

Original Article

***Streptococcus agalactiae* colonization and screening approach in high-risk pregnant women in southern Brazil**

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Abstract

Introduction: Considering that Group B *Streptococcus* (GBS) persists as an important cause of neonatal morbidity and mortality, the objective of this study was to evaluate the frequency of maternal colonization by GBS, comparing the culture by the Granada broth with the GeneXpert real-time PCR diagnostic methods and the impact of chemoprophylaxis in high-risk pregnant women.

Methodology: A prospective cohort of 110 pregnant women hospitalized for gestational complications was formed and recruited following interview and collection of rectovaginal swabs.

Results: The frequency of maternal colonization was 28.2% and statistically associated with Capurro > 37 weeks ($p = 0.030$) and neonatal infection ($p = 0.008$). Chemoprophylaxis was offered to 80% of those colonized. Among the pregnant women treated, a fivefold reduction in the rate of prematurity and rate of neonatal infection was observed. The sensitivity was 76.6% and 86.6% in culture and PCR, respectively, with an optimal index of agreement between the methods ($K = 0.877$). Grenade culture was considered an easy and low-cost method, while GeneXpert presented higher cost and error rate of 10%. However, 23.3% of the pregnant women were diagnosed exclusively by GeneXpert and the results were obtained in two hours.

Conclusions: This study showed a significant prevalence of maternal colonization for GBS and that both culture and molecular methods had peculiarities that allow different applicability, with the culture being feasible for antenatal screening and in the hospital for high-risk pregnant women with no sign of imminent delivery and GeneXpert being prioritized for situations of preterm birth.

Key words: *Streptococcus agalactiae*; prevalence; premature labor; high-risk pregnancy; Granada medium; GeneXpert.

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Introduction

Streptococcus agalactiae, also known as group B streptococcus (GBS), is related to invasive infections in neonates, such as sepsis, meningitis and pneumonia, and is the main cause of neonatal sepsis in developed countries [1]. Although GBS infections are not restricted to neonates, 60 to 70% of all streptococcal diseases affect this population, especially premature infants [2].

Despite having the gastrointestinal tract as a reservoir, GBS is able to adhere to the urogenital epithelium of the pregnant woman and can ascend to the uterine cavity and amniotic membranes [3]. At the time of delivery, maternal vaginal colonization with GBS is the most important risk factor for neonatal sepsis, increasing the risk approximately 200 times [4]. In addition, there is consistent evidence that maternal colonization due to GBS increases the incidence of

preterm delivery, which is an independent risk factor for early sepsis, having a case-fatality rate eight times greater than term newborns [5,6].

Worldwide, the prevalence of maternal colonization with GBS is estimated between 10% and 35%, with important variations according to region, ethnicity and socioeconomic status [7]. Although the epidemiology of GBS is well-documented in developed countries, its impact within the developing world is still unclear. Some studies suggest that rates of streptococcal disease are underestimated in these countries, with GBS being the predominant pathogen in neonatal sepsis and a fatality rate three times higher than in developed countries [2,8].

Since 2002, the *Centers for Disease Control* (CDC) has recommended screening between the 35th and 37th weeks of gestation using rectovaginal cultures with enriched selective medium as well as intrapartum

chemoprophylaxis for pregnant women colonized by GBS [9]. Recognizing the impact of streptococcal infection in preterm infants, in its latest update, the CDC recommended the expansion of laboratory methods with emphasis on chromogenic methods such as liquid cultures in Granada broth and rapid identification tests, such as real-time polymerase chain reaction (PCR) [10]. Commercial kits, such as GeneXpert, perform molecular detection of GBS in a few hours, being an excellent alternative for intrapartum use for women who have premature rupture of membranes (PROM) and preterm labor.

In Brazil, there is no national recommendation for GBS screening and chemoprophylaxis, despite the high prevalence of maternal colonization and increasing rates of prematurity and high-risk gestation in the country [11-13]. Prematurity is a public health problem in Brazil, since Brazil is among the ten countries with the highest rates of preterm birth in the world, with approximately 279 thousand cases per year [14]. In addition, it is known that 10 to 20% of pregnancies are high-risk, which are those with a higher chance of unfavorable outcomes due to some disease or injury closely related to prematurity [15-17].

Considering the reality of prematurity in Brazil coupled with the scarcity of national studies on GBS colonization in pregnant women at increased risk for preterm birth, a prospective study was conducted to evaluate the prevalence of maternal colonization with GBS using culture and real-time PCR as methods for diagnosis in high-risk pregnant women admitted to a referral hospital in the south of the country.

Methodology

Study design

This is a prospective cohort study which included all pregnant women hospitalized for obstetrical and/or clinical complications in the maternity hospital of Dr. Miguel Riet Correa Jr. University Hospital, a reference for high-risk gestation in the city of Rio Grande, southern Brazil, in the period from March to July 2016. Obstetric complications were those strictly related to the gestational process, such as premature labor, while clinical complications were events involving other organs and systems independent of pregnancy, such as hypertension and diabetes. Exclusions were due to abortion. Pregnant women with no clinical complications hospitalized for term delivery (> 37 weeks) were considered low gestational risk.

A total of 110 pregnant women that signed the consent form were interviewed through an epidemiological questionnaire, had a sample of

rectovaginal swab collected at the time of admission and were followed-up until the end of delivery of the neonate. The sociodemographic variables considered were age, color, marital status, schooling and per capita income. The obstetric variables analyzed were gestational age and diagnosis at hospitalization, parity, history of preterm birth, number of prenatal consultations, PROM presence, delivery route and puerperal infection. The neonatal variables observed were gestational age at birth calculated using the Capurro method, birth weight, severe early infections (sepsis, meningitis and pneumonia) and neonatal death. The neonatal outcome was evaluated through the chart, with premature neonates being considered with Capurro less than 37 weeks at birth and low-weight neonates being those weighing <2,500 g regardless of gestational age [18]. For the definition of neonatal infection, we used the criteria the presence of clinical signs and suggestive laboratory tests and need for transfer to the intensive care unit recorded in medical records.

Microbiological tests

For each pregnant woman, two swabs were collected for the GBS survey with the same proceeding. Each swab was inserted into vaginal introitus without a speculum to collect from the distal vaginal and afterwards, from the anal orifice. The two swabs were put in the same Stuart transport medium, taken to the laboratory and then processed by the two methods (culture and molecular).

Culture method: a swab was seeded in liquid culture in the Granada (Biomerieux, Marcy-l'Étoile, France) and incubated for 24-48 hours at 37°C. In reading the results, a positive culture was considered when there was presence of orange pigment of any hue, while the absence of pigment characterized the culture as negative.

Molecular diagnosis: the second swab was transferred to designated chamber of the Xpert® GBS cartridge and it was loaded in the Cepheid's GeneXpert System and performed according to the manufacture's protocol. This test utilizes real-time PCR, integrating the extraction, amplification and identification stages of the *cfb* gene in an automated manner, with processing time between 32 and 52 minutes until the final result [19].

For ethical reasons, positive cases were reported to the medical team for the institution of chemoprophylaxis for early neonatal infection, with ampicillin being the drug of choice and administration of 2 g (attack dose) at the time of diagnosis followed by 1 g every 6 h until or during 48 hours in cases where

there was no evolution of labor. Chemoprophylaxis administered for a minimum of 4 hours was considered appropriate.

For the analysis of the diagnostic methods, only pregnant women with a valid result for both methods were considered. The performance of the methods was evaluated in relation to the total number of cases

detected by calculations of sensitivity, specificity and Kappa index. The sum of methods was considered the gold standard. The statistical analysis was obtained through the SPSS 18.0 program, with descriptive and bivariate analysis of the variables, using the chi-square test with a significance level of 95%, being considered significant $p \leq 0.05$.

Table 1. Obstetric and neonatal variables according to the detection of GBS.

Obstetric and neonatal profile	Comparison between groups with and without diagnosis of GBS		Total	Bivariate analysis
	Pregnant women with GBS	Pregnant women without GBS		
Variables (N = 110)	n (%)	n (%)	Average/frequency (%)	p value
Gestational age (110)	31	79	110	
≤ 33 week+6d	12 (38,7)	47 (59,5)	59 (53,6)	
≥34 week ≤ 36+6 week	12 (38,7)	18 (22,8)	30 (27,3)	0,126
≥ 37 week	7 (22,6)	14 (17,7)	21 (19,1)	
Hospital diagnosis (110)				
Premature Labor/PROM	12 (38,7)	32 (40,5)	44 (40,0)	
Chronical diseases	14 (45,2)	27 (34,2)	41 (37,3)	0,457
Pyelonephritis	5 (16,1)	20 (25,3)	25 (22,7)	
Parity (110)				
Primiparous	18 (58,0)	33 (41,8)	51 (46,4)	0,123
Multiparous	13 (42,0)	46 (58,2)	59 (53,6)	
Prior prematurity(59)*				
Yes	4 (30,8)	10 (21,7)	14 (23,7)	0,499
No	9 (69,2)	36 (78,3)	45 (76,3)	
Prenatal consultations (107)**				
≤ 5 consultations	10 (33,3)	40 (52,0)	50 (46,7)	0,083
≥ 6 consultations	20 (66,7)	37 (48,0)	57 (53,3)	
PRM (105)***				
Yes	7 (23,3)	15 (20,0)	22 (20,9)	0,704
No	23 (76,7)	60 (80,0)	83 (79,1)	
Delivery route (105)***				
Vaginal	17 (56,7)	38 (50,7)	55 (52,3)	0,578
Caesarean	13 (43,3)	37 (49,3)	50 (47,7)	
Puerperal infection (109)#				
Yes	1 (3,3)	2 (2,5)	3 (2,7)	0,840
No	29 (96,7)	77 (97,5)	106 (97,3)	
Capurro (105)***				
≤ 36 week + 6d	5 (16,7)	29 (38,7)	34 (32,4)	0,029
≥ 37 week	25 (83,3)	46 (61,3)	71 (67,6)	
Weight birth (105)***				
≤ 2.500g	11 (36,7)	28 (37,3)	39 (37,1)	0,949
≥ 2.501g	19 (63,3)	47 (62,7)	66 (62,9)	
Neonatal infection (105)***				
Yes	6 (20,0)	3 (4,0)	9 (8,5)	0,008
No	24 (80,0)	72 (96,0)	96 (91,5)	
Neonatal death (105)***				
Yes	0 (0,0)	2 (2,7)	2 (1,9)	0,366
No	30 (100)	73 (97,3)	103 (98,1)	

* Excluding primigravidae for analysis of the history of prematurity; ** Excluded three pregnant women without prenatal care; *** Excluded five stillbirth cases; # Excluded one abortion case; PROM: premature rupture of membranes.

Ethics approval and consent of participants

This research followed the precepts brought by Resolution 466/2012 of the National Council of Health, which regulates research involving human subjects. The Ethics Committee for Research in Healthcare – FURG approved the study under number 42/2016. Informed consent was obtained from all individual participants included in this study.

Conflict of interests

The authors informed that the GeneXpert GBS test kits were provided by the manufacturer Cepheid Company) in donation form, without any interference in the study design, result analysis and manuscript writing process. The authors evaluated the test performance in accordance with the manufacturer's standards and have the right to publish such results, even if unfavorable to the manufacturer of the donated tests.

Results

Sociodemographic characteristics and prenatal coverage

A total of 110 pregnant women hospitalized for high-risk gestation were included. For this sample sized, the study had 80% power to detect prevalence ratios of 2.5 or more, with frequency of exposure between 20 and 50% and 95% confidence level. The mean maternal age was 26 (15-42) years, with a predominance of white pregnant women (77.3%), with companion (62.7%) and per capita income lower than a national minimum wage (78.2%). Although more frequent in adolescents, GBS colonization was homogeneously distributed between the groups, and there was no statistically significant association between the sociodemographic variables evaluated.

The prenatal coverage rate reached 97.2%, and 78 pregnant women (70.9%) had follow-up in the public health system, 29 (26.4%) in the private sector and 3 (2.7%) no follow-up. Regardless of the study, the

screening rate for GBS through culture between 35-37 weeks gestation in the public prenatal setting was nil (0/78) and 6.8% (2/29) in the private setting. The prenatal result was concordant with the intrapartum rate performed in the study in both cases.

Obstetric and neonatal variables and GBS association

The mean gestational age at admission was 32 (18-39) weeks, and the most frequent diagnosis was preterm labor and PROM, totaling 40% of the cases. The frequency of maternal colonization due to GBS by both methods was 28.2% (31/110) and was more pronounced in primigravida and carriers of chronic diseases such as hypertension and diabetes. However, there was no statistically significant association between the obstetric variables described and the GBS colonization (Table 1).

Among the three pregnant women who did not receive prenatal care, one was an adolescent drug abuser and was colonized by GBS, progressing to abortion at 20 weeks gestation. In addition, four cases of intrauterine fetal death occurred due to syphilis (2) and arterial hypertension (2). No maternal presence of GBS was found in these four cases of fetal death. These five losses were excluded for the analysis of gestational and neonatal outcome variables.

Chemoprophylaxis with ampicillin was appropriately offered to 80% of the colonized mothers (24/30), excluding the case of abortion. Due to the advanced stage of labor at admission, six colonized pregnant women had chemoprophylaxis considered inadequate (time <4 hours). Among these six women, four had a gestational age of less than 37 weeks, evolving into preterm birth. There was also another premature birth among the GBS colonized, which received adequate chemoprophylaxis and evolved to premature delivery after 10 days of PROM (Table 2).

There were 34 premature births in the study, with a mean gestational age at birth of 33.6 weeks, representing a premature birth rate of 32.3% (34/105).

Table 2. Proportion of unfavorable neonatal outcomes according to chemoprophylaxis.

Unfavorable neonatal outcomes	Chemoprophylaxis GBS +				Total (n = 30)
	Yes (n = 24)	%	No (n = 6)	%	
Prematurity birth	1	4,2	4	66,6	5
	23	95,8	2	33,3	25
Low birth weight	6	25	4	66,6	10
	18	75	2	33,3	20
Neonatal infection	4	16,7	2	33,3	6
	20	83,3	4	66,6	24
Neonatal death	0	0	0	0	0
	0	0	0	0	0

* Birth weight < 2.500g.

Among pregnant women colonized by GBS, the rate of prematurity was 16.6% (5/30) and reached 38.6% (29/75) among noncolonized women. The maternal colonization rate by GBS was 35.2% (25/71) among full-term neonates, while in the premature neonates group the maternal colonization rate was 14.7% (5/34) at the time of hospital admission showing a significant association between GBS colonization and Capurro over 37 weeks ($p = 0.030$).

There were nine cases of neonatal infection in the study and the frequency of neonatal infection reached 20% (6/30) among colonized women, while 4% (3/75) of the noncolonized group had the same outcome. Maternal colonization by GBS was twice as high among infants with infection when compared to the group without infection ($p = 0.008$). Among the six cases of neonatal infection with maternal colonization, four were born premature (66.6%) with chemoprophylaxis considered inadequate, demonstrating that the premature group was more affected by this gap in the therapeutic offer. The respiratory manifestation was the most common neonatal infection among the group with maternal colonization, accounting for 83.3% (5/6) of the cases, while syphilis infection predominated among the no colonized group, with 66.6% (2/3) of the cases. Although chemoprophylaxis was instituted, there was one case of neonatal sepsis in a preterm infant of a mother colonized within ten days of PROM. There was no bacteriological confirmation of the presence of GBS in cases of respiratory infection and neonatal sepsis, and it was not possible to affirm that it was the causative agent of the infections. There were two cases of neonatal death due to extreme prematurity, and no maternal colonization due to GBS was detected in either case.

Frequency of GBS and assessment of diagnostic methods

The overall GBS frequency detected by both methods was 28.2% (31/110). Of the 110 pregnant women included in the study, 97 presented a valid result for both tests. Thirteen (11.8%) were excluded by error (11) or invalid result (2) in the molecular analysis

through GeneXpert, with 5007 being the predominant error (8), followed by 2008 (3). According to the manufacturer's manual, errors 5007 and 2008 indicate, respectively, failure in probe control and pressure exceeded with high sample viscosity as the probable cause in both errors. Invalid results indicated failure in sample processing control with inhibition of the PCR-reaction likely resulted from the presence of blood in the sample. One of the cases discarded due to error in GeneXpert presented positive result through the culture. Among the valid results, a total of 30 GBS positive cases were detected, and 63.4% (19) were positive in both methods, 13.3% (4) only in the culture and 23.3% (7) exclusively in GeneXpert, according to Table 3.

The culture showed a GBS colonization frequency of 23.7% (23/97), whereas the PCR showed 26.8% (26/97). The culture demonstrated sensitivity and specificity of 76.6% and 100% relative to the total number of valid cases, while GeneXpert demonstrated 86.6% and 100%, respectively. The overall agreement index between the methods was 88.6%, and the Kappa index = 0.877. The average time from processing the sample to obtaining the diagnostic result was 24 hours for the culture with unit cost of US \$1.48 and 1 hour for GeneXpert with a unit cost of US \$43.17 without considering the value the equipment.

Discussion

Although the epidemiology of GBS is well documented in the developed world, it is believed that the prevalence of streptococcal disease is underestimated in developing countries due to the use of inadequate diagnostic techniques and collection. [20,21]. This study showed a high prevalence of maternal colonization (28.2%) when compared to the worldwide rate of 17.9% and to the European and North American rates between 15% and 20% (7). The prevalence in this study was also high relative to other Brazilian studies with rates between 9.8% and 22.5%, and similar to the study by Nomura (4), which showed a prevalence of 27.6% [22-24].

Table 3. Comparison between culture and PCR as diagnostic methods for GBS.

Methods		Total case		Sensitivity	Specificity	Global concordance	Kappa	Unit cost
		Pos	Neg					
Culture	Pos	23	0	76,6%	100%	88,6%	0,877	US\$1,48
Granada	Neg	7	67					
Molecular	Pos	26	0	86,6%	100%			
GeneXpert	Neg	4	67					

Pos: positive; Neg: negative.

In our study, the GBS colonization was widespread, without significant variations in any specific risk group. Appropriate prenatal care is considered one of the best prognostic indicators of obstetric and neonatal outcomes, since it allows the early detection and management of critical illnesses which typically carry a higher risk of complications [25]. In this study, despite the high prenatal coverage, it can be verified that there is no routine antenatal screening for GBS in the public and private spheres. Developed countries that show significant reduction in the incidence of neonatal streptococcal disease have in the past invested in the expansion of antenatal screening [26]. Despite strong global evidence of the benefit of antenatal screening for GBS through culture, there is no consensus or official recommendation in Brazil for the screening of GBS during pregnancy and cost-effectiveness studies are absent in the country [18].

Relative to the general prematurity rate, we observed 32.3% due to the high-risk gestation profile of patients, in line with other Brazilian referral services for high-risk pregnancies, which have reported rates between 34% and 50% [16,27]. However, in the group of patients colonized by GBS, a reduction in the prematurity rate (16.6%) can be observed, with a significant association between GBS colonization and Capurro over 37 weeks. This finding was attributed to chemoprophylaxis for GBS that was offered to 80% of those colonized at the time of diagnosis, suggesting a potential protective effect for the onset of preterm birth. Our data corroborate a study that showed 87% of pregnant women treated for GBS had full term delivery and that mothers who had premature labor were less likely to receive chemoprophylaxis. [26].

In this study, maternal colonization was strongly associated with the outcome of neonatal infection, since the frequency was five times higher in colonized mothers. Also in 1986, Boyer and Gotoff [28] observed that the administration of intrapartum antibiotics to women colonized with some risk factor present (premature labor, PROM or fever) reduced GBS vertical transmission from 51% to 9% and the early neonatal sepsis rate from 6% to 0%. A Brazilian study reported a significant association between maternal endocervical colonization and infection and neonatal death, being more frequent in women with gestational age of less than 37 weeks and GBS as the most prevalent microorganism [29].

This study pointed out that the cases of infection had a more pronounced impact on preterm infants who did not receive chemoprophylaxis. It is estimated that 25 to 40% of preterm births are the result of ascending

bacterial infections in which bacteria penetrate the cervical barrier and intrauterine space, triggering physiological events associated with preterm labor, including increased inflammatory cytokines, rupture of amniotic membranes and contractions [30]. Recently, the role of hyaluronic acid in the epithelial barrier of the uterine cervix, important in protecting against ascending infection and preterm delivery, has been implicated. Interestingly, studies demonstrate that GBS produces hyaluronidase, an enzyme capable of degrading hyaluronic acid, activating a cascade of inflammatory signaling, and there is evidence that massive colonization is the main risk factor for prematurity associated with GBS [31].

Although this study did not show a significant association between neonatal and puerperal infection at delivery route, some studies indicate this relationship. A recent cohort of 1,815 mother and baby binomials corroborated that maternal vaginal colonization by GBS is the most important risk factor for early neonatal disease, highlighting the potential for vertical transmission of GBS. In addition, it pointed to a significant association between maternal colonization and neonatal disease at vaginal delivery and the presence of episiotomy [32]. Previous studies have indicated that cesarean section was able to significantly reduce the vertical transmission rate of GBS; however, due to GBS's ability to cross intact amniotic membranes, cesarean section is unable to completely prevent this transmission [33,34]. In addition, cesarean section is related to an increase in puerperal infection. It is estimated that puerperal endometritis occurs in about 5% of all vaginal deliveries, while in cesarean sections it rises to 10% in developed countries, with GBS being the most common cause of puerperal endometritis [35]. Thus, the focus of GBS infection prevention is not the definition of the mode of delivery, but the implementation of screening actions and intrapartum prophylaxis.

Molecular diagnosis through GeneXpert demonstrated superior sensitivity to culture (86.6% vs 76.6%), as well as rapid detection, simple and automated processing. However, it presented an error rate and invalid results of greater than 10%, in addition to a cost approximately thirty times higher than that of the culture. Other authors reported sensitivity greater than 90% in GeneXpert when compared to culture, provided that the initial enrichment in selective broth was used [36,37]. This study followed the recommendations of the manufacturer, whose protocol does not involve any process for the enrichment and decontamination of samples, despite the presence of

mucus and blood inherent in the birthing process. Our findings suggest that the main advantage of the test is the practicality and speed of testing the direct sample, however, its performance is influenced by factors such as viscosity, presence of blood, mucus and other materials such as lubricant, which can physically interfere with the assay by inhibiting the PCR reaction. A French study found an error rate of 10.8% when using GeneXpert, attributing this to the significant presence of vaginal mucus and its important role in the inhibition of PCR, concluding that this method, without prior enrichment, is not sensitive enough for routine use [38].

The Granada broth is a selective chromogenic method that explores the ability of the GBS to synthesize a specific orange pigment called granadaene. The method allowed direct inoculation of the smear with identification in 24 hours [39]. In addition to simple and rapid processing (up to 2 min), it demonstrated a near-PCR detection capacity when the total number of cases was evaluated, detecting 23 of the 30 cases considered positive, whereas the PCR detected 26. The agreement between the methods was considered optimal through of the Kappa index (> 0.81) suggesting that culture in Granada medium, despite the lower sensitivity, can be considered as a reliable method of screening for GBS.

An American study estimated a prevalence of intrapartum colonization in 23.6% of the women through PCR and 23.8% through culture, demonstrating that there was no significant difference between the detection capacity of the methods, despite the higher sensitivity (90.8%) of GeneXpert [40]. Joubrel *et al.* (2014) compared five other selective tests with Granada medium and reported sensitivity and specificity of 96% and 100%, respectively [41]. Although it presents good sensitivity and specificity for the detection of GBS, it is known that approximately 2% to 5% of the strains are granadaene negative, that is, not producing the typical pigment, generating false negative results [42]. In our study, the sensitivity of Granada was 76.6%, and seven pregnant women presented positive PCR with negative culture. The absence of growth in the culture can be justified by the presence of non-pigment-forming strains and by the detection of genetic material of nonviable bacteria by GeneXpert, characterizing a false positive result in PCR [43]. In contrast, three culture positive samples were negative on GeneXpert. Although other microorganisms are capable of producing light yellow pigment, many studies indicate a high specificity (100%) for detecting GBS, considering the probability of false positive results in Granada as low [31,41,44,45].

When taken into account, this study revealed a high prevalence of maternal colonization for GBS when compared to the worldwide rate, providing evidence for the importance of screening for GBS in the high-risk gestational population. In addition, the study pointed to the benefit of chemoprophylaxis for GBS for the prevention of neonatal infections, also suggesting a potential protective effect in the prevention of prematurity in high-risk pregnant women. Both the Granada broth culture and GeneXpert demonstrated advantages with an optimal agreement index between the methods, indicating that both could be adopted as diagnostic tools. Additional comprehensive national studies focused on the analysis of cost-effectiveness are essential to define the most feasible strategy for supporting the expansion of GBS control programs.

Conclusion

When taken into account, this study revealed a high prevalence of maternal colonization for GBS when compared to the worldwide rate, providing evidence for the importance of screening for GBS in the high-risk gestational population. In addition, the study pointed to the benefit of chemoprophylaxis for GBS for the prevention of neonatal infections, also suggesting a potential protective effect in the prevention of prematurity in high-risk pregnant women. Both the Granada broth culture and GeneXpert demonstrated advantages with an optimal agreement index between the methods, indicating that both could be adopted as diagnostic tools. Additional comprehensive national studies focused on the analysis of cost-effectiveness are essential to define the most feasible strategy for supporting the expansion of GBS control programs.

Authors' contributions

JZR: conceptualization, methodology, investigation, resources, writing – original draft preparation; JF: investigation; VR: investigation; CVG: conceptualization, methodology, formal analysis; PEAS: conceptualization, methodology, resources, writing review; AVG: conceptualization, methodology, resources, writing review, supervision and project administration.

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