach have never been compared in countries where only the risk-based approach is recommended. Using intrapartum rectovaginal culture for GBS as the gold standard, the aim of the present study was therefore to compare the performance of the risk-based approach with the culture-based screening approach in predicting rectovaginal colonization with GBS in a Danish cohort of unselected pregnant women.

2. Material and methods

Women attending the prenatal clinic at Lillebaelt Hospital, Kolding, Denmark (approximately 3200 deliveries per year) at 29 weeks of pregnancy between April 1, 2013, and June 30, 2014, were invited to join a prospective observational study. Studies of this population have been published previously [7, 8]. Detailed information on oral antibiotic use during pregnancy was obtained from registered data in both

hospital medical records and the Danish Medical Agency's Register of non-hospitalized patient use, which included records on all drug prescriptions filled at any Danish pharmacy. All participants gave both written and verbal informed consent before the study began. The study was approved by the Regional Scientific Ethical Committees for Southern Denmark and the Danish Data Protection Agency.

Exclusion criteria were women who were treated with antibiotics after 35 weeks of pregnancy, women with preterm labor (before 37^{+0} weeks of pregnancy), women aged under 18 years, and women with a communication barrier.

The attending midwives on the delivery ward recorded the presence of risk factors for EOGBS: bacteriuria during current pregnancy, previous neonate with EOGBS, temperature above 38.0 ℃ during labor, and ROM for more than 18 hours.

At 35–37 weeks of pregnancy, the participants obtained a self-administered vaginal and rectal swab (E-Swab, Copan Diagnostics, Brescia, Italy) sample for GBS culture during a planned visit to the outpatient clinic [9, 10]. The participants were instructed on how to use the swabs correctly by written information, simple illustrations, and two instructional videos. The vaginal swab was rotated 1.5–2 cm inside the vagina, and the rectal swab 1.5–2 cm beyond the anal sphincter. During labor, vaginal and rectal swab samples (reference standard) were obtained by a midwife.

All samples were collected using nylon flocked swabs submerged separately into 1 mL of E-Swab transport medium (E-Swab, Copan Diagnostics, Brescia, Italy).

Samples were cultured immediately on arrival at the laboratory; if received after 8:00PM, they were kept at 4 ℃ until the next morning. Direct plating of the specimen was performed by streaking the E-Swab specimen on a selective Granada agar plate. The vaginal and rectal swab samples from the participant were seeded on different sides of the same Granada agar plate (BioMérieux, Spain). The Granada agar plates were incubated immediately after seeding in a CO_2-containing atmosphere at 35℃. The results of the paired vaginal and rectal samples were referred to in this study as rectovaginal culture.

All samples were analyzed at the Department of Clinical Microbiology, Lillebaelt Hospital, Vejle, Denmark. All GBS-like colonies (identified by their orange color on Granada agar plates) were routinely confirmed as *Streptococcus agalactiae* using the Microflex LT MALDI-TOF system (Bruker Daltonik, Germany).

STATA Statistics/Data Analysis software version 14 (StataCorp LP, College Station, TX, USA) was used for the statistical analysis. Sensitivity, specificity, positive predictive values (PPV), negative predictive values (NPV), and positive likelihood ratio (LH^+), including 95% confidence intervals (CI), were calculated for prepartum GBS screening using the intrapartum culture of a rectovaginal swab sample as the gold standard.

3. Results

Of the 2343 women invited to participate in the present study, 902 women were enrolled (Figure 1).

Using the risk-based approach, among the 902 participants (Table 1), 12% (108) had one or more risk factors for EOGBS, and 17% (155) had rectovaginal colonization of GBS during labor (Table 2). This GBS colonization rate was 30% (32/108) among those with risk factors and 15% among those without risk factors (123/794), giving an OR of 2.3 (95% CI 1.5–3.6). Altogether, the risk-based approach provided a sensitivity of 21% (32/155), a specificity of 90% (671/747), PPV of 30% (32/108), NPV of 85% (671/794), and LH^+ of 2 (Table 3). Of note, 63% of the participants with GBS bacteriuria during pregnancy had rectovaginal GBS colonization during labor (Table 2).

Using the culture-based approach, the rectovaginal culture for GBS at 35 to 37 weeks of pregnancy was positive in 17% (n=156) of the cohort giving a sensitivity of 78% (n=121), a specificity of 95%, PPV of 78%, NPV of 95%, and LH^+ of 17, using intrapartum rectovaginal GBS culture as the reference standard. This gives an OR of 72 (95% CI 43.5-120.5) (Table 3). Prepartum screening showed that 9.0% (81/902) were colonized only in the vagina (sensitivity in predicting intrapartum carriage of GBS: 52%; specificity: 98%), whereas 13% (n=114) were colonized only in the rectum (corresponding sensitivity 74% and specificity 96%).

4. Discussion

Examining a Danish cohort of unselected pregnant women, the authors of the present study found that culture-based screening at 35 to 37 weeks of pregnancy performed better than a risk-based approach for prediction of intrapartum rectovaginal colonization with group B streptococci (LH^+ 17 vs 2).

A strength of the present study was that it included a relatively high number (902) of unselected pregnant women, none of whom received antibiotics after 35 weeks of pregnancy. It could be perceived as a limitation that the use of direct plating on Granada agar differs from the standard recommended by CDC of using Lim broth before plating. The difference in the detection rates between the direct plating on the Granada medium and plating after prior Lim broth enrichment is only 4% [11]. Granada medium cannot detect non-hemolytic GBS, thereby potentially decreasing the sensitivity of this culture medium for GBS screening [5]. However, the frequency of non-hemolytic GBS isolates is only 1% among invasive GBS strains [12].

The self-administered swab sampling could also be considered as a limitation; however no significant difference was observed in the number of positive findings between the prepartum vaginal swab samples obtained by the women (n=100) and the intrapartum vaginal swab samples collected by midwives (n=104) (OR 0.96, 95% CI 0.7–1.3, thus supporting the principle of self-administered swab sampling.

To our knowledge, no systematic comparison of a risk-based strategy and a prepartum culture strategy for prediction of intrapartum rectovaginal carriage of GBS had previously been performed in a country at low risk for EOGBS such as Denmark, where the risk-based approach alone has been used to date. The GBS carriage rate in the present study was 17% compared to 10%–29% in other studies [13–16]. This variation could be attributable to differences between populations and the use of different GBS detection methods, especially differences in the use of broth enrichment [15, 17]. The difference between vaginal and rectal culture carriage (9% vs 13%, respectively) at 35 to 37 weeks of pregnancy has also been shown in other studies. This supports the hypothesis that the gastrointestinal tract is the primary

reservoir of GBS, and that vaginal colonization indicates the spread of GBS from the rectum [14, 15].

The present study indicated that culture-based screening performed better than the risk-based approach for identification of women in labor with rectovaginal colonization of GBS. This may explain why most neonates with EOGBS are delivered by women without risk factors [2, 4, 18, 19].

The findings of the present study were, to some extent, supported by prior publications. Daniels and colleagues [20] found that 29% of the women with one or more risk factors were actually carrying GBS, and up to 19% without risk factors were GBS carriers. Furthermore, longitudinal studies of GBS carriage have demonstrated that approximately 50% of all pregnant women remain GBS-negative during pregnancy, 20%–40% are intermittently GBS-positive, and 10%–30% are GBS-positive at each examination [16, 17, 21]. However, it was surprising to find that 78% of the GBS culture-positive cases at 35 to 37 weeks of pregnancy were still GBS-positive during labor in the present study population. El Helali [22] and colleagues found this figure to be 58% in a French population.

Screening in order to prevent rare diseases such as EOGBS may not be cost-effective, as it may be expensive and associated with a high false positive rate, causing unnecessary use of antibiotics. If the unnecessary use of antibiotics is considered to be problematic because of the possible negative influence on the microbiome of the neonate [23, 24], increased incidence of antibiotic drug resistance, and a risk of anaphylaxis in the mother [25], other strategies could potentially be considered such as rapid and accurate intrapartum bedside tests for rectovaginal carriage of GBS [7, 8].

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Conflict of interests

The authors have no conflicts of interest.

Author contributions

All authors contributed to the conception and design of the study, the collection, analysis and interpretation of data, and writing and revising the manuscript. All authors approved the final published version of the article.

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Figure 1 Flow chart of participant enrollment.

Table 1 Concordance between prediction of intrapartum GBS colonization detected by risk-based approach and rectovaginal prepartum culture.

Variable	Rectovaginal intrapartum culture (Reference standard) (n=902)		
	Positive	Negative	Total
Participants having specified risk factor			
Positive	32	76	108
Negative	123	671	794
Rectovaginal prepartum culture			
Positive	121	35	156
Negative	34	712	746
Total	155	747	902

Abbreviation: GBS, group B streptococci.

Table 2 Intrapartum rectovaginal GBS carriage rates and risk factor status (n=902). [a]

Participants having specified risk factor	Intrapartum rectovaginal culture GBS-positive rate
EOGBS in previous delivery	0/1 (0)
GBS bacteriuria during current pregnancy	19/30 (63)
Fever (≥38.0°C)	1/9 (11)
ROM ≥18 hours	12/68 (18)
One or more risk factors	32/108 (30)
No risk factor present	123/794 (15)
Total	155/902 (17)

Abbreviation: EOGBS, early-onset group B streptococci; GBS, group B streptococci; ROM; rupture of membranes.

[a] Values given as number/denominator (percentage).

Table 3 Performance characteristics of GBS by risk-based screening and rectovaginal culture at 35–37 weeks of pregnancy using rectovaginal intrapartum culture as the reference standard.[a]

Variable	One or more Risk factors (n=902)	Rectovaginal culture samples at 35–37 weeks of pregnancy (n=902)
Sensitivity	32/155 (21 [15–28])	121/155 (78 [71–84])
Specificity	671/747 (90 [87–92])	712/747 (95 [94–97])
PPV	32/108 (30 [22–38])	121/156 (78 [70–84])
NPV	671/794 (85 [83–86])	712/746 (95 [94–97])
LH^+	2 (1–3) [b]	17 (12–23) [b]

Abbreviations: CI, confidence interval; GBS, group B streptococci; LH+, positive likelihood ratio; NPV, negative predictive value; PPV, positive predictive value.

[a] Values are given as number/denominator (percentage [95% CI]), unless indicated otherwise.

[b] Value given are absolute numbers (95% CI).