

Group B Streptococcus screening with antenatal culture and intrapartum polymerase chain reaction: A prospective cohort study

Marlene Samantha Sze Minn Goh^{*1} MBBS, Hong Ying Tan^{*2} MBBS, Yan Shun Ng^{*1} MB BCh BAO, Ilka Tan³ FRCOG, Kee Thai Yeo^{**2,4,5} MD, Chee Wai Ku^{**5,6} MRCOG, Manisha Mathur^{**1} FRCOG

Dear Editor,

Group B Streptococcus (GBS) is a common genital and gastrointestinal tract commensal in healthy women. Vertical transmission of GBS may cause neonatal early-onset GBS disease (EoGBS), and this is prevented by intrapartum antibiotic prophylaxis (IAP). Notably, intermittent GBS colonisation,¹ coupled with long turnaround time of GBS culture, challenges the accuracy of conventional antenatal GBS screening in predicting carriage during labour, especially for those without prior antenatal GBS screening. Polymerase chain reaction (PCR) offers a rapid and accurate alternative, demonstrating 98.5% sensitivity and 99.6% specificity, surpassing the 58.3% positive predictive value of antenatal culture screening in a retrospective study,² resulting in the reduction of EoGBS from 1.01 to 0.21 per 1000 live-births. This study aimed to compare the sensitivity and specificity of intrapartum GBS PCR to antenatal GBS swab culture, using intrapartum GBS culture as a reference for maternal colonisation status.

This cross-sectional study from March 2021 to December 2021 in KK Women's and Children's Hospital included pregnant women aged ≥ 21 years, ≥ 37 weeks' gestation, with antenatal swab culture (COPAN M40 Amies Agar Gel Transystem, COPAN, US) for GBS broth culture collected within 5 weeks (window of validity as per American College of Obstetrics and Gynaecology)³ prior to delivery, and intact membranes with no leaking liquor at presentation. Those with spontaneous rupture of membranes, in labour < 37 weeks' gestation, and who received antibiotics after 35 weeks of gestation or after routine antenatal GBS screening were excluded. Informed consent was obtained. This study is approved by the SingHealth Centralised Institutional Research Board (CIRB

2020/2126). Medical records were accessed for demographic and clinical information related to labour and delivery.

During labour, double-vaginal swab was collected prior to antibiotics administration. One was sent for intrapartum culture (as per antenatal swab), while the other was processed as a point-of-care test, using Cepheid collection device as transport medium before being loaded into an Xpert GBS cartridge. The Xpert GBS PCR assay (Cepheid, Sunnyvale, CA, US) was performed using the Cepheid GeneXpert device, according to manufacturer's protocol. Results were reported in the Cepheid GeneXpert software. Patients with positive antenatal GBS culture were covered with IAP as per hospital guidelines regardless of intrapartum results. Patients with negative antenatal GBS culture but positive intrapartum PCR result were offered IAP.

Continuous data were presented as mean $\pm$ standard deviation (SD), while categorical data were presented as frequencies (percentages). Diagnostic measures were reported using sensitivity, specificity and area under the curve (AUC) from receiver operating curve with a 95% confidence interval (CI). Gwet's AC1 agreement was reported between antenatal and intrapartum cultures, and between intrapartum culture and PCR. Sensitivity and specificity from antenatal culture and intrapartum PCR were compared using McNemar tests of paired design. All tests were two-sided, and $P < 0.05$ was statistically significant. All analyses were performed in SAS version 9.4 software (SAS Institute, Cary, NC, US).

Among 170 participants, 86 (50.6%) had positive and 84 (49.4%) had negative antenatal GBS culture. Their mean age was 30.6 ± 4.6 years, mean body

The Annals is an open access journal, allowing non-commercial use under CC BY-NC-SA 4.0.

¹ Department of Obstetrics and Gynecology, KK Women's and Children's Hospital, Singapore

² Yong Loo Lin School of Medicine, National University of Singapore, Singapore

³ Department of Maternal Fetal Medicine, KK Women's and Children's Hospital, Singapore

⁴ Department of Neonatology, KK Women's and Children's Hospital, Singapore

⁵ Duke-NUS Medical School, Singapore

⁶ Department of Reproductive Medicine, KK Women's and Children's Hospital, Singapore

* Joint first authors

** Joint last authors

Correspondence: Dr Chee Wai Ku, Department of Reproductive Medicine, KK Women's and Children's Hospital, 100 Bukit Timah Road, Singapore 229899.

Email: gmskcw@nus.edu.sg

Table 1. Detection of GBS status by antenatal culture and intrapartum PCR, compared to intrapartum culture as the reference standard.

		Intrapartum culture		
		Positive	Negative	Total
Antenatal culture	Positive	35	51	86
	Negative	3	81	84
	Total	38	132	170
Intrapartum PCR	Positive	33	25	58
	Negative	4	105	109
	Total	37	130	167

GBS: Group B Streptococcus; PCR: polymerase chain reaction

mass index was 29.7±5.7 kg/m², and mean gestational age at delivery was 39.1±0.9 weeks. Most were nulliparous (50.6%), without gestational diabetes (81.8%), and delivered vaginally (84.7%). None of the neonates developed EoGBS sepsis. The mean duration required for intrapartum PCR was 54±3 minutes.

The detection of GBS status by antenatal culture and intrapartum PCR was compared with intrapartum culture as the reference standard (Table 1). Antenatal culture and intrapartum PCR have sensitivities comparable to those of intrapartum culture at 92.1% (95% CI 78.6–98.3) and 89.2% (95% CI 74.6–97.0), respectively. However, intrapartum PCR has a higher specificity of 79.6% (95% CI 71.7–86.1) compared to 61.4% (95% CI 52.5–69.7) for antenatal culture. AC1 (71.7% versus 40.8%), AUC (0.85 vs 0.77) and odds ratio (OR) (30.8 vs 16.1) of intrapartum PCR were also higher. Furthermore, the false positive rates of intrapartum PCR (19.2%, 25 of 130) were lower than those of antenatal culture (38.6%, 51 of 132).

Three (1.8%) women had inconclusive PCR results, 2 of which were antenatal and intrapartum culture negative, and 1 was antenatal and intrapartum culture positive. Six participants (3.5%) had discordant results. Intrapartum PCR did not detect the positive GBS colonisation status of 3 (1.8%) women determined by intrapartum culture. Another 3 (1.8%) women had a change in GBS status (from negative antenatal culture to positive intrapartum culture), 2 of whom were correctly identified as positive with intrapartum PCR.

There is increasing evidence supporting nucleic acid amplification tests for intrapartum GBS screening,⁴ due to higher sensitivity, specificity and rapid 1–2 hour turnaround time. The Cepheid Xpert GBS test used in this study is also the only in vitro diagnostic test that meets the criteria of

Centers for Disease Control and Prevention for rapid intrapartum GBS testing without requiring 24-hour Lim broth enrichment⁵ and has shown to have comparable results.⁶ In this study, intrapartum PCR demonstrated comparable sensitivity and superior specificity compared to antenatal culture, with higher AC1, AUC and OR. With a disease prevalence of 22% (38 of 170), despite the modest sample size of 170, this study achieves over 85% power to detect change in sensitivity from 50% to 75% using a two-sided binomial test and 100% power to detect change in specificity from 50% to 80% using a two-sided binomial test at the target significance level of 5%.

In this study, 51 (59.3%, 51 of 86) participants experienced a change in GBS status from positive antenatal to negative intrapartum GBS colonisation, which resulted in unnecessary IAP use for over half the participants. This overuse impacts maternal and neonatal microbiomes, affecting infants' immune and metabolic functions,⁷ and increases treatment cost, which could potentially be used to offset any additional cost of PCR testing. Notably, PCR detected 2 of 3 women with negative antenatal GBS culture but subsequently positive intrapartum GBS culture, highlighting its potential in preventing missed opportunities for IAP.

Admittedly, intrapartum PCR has limitations. Three (1.8%) participants had inconclusive PCR results, lower than similar studies reporting up to 13.6% invalid results.^{8,9} This can be minimised by repeating the test, which has shown to increase success rate from 86.4% to 91.3%. Among 4 with negative intrapartum PCR but positive intrapartum culture, 3 had positive antenatal culture results, potentially missing the opportunity for IAP if they were screened with intrapartum PCR only. The presence of such discordant results is possibly due to sampling or processing errors.^{2,8} In

addition, we acknowledge that recto-vaginal swabs are recommended for GBS screening, instead of vaginal swabs, which was the routine practice in this centre due to cultural reasons. This may have affected the sensitivity of GBS detection. However, vaginal swabs were consistently used for the antenatal and intrapartum swab cultures and PCR.

Intrapartum PCR has shown comparable sensitivity and superior specificity in detecting GBS colonisation. It provides an alternative strategy for the universal screening of GBS, especially in those who have missed out on antenatal screening.

Keywords: *Group B Streptococcus, Group B Streptococcus screening, intrapartum screening, obstetrics and gynaecology, polymerase chain reaction*

REFERENCES

1. Goodman JR, Berg RL, Gribble RK, et al. Longitudinal Study of Group B Streptococcus Carriage in Pregnancy. *Infect Dis Obstet Gynecol* 1997;5:237-43.
2. 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.
3. The American College of Obstetricians and Gynecologists Committee Opinion No. 797. Prevention of group B streptococcal early-onset disease in newborns. *Obstet Gynecol* 2020;135:e51-72.
4. American Society for Microbiology. Guidelines for the Detection and Identification of Group B Streptococcus, 29 July 2021. <https://asm.org/Guideline/Guidelines-for-the-Detection-and-Identification-of-> Accessed 23 May 2022.
5. Cepheid. Group B Strep (GBS) Intrapartum Molecular Test - XpertGBS. https://web-support.cepheid.com/en_CA/tests/Sexual-Health/Xpert-GBS. Accessed 18 May 2022.
6. Buchan BW, Faron ML, Fuller D, et al. Multicenter Clinical Evaluation of the Xpert GBS LB Assay for Detection of Group B Streptococcus in Prenatal Screening Specimens. *J Clin Microbiol* 2014;53:443-8.
7. Kotwani A. Overuse of Antibiotics in Pregnancy: Beyond Antimicrobial Resistance. In: Mehta S, Grover A, eds. *Infections and Pregnancy*. Springer 2022:641-50.
8. Mueller M, Henle A, Droz S, et al. Intrapartum detection of Group B streptococci colonization by rapid PCR-test on labor ward. *Eur J Obstet Gynecol Reprod Biol* 2014;176:137-41.
9. Plainvert C, El Alaoui F, Tazi A, et al. Intrapartum group B Streptococcus screening in the labor ward by Xpert® GBS real-time PCR. *Eur J Clin Microbiol Infect Dis* 2018;37:265-70.