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Performance of BD MAX Group B Streptococcus (GBS) Assay without Enrichment for the Detection of GBS

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Group B streptococcus (GBS) is an important pathogen causing neonatal early-onset disease. We evaluated the diagnostic performance of BD Max GBS assay (Becton Dickinson, Franklin Lakes, NJ, USA) without enrichment (direct BDM) for detecting GBS using vaginal and rectal specimens in comparison with culture. In total, 716 specimens collected from 358 pregnant women between June 2018 and May 2020 were included in this study. Bacterial culture was performed using ChromID Strep B agar (bioMérieux, Marcy-l'Étoile, France), and species identification results were confirmed using the VITEK-MS system (bioMérieux). The sensitivity of direct BDM for vaginal and rectal specimens was 75.0% and 100%, respectively. Thirteen specimens showed discrepant results: 10 false-negative results in the vaginal specimens and three false-positive results in the rectal specimens. The overall agreement between direct BDM and culture was 98.9% (354/358). The final sensitivity and specificity of direct BDM were 98.5% and 99.0%, respectively. Discrepant results—one false-negative and three false-positives—were obtained for four specimens. Direct BDM shows a good diagnostic performance and will be useful for GBS screening within a few hours.

Key Words: Group B streptococcus, BD Max, Performance, Sensitivity, Specificity

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Group B streptococcus (GBS) is an important pathogen causing neonatal early-onset disease (EOD) with high morbidity and mortality rates [1-3]. The American College of Obstetricians and Gynecologists has reported that the transmission of GBS from the mother's gastrointestinal tract and urogenital organs is a recognized risk factor for early-onset GBS disease [4]. Rapid and accurate identification of GBS colonization in pregnant women is important for appropriate intrapartum antibiotic prophylaxis and the prevention of EOD [5, 6].

The US Centers for Disease Control and Prevention (CDC) recommends antepartum vaginal/rectal culture in all pregnant women between 35 and 37 weeks as the gold standard [7]. However, conventional culture is insufficient to reflect the GBS colonization status, which commonly changes during pregnancy [8, 9]. Recently, real-time PCR was introduced for GBS screening, significantly reducing the turnaround time [10]. However, PCR requires enrichment and is therefore not suitable as an intrapartum GBS assay.

We evaluated the BD Max GBS assay (Becton Dickinson, Franklin Lakes, NJ, USA) without enrichment (direct BDM) in comparison with culture for the detection of GBS using vaginal and rectal specimens. The Institutional Review Board of Inje University Busan Paik Hospital, Busan, Korea (approval number 20-0151) approved this study with participant consent exemption.

In total, 716 specimens collected from 358 pregnant women between June 2018 and May 2020 were assessed. Vaginal and rectal specimens were collected in pairs into E-Swab transport medium (E-Swab, Copan Diagnostics, Brescia, Italy). The specimens were stored at -70°C until use.

Bacterial culture without enrichment was performed using ChromID StrepB agar (bioMérieux, Marcy-l'Étoile, France), and the species identification results were confirmed using matrix-assisted laser desorption/ionization time-of-flight on the VITEK-MS system (bioMérieux). The PCR-based BD Max GBS assay was performed according to the manufacturer's instructions. This assay automatically extracts DNA from specimens and amplifies a 124-bp region of the *cfb* gene from the GBS genome.

Our study has two major methodological differences compared to other studies on conventional BD Max GBS assay. First, we inoculated the specimens into specimen preparation reagent without an enrichment step. Second, the vaginal and rectal specimens were tested separately in contrast to the manufacturer's recommendation to mix vaginal and rectal specimens before the specimen preparation step.

We calculated the sensitivity and specificity of direct BDM for each specimen type on the basis of the culture results. The diagnostic performance of direct BDM was assessed using the combined results from the vaginal and rectal specimens obtained from the 358 pregnant women. The combined result for direct BDM and the culture was considered positive if the result of either the vaginal specimen or the rectal specimen was positive.

For the 716 specimens, the positive rates of direct BDM and culture were 13.3% (N=95) and 14.2% (N=102), respectively. The overall agreement between the BD Max GBS assay and culture was 98.2% (703/716) (Table 1).

The sensitivity and specificity of direct BDM for vaginal specimens were 75.0% and 100%, respectively. There were 10 discrepant results, and all were false-negatives on direct BDM. For rectal specimens, the sensitivity and specificity were 100% and 99.0%, respectively. Three discrepant results were all false-positives in direct BDM.

The overall diagnostic performance of direct BDM in all the specimens is shown in Table 2. A culture result was considered positive if either the vaginal or the rectal specimen yielded a positive result. The results of direct BDM were interpreted in the same way. The positive rates of direct BDM and culture were 19.0% (68/358) and 18.4% (66/358), respectively. The overall agreement between direct BDM and culture was 98.9% (354/358). The final sensitivity and specificity of direct BDM in the 358 women were 98.5% and 99.0%, respectively, when combined results were used. Discrepant results were found for four women, with one false-negative and three false-positive results.

Nine vaginal specimens tested negative in direct BDM despite that all the vaginal cultures, rectal cultures, and rectal direct BDM for these women yielded positive results (Table 3). Twenty-six rectal specimens yielded positive results in culture and direct BDM, whereas the corresponding vaginal specimens tested negative in culture and direct BDM. Three vaginal specimens tested

Table 1. Comparison of direct BDM with culture

Culture	Direct BDM					
	Total (N=716)		Vagina (N=358)		Rectum (N=358)	
	Positive	Negative	Positive	Negative	Positive	Negative
Positive	92	10	30	10	62	0
Negative	3	611	0	318	3	293
Sensitivity (%) (95% CI)	90.2 (82.3-94.9)		75.0 (58.5-86.8)		100 (92.7-100)	
Specificity (%) (95% CI)	99.5 (98.5-99.9)		100 (98.5-100)		99.0 (96.8-99.7)	

Abbreviations: BDM, BD Max GBS assay; CI, confidence interval.

Table 2. Diagnostic performance of direct BDM in specimens obtained from 358 pregnant women

Culture	Direct BDM (N=358)					
	Vagina or rectum		Vagina		Rectum	
	Positive*	Negative	Positive	Negative	Positive	Negative
Positive*	65	1	30	36	62	3
Negative	3	289	0	292	3	290
Sensitivity (%) (95% CI)	98.5 (90.7-99.9)		45.5 (33.3-58.1)		95.4 (86.2-98.8)	
Specificity (%) (95% CI)	99.0 (96.8-99.7)		100 (98.4-100)		99.0 (96.8-99.7)	

*A positive result for either the vaginal or the rectal specimen was considered a positive result.
Abbreviations: BDM, BD Max GBS assay; CI, confidence interval.

Table 3. Discrepant results between culture and direct BDM in vaginal and rectal specimens

Culture (vagina/rectum) (N=358)	Direct BDM (vagina/rectum)			
	P/P (N=27)	P/N (N=3)	N/P (N=38)	N/N (N=290)
P/P (N=36)	27		9	
P/N (N=4)		3		1
N/P (N=26)			26	
N/N (N =292)			3	289

Abbreviations: BDM, BD Max GBS assay; P, Positive; N, Negative.

positive in both culture and direct BDM, whereas the corresponding rectal specimens tested negative by both methods.

In recent years, a few FDA-approved PCR assays for rapid GBS detection have been introduced in clinical laboratories [4, 11]. These assays have the prominent advantages of a short turnaround time (within several hrs) and accurate performance [9, 10, 12]. However, most PCR assays for GBS screening require enrichment before amplification, which takes more than 18 hrs according to the CDC recommendation . Some studies have shown the limited utility of intrapartum specimens for PCR-based GBS screening as GBS colonization can change during pregnancy [9, 13]. In urgent situations, such as premature labor, or when information for prenatal care is lacking, final results have to be reported more rapidly. Direct BDM would be helpful for appropriate diagnosis and prophylaxis of GBS.

Direct BDM showed a good diagnostic performance, with a high sensitivity (98.5%) and specificity (99.0%) based on combined results. Riedlinger, *et al.* [14] reported a sensitivity and specificity of BDM of 95% and 96.7%, respectively, despite the inclusion of an enrichment procedure. Concerning direct BDM, Silbert, *et al.* [15] reported good performance, although the sensitivity of direct BDM (92.7%) was lower than that of BDM with enrichment (99.1%), whereas Ellem, *et al.* [16] reported a sensitivity and specificity of 98.4% and 100.0%, respectively, for the BD Max GBS assay without enrichment and of 100% and 100%, respectively, when enrichment was included. From our results, we conclude that the BD Max GBS assay can be used without enrichment for GBS screening.

Our study had some strengths. We tested two (vaginal and rectal) specimen types independently and found that they can render different results. Rectal specimens showed a better clinical sensitivity for GBS detection (95.4%) than vaginal specimens (45.5%), as also reported by Madani, *et al.* [17]. We presume that the colon is a major reservoir of GBS. However, it is appropriate to use mixed specimens as for three women, only the vaginal specimen tested positive.

The sensitivity of direct BDM was significantly lower in vaginal specimens (75%) than in rectal specimens (100%) when we compared the results of direct BDM with those of culture. For nine vaginal specimens, direct BDM showed negative results, although vaginal culture, rectal culture, and rectal direct BDM yielded positive results. We did not determine why these false-negative results occurred, but we presume they did so owing to the presence of PCR inhibitors in vaginal secretions. Three rectal specimens yielded false-positive results by direct BDM. We hypothesize that these may represent true-positive findings of direct BDM given the higher performance of real-time PCR.

This study had a few limitations. First, we did not include BDM with enrichment; thus, we could not compare the results of direct BDM with those of BDM with enrichment. Second, we did not conduct retesting for the discrepant results between direct BDM and culture.

In conclusion, direct BDM shows good diagnostic performance and would allow GBS screening within a few hrs and appropriate prophylaxis. The study results support the use of direct BDM for rapid and accurate detection of GBS-colonized in pregnant women.

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AUTHOR CONTRIBUTIONS

Um S, Her J, and Kim SH designed the study, performed the experiments, analyzed the data, and wrote the original draft of the manuscript. Song SA and Kim YN contributed their valuable review. Shin JH participated in the study design and the writing, editing, and reviewing of the manuscript. All authors reviewed and approved the final version of the manuscript.

CONFLICTS OF INTEREST

No potential conflicts of interest relevant to this article have been reported.

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