The Journal of Maternal-Fetal & Neonatal Medicine

ISSN: 1476-7058 (Print) 1476-4954 (Online) Journal homepage: http://www.tandfonline.com/loi/ijmf20

Accuracy of a rapid real-time polymerase chain reaction assay for diagnosis of group B Streptococcus colonization in a cohort of HIV-infected pregnant women

Maria Isabel S. Gouvea, Esau C. Joao, Maria de Lourdes B. Teixeira, Jennifer S. Read, Sergio E. L. Fracalanzza, Claudia T. V. Souza, Maria José de Souza, Helio M. Torres Filho, Cassiana C. F. Leite & Pedro E. A. A. do Brasil

To cite this article: Maria Isabel S. Gouvea, Esau C. Joao, Maria de Lourdes B. Teixeira, Jennifer S. Read, Sergio E. L. Fracalanzza, Claudia T. V. Souza, Maria José de Souza, Helio M. Torres Filho, Cassiana C. F. Leite & Pedro E. A. A. do Brasil (2016): Accuracy of a rapid real-time polymerase chain reaction assay for diagnosis of group B Streptococcus colonization in a cohort of HIV-infected pregnant women, The Journal of Maternal-Fetal & Neonatal Medicine, DOI: 10.1080/14767058.2016.1205021

To link to this article: http://dx.doi.org/10.1080/14767058.2016.1205021

THE JOURNAL OF MATERNAL-FETAL & NEONATAL MEDICINE

http://informahealthcare.com/jmf
ISSN: 1476-7058 (print), 1476-4954 (electronic)

J Matern Fetal Neonatal Med, Early Online: 1–6
 DOI: 10.1080/14767058.2016.1205021

Taylor & Francis
Taylor & Francis Group

ORIGINAL ARTICLE

Accuracy of a rapid real-time polymerase chain reaction assay for diagnosis of group B *Streptococcus* colonization in a cohort of HIV-infected pregnant women

Maria Isabel S. Gouvea[1,2], Esau C. Joao[1], Maria de Lourdes B. Teixeira[1,2], Jennifer S. Read[3], Sergio E. L. Fracalanzza[4], Claudia T. V. Souza[2], Maria José de Souza[5], Helio M. Torres Filho[6], Cassiana C. F. Leite[6], and Pedro E. A. A. do Brasil[2]

[1]Infectious Diseases Department, Hospital Federal dos Servidores do Estado, Rio de Janeiro, Brazil, [2]Instituto Nacional de Infectologia Evandro Chagas – Fiocruz, Rio de Janeiro, Brazil, [3]Department of Epidemiology and Biostatistics, University of California at San Francisco, San Francisco, CA, USA, [4]Laboratório de Bacteriologia Médica do Instituto de Microbiologia Prof. Paulo de Góes, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil, [5]Department of Bacteriology, Hospital Federal dos Servidores do Estado, Rio de Janeiro, Brazil, and [6]Laboratório Richet, Núcleo de Apoio à Pesquisa Clínica, Rio de Janeiro, Brazil

Abstract

Objective: There are limited data regarding Xpert performance to detect Group B *Streptococcus* (GBS) in HIV-infected pregnant women. We evaluated the accuracy of a rapid real-time polymerase chain reaction (PCR) test in a cohort of HIV-infected women.

Methods: At 35–37 weeks of pregnancy, a pair of combined rectovaginal swabs were collected for two GBS assays in a cohort of sequentially included HIV-infected women in Rio de Janeiro: (1) culture; and (2) real-time PCR assay [GeneXpert GBS (Cepheid, Sunnyvale, CA)]. Using culture as the reference, sensitivity, specificity, positive and negative-likelihood ratios were estimated.

Results: From June 2012 to February 2015, 337 pregnant women met inclusion criteria. One woman was later excluded, due to failure to obtain a result in the index test; 336 were included in the analyses. The GBS colonization rate was 19.04%. Sensitivity and specificity of the GeneXpert GBS assay were 85.94% (95% CI: 75.38–92.42) and 94.85% (95% CI: 91.55–96.91), respectively. Positive and negative predictive values were 79.71% (95% CI: 68.78–87.51) and 96.63% (95% CI: 93.72–98.22), respectively.

Conclusions: GeneXpert GBS is an acceptable test for the identification of GBS colonization in HIV-infected pregnant women and represents a reasonable option to detect GBS colonization in settings where culture is not feasible.

Keywords

Culture, group B *Streptococcus*, HIV, real-time polymerase chain reaction

History

Received 20 February 2016
Revised 30 May 2016
Accepted 19 June 2016
Published online 13 July 2016

Introduction

During pregnancy, vaginal and rectal colonization of women have been implicated in the vertical transmission of Group B *Streptococcus* (GBS). About 50% of colonized pregnant women transmit GBS to their infants, of whom 1–2% develop invasive disease [1,2]. Two neonatal syndromes have been recognized, (a) early-onset disease (<7 days of life, mainly in the first 24 h), which most commonly presents as sepsis, pneumonia and less frequently as meningitis, and (b) late-onset disease (≥ 7 and ≤ 90 days of life), which usually presents with bacteremia, otitis media, arthritis, endocarditis and osteomyelitis [3,4]. Due to advances in neonatal care, mortality associated with early-onset disease declined substantially from 50% in the 1970s to 4–6% in the 1990s [1,5]. Nevertheless, mortality rates are still high in preterm infants and can reach 30% among those at ≤ 33 weeks of gestation. Moreover, long-term neurologic sequelae have been described among survivors, being more frequently associated with late-onset disease [1,3,5]. Two main strategies are currently recommended for the prevention of neonatal disease: (a) universal maternal GBS screening at 35–37 weeks of gestation; and (b) risk-based prevention (for those at increased risk of neonatal disease) [1,6–9] . Some countries have adopted a policy with these two strategies combined [1,6,10]. With implementation of intrapartum antibiotic prophylaxis (IAP) in all colonized women and in pregnant women who are at risk of GBS colonization, there has been a dramatic reduction in the prevalence of early neonatal disease over the last decade [1,2]. However, neonatal morbidity and mortality associated with GBS infection is still a concern even in developed countries [1,2].

Despite its limitations, culture is still considered the gold standard for GBS diagnosis [1]. According to the Centers for Disease Control and Prevention (CDC), and other GBS

Address for correspondence: Maria Isabel Gouvea, Infectious Diseases Department – Hospital Federal dos Servidores do Estado, Rua Sacadura Cabral, 178, 4° andar – anexo IV – Pesquisa Clínica, Saúde – Rio de Janeiro RJ, CEP: 20221-903, Brazil. Tel: 55-21-2518-1594. Fax: 55-21-2263-7135. E-mail: bebelsgouvea@uol.com.br

prevention guidelines [1,11], the universal screening approach should be performed at 35–37 weeks of gestation, with specimens obtained from vaginal and rectal sites and using broth enrichment [1,11]. Its limitations were previously described as follows: (a) time-consuming; (b) a low negative predictive value; and (c) accuracy varying depending on the timing or site of specimen collection, as well as the experience of laboratory professionals [1,5,12]. Even in the best scenario, sensitivity was estimated at 54.3% to 83.3% [13,14]. Additionally, a subset of pregnant women will not have the benefit of testing with cultures, namely women presenting at delivery [1], presenting late for prenatal care (e.g. after 37 weeks of gestation), or delivering preterm [15]. Culture cannot be performed for these groups due to the time required for results to become available and, consequently, the window for IAP will be lost.

Many rapid molecular-based tests have been developed as an alternative to culture to detect GBS colonization [16–18]. Among these, reverse transcriptase polymerase chain reaction (RT-PCR) has been used and has shown good accuracy compared to antepartum and intrapartum cultures in the general population of pregnant women [1,16,17,19]. In the last decade, the GeneXpert GBS system (Xpert) [20], a fully automated RT-PCR assay, has been developed and used for rapid diagnosis. This system integrates the steps of DNA extraction, amplification and detection. It targets a 3′ DNA region adjacent to the *cfb* gene and can be used in different settings, such as antepartum and intrapartum screening [20–22].

The Xpert performance has been previously reported as having high accuracy in the general population of pregnant women [22–24]. However, there is no specific recommendation regarding rapid test screening for GBS in HIV-infected pregnant women. The culture performance for GBS screening in HIV-infected pregnant women may be impaired by the chronic use of antibiotics for opportunistic infections prophylaxis in this population. Currently, there are no specific data regarding the performance of culture or GBS molecular rapid tests performances in a population of HIV-infected pregnant women. In order to generate data regarding GBS screening of HIV-infected pregnant women, the aim of this study was to evaluate the accuracy of the Xpert assay for antepartum diagnosis of GBS colonization in a cohort of HIV-infected pregnant women.

Methods

Study design and ethical statement

This analysis was embedded within a prospective cohort study conducted at a referral center for the prevention of mother-to-child transmission (PMTCT) of HIV in Rio de Janeiro. The study was reviewed and approved by the local institutional review board (study number 000.464). All the study subjects provided written informed consent. A cohort of HIV-infected pregnant women was established in 1996 at Hospital Federal dos Servidores do Estado (HFSE), Rio de Janeiro, Brazil and data from this cohort have been described in detail previously [25]. HFSE is a public tertiary hospital, funded by the Ministry of Health.

Participants

The study population for this analysis comprised women sequentially enrolled in the prospective cohort study at HFSE from June 2012 to February 2015. Eligibility criteria for this analysis were as follows: (a) confirmed of HIV infection (according to Brazilian and US guidelines); (b) willingness and ability to sign inform consent (older than 18 years or ≤ 18 years with consent signed by a legal guardian/parent); (c) agreement to have ano-vaginal swabs collected; (d) gestational age of 35–37 weeks; and (e) intention to deliver at HFSE. Exclusion criteria were as follows: (a) use of topical (vaginal) antibiotics in the week prior to swab collection; (b) use of oral (systemic) antibiotics in the month prior to swab collection; (c) subsequent pregnancies during the study period (only the first pregnancy was included); and (d) inability to have culture or Xpert result.

Data and specimen collection

Sociodemographic characteristics, laboratory data, maternal and neonatal outcomes were obtained from medical records or extracted from the cohort database. Two combined vaginal/rectal specimens were collected from pregnant women at 35–37 weeks' gestation, one with a Rayon swab, for GBS culture (inserted in Stuart transport medium) and the other with a Cepheid collection device for the Xpert assay [20] (Cepheid, Sunnyvale, CA). First, excessive secretions from the vagina were wiped away prior to sampling secretions and no sterile gel was used during vaginal exam. Then, the lower one-third of the vagina was sampled with both swabs, with each swab being inserted through the anal sphincter for rectal sampling [1]. The two swabs were brushed together for a better sample distribution. Only the GBS culture results were used for clinical decision-making regarding IAP.

Reference standard

Cultures were performed at the institution laboratory. Swabs were inoculated into Todd-Hewitt broth containing nalidixic acid (15 μg/l) and gentamicin (8 μg/l) and incubated at 37 °C in 5% CO_2 for 24 h. Subcultures were performed on 5% sheep blood agar for the isolation of GBS. After overnight incubation, broth cultures showing no visible turbidity were reincubated and subcultured in sheep blood agar after 48 h. Traditional physiological, biochemical methods and the Vitek 2 system (bioMérieux, Hazelwood, MO) were used for GBS identification. Laboratory personnel performing cultures were blinded to the Xpert results.

Index test

Xpert tests were processed in a quality-certified external laboratory (Laboratório Richet). This platform automates and integrates sample lysis, nucleic acid purification and amplification and detection of the target sequence (3′ DNA region adjacent to the *cfb* gene of GBS) in complex samples using real-time PCR (Cepheid, Sunnyvale, CA). In case of invalid or erroneous results, the assays can be retested until either a positive or negative result are obtained [20]. All Xpert tests were stored and conducted within 96 h of swab collection. For this study, Xpert results were defined as follows: POSITIVE,

NEGATIVE, INVALID, ERROR and NO RESULT, according to manufacturer. The Xpert result was blinded to all health professionals providing care to research participants, including those conducting GBS culture.

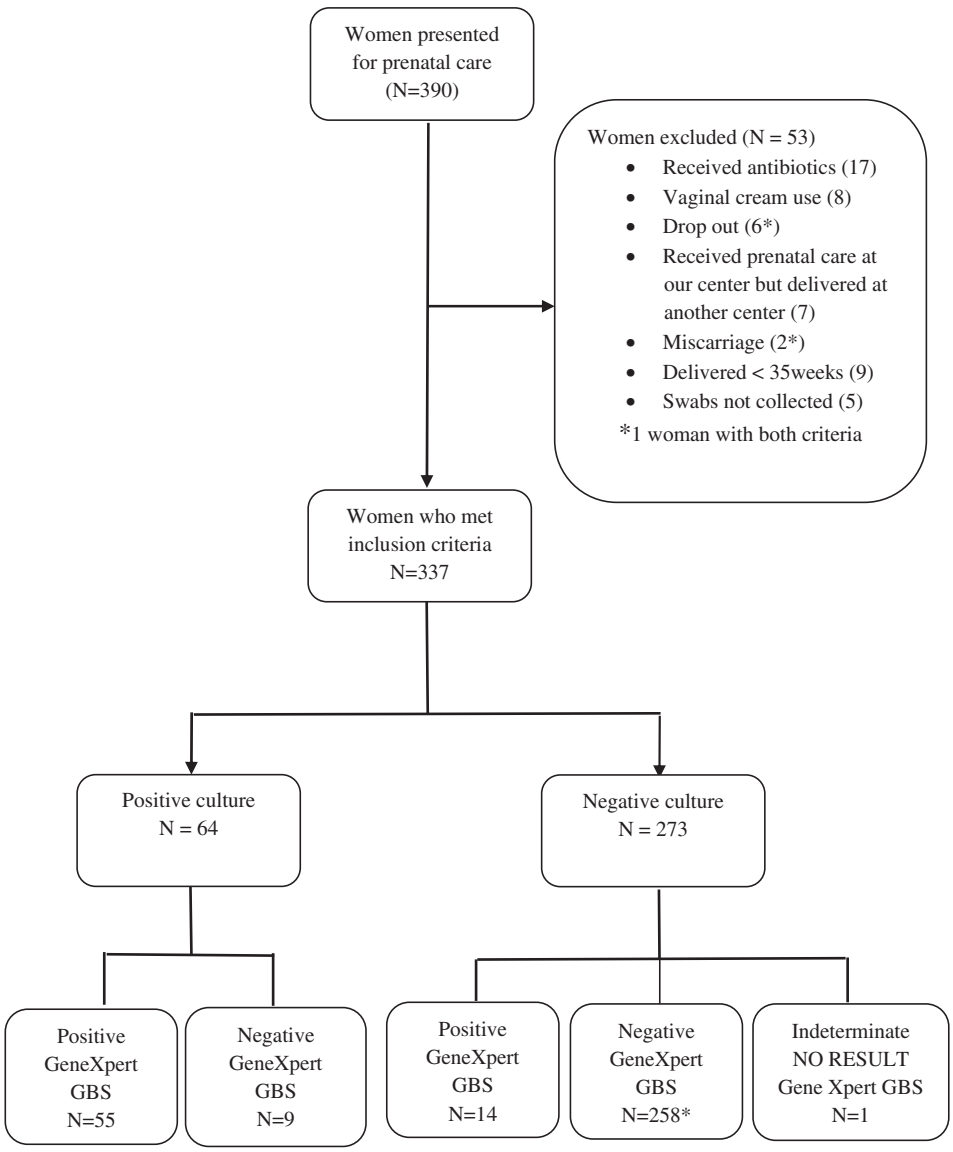
Analysis plan

Data are presented as median and interquartile range (IQR) for continuous measures and frequency and proportion for categorical variables. For continuous variables, the Mann–Whitney test was used to compare subgroups where appropriate. Chi-square or Fisher's exact tests were used to compare proportions. A p value of <0.05 was considered significant.

The sensitivity, specificity, positive and negative predictive values, and likelihood ratios, with their respective binomial 95% confidence intervals, were calculated. Accuracy was defined as the proportion of sample correctly classified by the test. The Youden J Index was defined as sensitivity plus specificity minus one. The area under the ROC curve is defined as the sum of sensitivity and specificity divided by two. All statistical analyses were performed using SPSS 17.0 for Windows (SPSS Inc., Chicago, IL) and R version 3.0.2 (R Foundation for Statistical Computing, 2013, Vienna, Austria) statistical software.

Results

A total of 390 HIV-infected pregnant women presented for prenatal care during the study period. Of those, 337 met inclusion criteria (Figure 1) and one was later excluded due to failure to obtain a result of the Xpert test (NO RESULT). (This participant was GBS culture negative (such that exclusion of this patient did not affect the sensitivity results). Among 336 HIV-infected pregnant women, 64 (19.05%) had positive GBS culture results, while 69 (20.54%) subjects had positive Xpert results. Nine women had a positive culture but a negative rapid test. Of the 272 culture-negative samples,



*One specimen initially with invalid result; after test was repeated, yielded a valid result (NEGATIVE) PCR (polymerase chain reaction)

Figure 1. Flow diagram: results of group B *Streptococcus* culture and real-time polymerase chain reaction (GeneXpert GBS) screening in HIV-infected pregnant women.

14 were positive with Xpert and 258 were negative with both methods. In initial testing, Xpert did not yield a result in two of the specimens. In one, the result was INVALID, but the assay was repeated and a negative result was obtained. In the other, even after retesting NO RESULT was obtained and this subject's data were excluded from the analyses.

The median age of women at enrollment was 27 years, and 76% were nonwhite (self-declared ethnicity). The median gestational age at entry was 17 weeks. There were no significant differences between the two subgroups (colonized versus noncolonized) in terms of the sociodemographic characteristics, laboratory data, and obstetric and neonatal outcomes (Table 1).

Xpert had a sensitivity of 85.94% (55/64), a specificity of 94.85% (258/272), a positive predictive value of 79.71% (55/69) and a negative predictive value of 96.63% (258/267). The positive likelihood ratio was 16.70 and the negative likelihood ratio was 0.15 (Table 2).

We also performed subanalyses to evaluate the performance of the Xpert assay in different categories of selected variables (data not shown). The sensitivity and specificity were calculated for age at first visit, CD4 (cell/mm^3) at entry and at delivery and viral load at entry and at delivery. The lowest sensitivity observed for each of these variables was 80.00%, 80.00%, 84.40%, 85.70% and 81.20%, respectively. All of these variables showed specificity greater than 92%. Therefore, there was no evidence that any of the sample characteristics significantly changed the Xpert performance.

Discussion

The main findings of this study are as follows: (1) Xpert provided acceptable accuracy for the diagnosis of GBS colonization in HIV-infected pregnant women; and (2) Xpert offers the opportunity to rapidly rule out GBS in circumstances where culture may not be feasible. In addition, there is no evidence to support that Xpert performance changes in different subgroups.

The accuracy results presented here are similar to previous reports from other authors describing Xpert use for antenatal diagnostics in the general population of pregnant women [21] and its accuracy is similar to the culture accuracy from swabs collected in similar pregnancy periods [19]. Park et al.

Table 2. Performance of GeneXpert GBS test for the detection of group B *Streptococcus* in the ano-genital region of HIV-infected pregnant women, compared with culture as reference ($N = 336$).

Parameters	Estimate	95% Confidence interval
Sensitivity (%)	85.94	75.38–92.42
Specificity (%)	94.85	91.55–96.91
Accuracy (%)	93.15	89.94–95.40
Positive-predictive value (%)	79.71	68.78–87.51
Negative-predictive value (%)	96.63	93.72–98.22
Positive-likelihood ratio	16.70	9.94–28.05
Negative-likelihood ratio	0.15	0.08–0.27
Youden index	0.81	0.72–0.89
Area under ROC curve	0.904	NA

Table 1. Characteristics of HIV-infected pregnant women and their infants, by GBS colonization status ($N = 336$)*.

Variables	Positive GBS culture *N* (%)	Negative GBS culture *N* (%)	Statistical test	*p* Value
Demographics				
Ethnicity ($n = 336$) (number, %)			Pearson Chi-square	0.195
Nonwhite	45 (70.3)	212 (77.9)		
White	19 (29.7)	60 (22.1)		
Age at entry (y) ($n = 336$) (median, IQR)	26 (23–30)	27 (23–33)	Mann–Whitney	0.088
Pregnancy-related characteristics				
Parity ($n = 336$) (number, %)			Pearson Chi-square	0.147
0	18 (28.1)	54 (19.9)		
≥1	46 (71.9)	218 (80.1)		
Type of delivery ($n = 336$) (number, %)			Pearson Chi-square	0.589
Vaginal	22 (34.4)	84 (30.9)		
Cesarean section	42 (65.6)	188 (69.1)		
Gestational age at entry ($n = 336$) (median, IQR)	19 (11.3–25.8)	17 (11.0–25.0)	Mann–Whitney	0.330
Neonatal outcomes				
Birth weight ($n = 335$) (number, %)			Pearson Chi-square	0.887
<2500 g	6 (9.4)	27 (10.0)		
≥2500 g	58 (90.6)	244 (90.0)		
Gestational age ($n = 333$) (number, %)			Fisher's exact test	0.751
<37 completed weeks of gestation	4 (6.2)	13(4.8)		
≥37 completed weeks of gestation	60 (93.8)	256 (95.2)		
HIV-related characteristics				
Viral load at entry (copies/mL) ($n = 336$) (number, %)			Pearson Chi-square	0.260
<50	16 (25.0)	51 (18.8)		
≥50	48 (75.0)	221 (81.2)		
Viral load at delivery (copies/mL) ($n = 333$) (number, %)			Pearson Chi-square	0.189
<50	35 (54.7)	171 (63.6)		
≥50	29 (45.3)	98 (36.4)		
CD4 (cells/mm^3) at entry ($n = 336$) (median, IQR)	461 (292–704)	421 (247–623)	Mann–Whitney	0.191
CD4 (cells/mm^3) at delivery ($n = 330$) (median, IQR)	578 (426–805)	543 (359–760)	Mann–Whitney	0.348

*From a total 337 patients who met inclusion criteria, 1 was excluded from this analysis due to failure in obtain a result of Xpert GBS test (NO RESULT).

evaluated the performance of this assay in 175 pregnant women between 35 and 39 weeks of gestation and showed a sensitivity and specificity of 86.7% and 95.6%, respectively. Others studies, also conducted among the general population of pregnant women, have reported higher sensitivities for RT-PCR than cultures, mainly when the test was performed for intrapartum diagnosis and when enrichment samples were used [13,15,23].

We found some discordant results (23/336) between culture and Xpert, which have also been described by other authors in general population [15,21]. A very low bacterial count and nonviable GBS may explain those cases with a negative culture result but a positive Xpert result (14/23). In these circumstances, only a PCR assay could detect GBS due to amplification with RT-PCR [21]. If this is universally true, then only Xpert will detect GBS in approximately 4% of all screened subjects, and the sensitivity of Xpert increases to 88.46% [79.50–93.81%].

Despite advances in the development of this platform, few studies have demonstrated good cost-effectiveness in intrapartum diagnostic use [21,22]. Xpert is still an expensive technology compared to GBS culture [1]. Another disadvantage is that the test does not provide antimicrobial susceptibility testing. GBS remains sensitive to penicillin, and non-beta lactam antibiotics should be used only in cases of seriously allergic patients. There is a global concern about the antibiotic susceptibility profile in these allergic women because resistance to clindamycin and erythromycin, the possible therapeutic alternatives, is rising worldwide [26]. Nevertheless, in this cohort, there were no penicillin-allergic women and all the isolates were penicillin-susceptible (as reported in a previous study with the same subpopulation at this center) [2].

Trained health professional can easily handle Xpert, as well as other rapid and point of care tests, and, as it is fully automated, results become available in less than 60 minutes. When compared with other molecular tests requiring manual handling, the automated system decreases the chance of contamination during specimen processing and shortens the length of time to the result [15]. Further, it has the advantage of allowing testing in high-risk groups, including women presenting at delivery or late for prenatal care (e.g. after 37 weeks of gestation) and women at risk of preterm delivery [19,24].

Many molecular technologies have been developed in the last decade, and the use of this automated diagnostic test has contributed to the prompt identification of GBS colonization, and consequently to the prevention of neonatal early onset disease, but there is still no consensus about the ideal scenario for replacement of culture by Xpert. In Brazil, the Ministry of Health and the Brazilian Federation of Gynecology and Obstetrics Associations (FEBRASGO) recommend universal screening after 34 weeks gestation for both HIV-infected and HIV-uninfected women [27,28], but the implementation of prevention policies varies greatly across several Brazilian states [29]. In our institution, we have successfully performed routine antenatal GBS screening by culture at 35–37 weeks gestation since 2008, and, in a different population of pregnant women, GBS prevalence was previously estimated as 31% [2].

Considering that Xpert screening is about three times more expensive than GBS culture screening for the patient, a possible cost-effective approach would be to use the Xpert assay combined with culture. A reasonable strategy would be to replace culture in some specific situations, such as threatened preterm delivery, in pregnant women with no prenatal care or presenting late (>37 weeks gestation) for care. The use of Xpert for GBS diagnosis is potentially beneficial for patients who are in continuously using prophylactic antibiotics for opportunistic infections, where culture is not feasible.

Our study had some limitations: (a) women who used antibiotics were not eligible and thus the performance of Xpert was not evaluated in this group of patients; (b) some HIV-infected women have indications for an urgent cesarean section, so we could not perform Xpert in the intrapartum setting where the best performance of the Xpert is expected [1,22,30]. Perhaps this explains the lower sensitivity profile in our study population; and (c) we evaluated Xpert on nonenriched samples and this also probably have affected our results.

In conclusion, this study confirmed that Xpert is a reasonable test for prenatal diagnosis of maternal colonization with GBS in HIV-infected pregnant women in our setting and represents a suitable option in circumstances where faster results are needed and culture is not feasible. However, the results of this study cannot support the routine use of rapid tests for prenatal diagnosis of GBS colonization when culture is available. Further studies regarding the use of this tool for intrapartum GBS screening and for the screening of patients with previous use of antibiotics, as well as cost-effectiveness analyses, should improve our understanding of the applicability of this assay in this setting.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the manuscript.

References

1. Verani JR, McGee L, Schrag SJ. Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention (CDC). Prevention of perinatal group B *Streptococcal* disease–revised guidelines from CDC, 2010. MMWR. Recommendations and reports: Morbidity and mortality weekly report. Recommendations and reports/Centers for Disease Control. 2010;59(RR-10):1–36.
2. Joao EC, Gouvêa MI, Menezes JA, et al. Group B *Streptococcus* in a cohort of HIV-infected pregnant women: prevalence of colonization, identification and antimicrobial susceptibility profile. Scand J Infect Dis 2011;43:742–6.
3. Gibbs RS, Schrag S, Schuchat A. Perinatal infections due to group B *Streptococci*. Obstet Gynecol 2004;104:1062–76.
4. Clifford V, Garland SM, Grimwood K. Prevention of neonatal group B *Streptococcus* disease in the 21st century. J Paediatr Child Health 2012;48:808–15.
5. Picard FJ, Bergeron MG. Laboratory detection of group B *Streptococcus* for prevention of perinatal disease. Eur J Clin Microbiol Infect Dis 2004;23:665–71.
6. Royal Australian and New Zealand College of Obstetricians and Gynaecologists - College Statements & Guidelines. Available from: https://www.ranzcog.edu.au/college-statements-guidelines.html [last accessed 2 Feb 2016].
7. Group B *Streptococcal* Disease, Early-onset (Green-top Guideline No. 36). Available from: https://www.rcog.org.uk/en/

guidelines-research-services/guidelines/gtg36/ [last accessed 2 Feb 2016].
8. Joao E, Gouvea MI, Freimanis-Hance L, et al. Institutional prevention policies and rates of group B *Streptococcus* infection among HIV-infected pregnant women and their infants in Latin America. Int J Gynaecol Obstet 2013;120:144–7.
9. Guía de Prevención y Tratamiento de las Infecciones Congénitas y Perinatales | Educación Permanente en Pediatría. Available from: http://www.ms.gba.gov.ar/sitios/pediatria/guia-de-prevencion-y-tratamiento-de-las-infecciones-congenitas-y-perinatales/ [last accessed 2 Feb 2016].
10. Homer CSE, Scarf V, Catling C, Davis D. Culture-based versus risk-based screening for the prevention of group B *Streptococcal* disease in newborns: a review of national guidelines. Women Birth 2014;27:46–51.
11. Money D, Allen VM, Society of Obstetrician and Gynaecologists of Canada. The prevention of early-onset neonatal group B *Streptococcal* disease. J Obstet Gynaecol Can 2013;35:939–51.
12. El Aila NA, Tency I, Claeys G, et al. Comparison of different sampling techniques and of different culture methods for detection of group B *Streptococcus* carriage in pregnant women. BMC Infect Dis 2010;10:285.
13. Davies HD, Miller MA, Faro S, et al. Multicenter study of a rapid molecular-based assay for the diagnosis of group B *Streptococcus* colonization in pregnant women. Clin Infect Dis 2004;39:1129–35.
14. Money D, Dobson S, Cole L, et al. An evaluation of a rapid real time polymerase chain reaction assay for detection of group B *Streptococcus* as part of a neonatal group B *Streptococcus* prevention strategy. J Obstet Gynaecol Can 2008;30:770–5.
15. 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 2015;53:443–8.
16. Feuerschuette OM, Serratine AC, Bazzo ML, et al. Performance of RT-PCR in the detection of *Streptococcus* agalactiae in the anogenital tract of pregnant women. Arch Gynecol Obstet 2012; 286:1437–42.
17. Honest H, Sharma S, Khan KS. Rapid tests for group B *Streptococcus* colonization in laboring women: a systematic review. Pediatrics 2006;117:1055–66.
18. Emonet S, Schrenzel J, Martinez de Tejada B. Molecular-based screening for perinatal group B *Streptococcal* infection: implications for prevention and therapy. Mol Diagn Ther 2013;17:355–61.
19. de Tejada BM, Pfister RE, Renzi G, et al. Intrapartum group B *Streptococcus* detection by rapid polymerase chain reaction assay for the prevention of neonatal sepsis. Clin Microbiol Infect 2011; 17:1786–91.
20. Cepheid Xpert GBS. Available from: http://www.cepheid.com/us/cepheid-solutions/clinical-ivd-tests/sexual-health/xpert-gbs [last accessed 2 Feb 2016].
21. Park JS, Cho DH, Yang JH, et al. Usefulness of a rapid real-time PCR assay in prenatal screening for group B *Streptococcus* colonization. Ann Lab Med 2013;33:39–44.
22. El Helali N, Nguyen J-C, 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.
23. Young BC, Dodge LE, Gupta M, et al. Evaluation of a rapid, real-time intrapartum group B *Streptococcus* assay. Am J Obstet Gynecol 2011;205:372.
24. Abdelazim IA. Intrapartum polymerase chain reaction for detection of group B *Streptococcus* colonisation. Aust N Z J Obstet Gynaecol 2013;53:236–42.
25. Calvet GA, João EC, Nielsen-Saines K, et al. Trends in a cohort of HIV-infected pregnant women in Rio de Janeiro, 1996–2004. Rev Bras Epidemiol 2007;10:323–37.
26. Panda B, Iruretagoyena I, Stiller R, Panda A. Antibiotic resistance and penicillin tolerance in ano-vaginal group B *Streptococci*. J Matern Fetal Neonatal Med 2009;22:111–14.
27. Recomendações para profilaxia da transmissão vertical do HIV e terapia antirretroviral em gestantes – 2010. Departamento de DST, Aids e Hepatites Virais. Available from: http://www.aids.gov.br/publicacao/consenso-recomendacoes-para-profilaxia-da-transmissao-vertical-do-hiv-e-terapia-antirretr [last accessed 2 Feb 2016].
28. Febrasgo. Available from: http://www.febrasgo.org.br/site/ [last accessed 2 Feb 2016].
29. Função JM, Narchi NZ. [A study of group B *Streptococcus* in pregnant women of eastern São Paulo]. Rev Esc Enferm USP 2013; 47:22–9.
30. Gavino M, Wang E. A comparison of a new rapid real-time polymerase chain reaction system to traditional culture in determining group B *Streptococcus* colonization. Am J Obstet Gynecol 2007;197:388.