Clinical performance of the WASPLab AI/IA-PhenoMATRIX™ software in detection of GBS from LIM-enriched cultures plated to CHROMID® Strepto B Chromogenic Media.

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Abstract

Group B *Streptococcus* (GBS) can be found colonizing about 25% of all healthy, adult women and is the leading infectious cause of early neonatal morbidity and mortality in the United States. The rate of early-onset neonatal infection is ~0.22 cases per 1,000 live births (2016) and can cause sepsis resulting in neurologic sequelae such as sight/hearing loss and cerebral palsy. The CDC recommends that vaginal/rectal swabs be collected between 35 to 37 weeks gestation to test the mother for carriage and prophylactic measures taken for colonized women.

This study was undertaken to evaluate the clinical performance of the WASPLab™ Artificial Intelligence/Interpretative Algorithm (PhenoMATRIX™[PM] Copan Diagnostics) in detection of GBS from LIM broth enriched cultures plated on CHROMID® Strepto B (ChromGBS) Chromogenic Media (bioMérieux) after 24 and 48 hours of incubation. The performance of the PhenoMATRIX was compared to manual culture review of the digital images and molecular detection of GBS (BD MAX, BD Diagnostics Systems). Discrepant results were adjudicated using a second molecular method (Cepheid GeneXpert GBS, Cepheid, Inc.).

A total of 486 vaginal/rectal swab samples were collected for the study. Specimens were determined to be positive if they had a positive molecular result and/or a confirmed GBS culture result. Thus, the overall detection of GBS was considered to be 94/486 (19.3%). The ChromGBS plus PM algorithm detected 88/94 (93.6%) GBS samples at 24 hours demonstrating a sensitivity and specificity of 93.6% and 79.9%, respectively. Increasing the incubation time to 48 hours increased GBS detection to 90/94 (95.7%) for a sensitivity of the ChromGBS plus PM of 95.7%, but specificity of 66.6%. Molecular detection of GBS resulted in 90/94 (95.7%) positive samples for an overall sensitivity of 95.74% with a specificity of 98.8%. Technologist read of ChromGBS without PM, detected 84/94 (89.4%) of positive GBS colonies by 48 hours for a sensitivity and specificity of 89.4% and 99.5%, respectively.

The use of ChromGBS in combination with the PM AI/IA System was equivalent to the sensitivity of molecular detection. Further, the algorithm never called a culture negative that was determined to be positive by manual reading and identified an additional six true positive specimens that were missed by manual digital image culture reading.

Introduction

Group B Streptococcus (GBS) has been recognized as a leading cause of infectious early neonatal morbidity and mortality in the United States. Early onset GBS disease in infection in newborns occurs within the first week of life. Patients typically present with respiratory distress, apnea or other constitutional signs of sepsis with mortality from early-onset GBS can range from 2-30%, with the highest rates among infants less than 33 weeks gestation.

The CDC recommends universal culture-based screening for GBS on all pregnant women using vaginal-rectal swabs collected at 35-37 weeks gestation. Approximately 10-30% of pregnant women are colonized with GBS during pregnancy. Following the first recommendations for screening, the rate of early-onset GBS disease has decreased from 1.7 cases per 1,000 live births (1993) to 0.22 cases per 1,000 live births (2016).

Culture of the Lim-broth enriched specimen is the gold-standard for detection of GBS. However, culture lacks sensitivity and requires 24-48 hours following enrichment for final identification. There are several commercially available nucleic acid amplification tests available for the detection of GBS that increase sensitivity and provide a faster result, but may suffer from a lack of specificity.

Based on previous studies describing the efficacy of the WASPLab artificial intelligence interpretive algorithm, PhenoMatrix (Copan Diagnostics) Chromogenic Detection Module (CDM) for detection of MRSA, VRE and Group A Streptococcus, we are evaluating the performance of the CDM on ChromID StreptoGBS (Chrom ID GBS) for the enhanced detection of GBS in enriched vaginal-rectal swabs compared to routine visual inspection and a molecular method.

Methods

Samples: 486 residual vaginal/Rectal swabs in LIM broth were enrolled in the study. LIM broths were incubated at 35-37°C for 18-24 as per standard laboratory procedures. 1mL of enriched LIM broth was aliquoted into empty sterile Copan 12 tubes for automated processing on the WASPLab.
GBS Culture: 30µl of LIM enriched cultures were inoculated by the WASP (Copan Diagnostics) onto one ChromID StreptoB Chromogenic Media plate (bioMerieux) and a Blood Agar Plate . Cultures were incubated in the WASPLab (Copan Diagnostics) incubator in ambient air at 35-37°C with digital images captured at initial planting (0 hours), 24 hours and 48 hours.
Culture Reading: Digital images of cultures were reviewed manually at 24 and 48 hours by a technologist and scored for the presence or absence of colonies resembling GBS. Morphologies consistent with GBS were confirmed using Gram stain, catalase reaction and latex Lancefield grouping.
Algorithm-Based Detection of GBS: Acquired images were analyzed by PhenoMatrix (Copan Italia) for the detection of colonies resembling GBS.
Discordant Analysis: Discrepant results between the PhenoMatrix and manual culture review were resolved by performing identification on discordant colonies.
Molecular Detection of GBS: All enriched LIM broths were tested by BD MAX GBS (BD Diagnostics).
Data analysis: To evaluate the performance between the culture methods and NAAT, the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) was determined by comparing the result of each method to the consensus result.

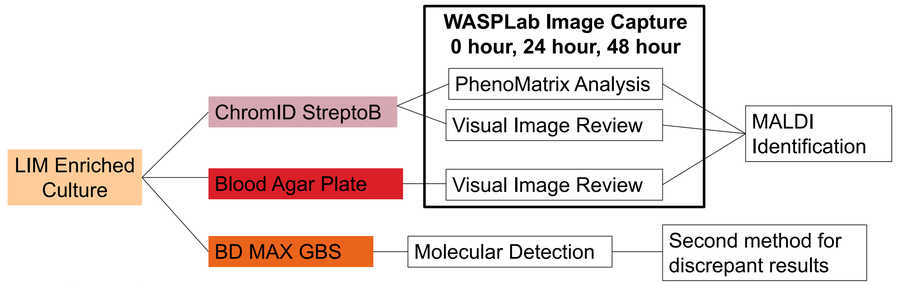


Figure 1.
Study workflow for detection of GBS. (Matrix Assisted Laser Desorption Ionization, MALDI)

Figure 2.
Range of color spectra selected for chromogenic detection of Group B Streptococcus on ChromID GBS Agar

Results

	Total Positive	TP	FP	FN	TN	Sensitivity	Specificity	PPPV	NPV
Manual Review 24h	74	73	1	21	391	77.7%	99.7%	98.7%	94.9%
PhenoMatrix 24 h	167	88	79	6	313	93.6%	79.9%	52.7%	98.1%
Manual Review 48h	86	84	2	10	390	89.4%	99.5%	97.7%	97.5%
PhenoMatrix 48 h	221	90	131	4	261	95.7%	66.6%	40.7%	98.5%
BD MAX	94	90	4	4	388	95.7%	98.9%	95.7%	99.0%

Table 1 Comparison the three methods for GBS detection. Total prevalence of GBS was 19.3% (94/486).

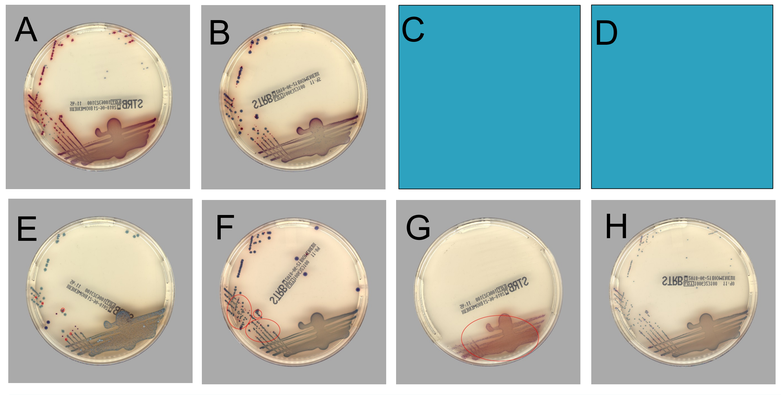
		Visual Image Review	
		Positive	Negative
PhenoMatrix	Positive	86	164
	Negative	0	236

Table 3. Comparison of PhenoMatrix to manual review. We calculated the performance of PhenoMatrix compared to manual review. The sensitivity was 100% (94.7-100%) specificity was 59.0% (54.0%-63.8%), PPV was 51.4% and NPV was 100%.

Table 4. Identification of PhenoMatrix detected/culture not detected isolates
When Phenomatrix detected an isolate that was not identified by manual review, MALDI-TOF was performed. An additional 4 *S. agalactiae* (GBS) isolates were detected by PhenoMatrix

Identification	Count
S. agalactiae	**6**
Specimen artifact	38
E. faecalis	51
E. faecium	17
S. anginosus	10
Lactobacillus sp.	7
Enterococcus sp.	6
S. mitis/oralis	6
Streptococcus sp.	3
E. coli	2
S. salivarius	2
Other	5
Unable to identify	7

Figure 3. Images of representative cultures on ChromID GBS. (A) PhenoMatrix (PM) positive/manual review (MR) positive GBS high abundance (B) PM positive/ MR positive GBS low abundance (C) PM positive/MR negative GBS true positive (D) PM positive/MR negative GBS true positive (E) PM Positive/MR negative. Isolates identified as *S. anginosus* (F) PM positive - non GBS. Isolates identified as *E. faecalis.* (G) PM positive – specimen artifact. (H) PM negative - non GBS



Conclusions

- The use of ChromGBS in combination with PhenoMatrix is equivalent in sensitivity to molecular detection of GBS.
- ChromGBS with PhenoMatrix lacks specificity due to overlap in color spectra for GBS and nonGBS isolates and color change produced by specimen artifact.
- ChromID GBS plus PhenoMatrix provides an efficient method for rapid screening of GBS negative cultures

Acknowledgements

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