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Research Article

Infectious Risk in Newborns of Mothers with Positive GBS 2016 - 2017

Orozco Fernandez Rodrigo*, Gonzales Gamarra Raiza G, Ruiz Serrano Cristina, García-Puente Mesa Luis M, Plaza Arranz Franciso J and Albi González M

Department of Gynecology and Obstetrics and Department of Pediatrics, Hospital Universitario Fundacion Jimenez Diaz, Madrid, Spain

***Corresponding Author:** Orozco Fernandez Rodrigo, Department of Gynecology and Obstetrics and Department of Pediatrics, Hospital Universitario Fundacion Jimenez Diaz, Madrid, Spain.

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Abstract

Introduction: Nowadays, group B *Streptococcus* (GBS) continues to be one of the main pathogens causing neonatal morbidity and mortality that affects 1 - 2% of newborns. Intravenous antibiotic prophylaxis has been shown to be effective in reducing neonatal infection by decreasing the incidence to 0,26 per 1000 live births.

Objectives: To analyze the neonatal infectious risk related to the presence of group B *Streptococcus* isolated in maternal rectovaginal culture and the relationship with intrapartum antiviral prophylaxis.

Materials and Methods: Transversal, descriptive, retrospective study. Population of study: newborns with positive maternal rectovaginal culture for GBS attended in the University Hospital Fundación Jiménez Díaz during the period between 2016 and 2017.

Results: The prevalence of GBS isolated in maternal rectovaginal culture was of 13.87% and 77.8% received complete intrapartum antibiotic prophylaxis. Of all the NBs born to mothers carrying SG, 17% required surveillance for infectious risk but only 1% developed overt sepsis.

Keywords: *Infectious Risk; Newborns; Mothers; Positive GBS*

Introduction

Nowadays, group B *Streptococcus* (GBS) continues to be one of the main pathogens causing neonatal morbidity and mortality that affects 1 - 2% of newborns, who will develop early neonatal infection in the form of septicemia, pneumonia or meningitis.

The GBS reservoir is located in the gastrointestinal and genitourinary tract, and the vagina presents an intermittent colonization over time, therefore, a vagino-rectal exudate should be performed during the last 5 weeks before delivery, since if it has been done with greater advance, the sample must be repeated. Rates of maternal vaginal colonization in Spain are between 10 - 20%.

The transmission to the newborn occurs during the beginning of labor or after the rupture of the amniotic membranes, reaching colonization rates of up to 50%, of which 1 - 2% of the newborns will develop infection, increasing the risk if there is prematurity, premature rupture of membranes of more than 18 hours, maternal fever, chorioamnionitis or a history of brother infected with GBS.

Intravenous antibiotic prophylaxis has been shown to be effective in reducing neonatal infection by decreasing the incidence to 0,26 per 1000 live births.

Objective of the Study

To analyze the neonatal results corresponding to the infectious risk related to the presence of group B *Streptococcus* isolated in maternal rectovaginal culture and the relationship with intrapartum antiviral prophylaxis.

Materials and Methods

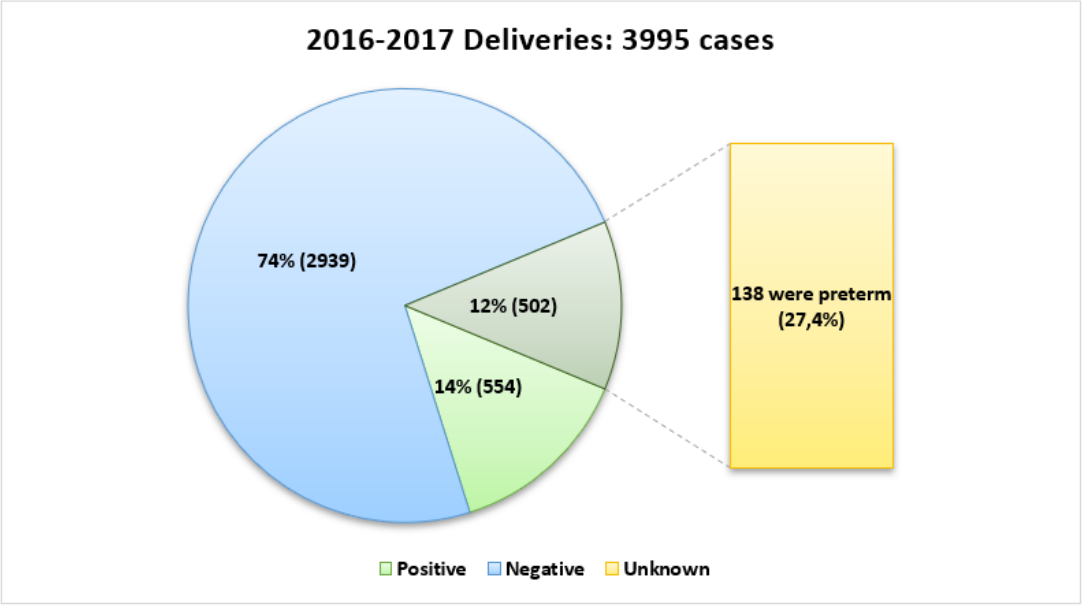
Transversal, descriptive, retrospective study. The population corresponded to the total of deliveries and newborns attended in the University Hospital Fundación Jiménez Díaz during the period between 2016 and 2017.

Those with positive culture for GBS were analyzed. A descriptive analysis was carried out using the Excel program.

Results

In our centre, data on births and newborns (NB) were collected and analyzed during the period between 2016 and 2017, obtaining a total of 3995 births (which was used as the population of study) and 4014 newborns (19 twins).

A total of 554 mothers with GBS were reported, constituting a prevalence of 13.87%. In 502 (12.6%) patients, vaginal exudate was not collected, of which 138 were preterm pregnant women (27.4%).



Graph 1: *GBS results in the population studied.*

During the period of labor, 77.8% received complete intrapartum antibiotic prophylaxis, while 22.4% received incomplete prophylaxis or did not receive it.

There were 559 NB (5 twins) children of mothers with GBS. 100 NB (17.9%) required admission in the neonatal unit due to infectious risk (risk factors associated with group B *Streptococcus*: hours of ruptured bag, maternal fever, prematurity), of which 92% were NB at term and 8%, preterm.

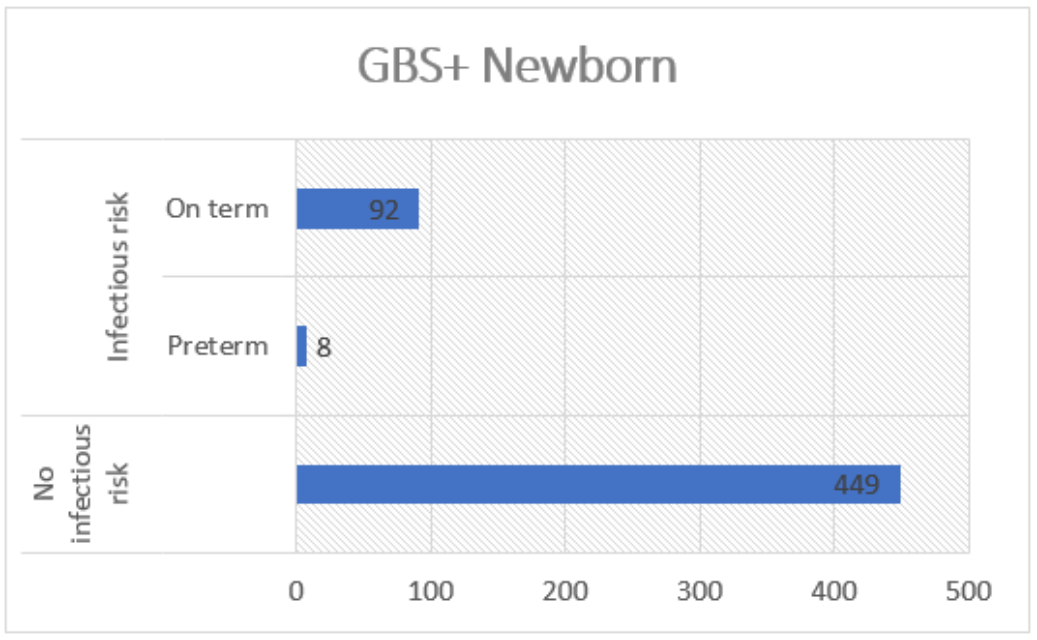
Among the infants admitted, 68% received complete prophylaxis, 20% received incomplete prophylaxis, and 11% did not needed it. 21% of the newborn required infectious screening and only 1% developed clinical sepsis that required antibiotic therapy.

	Average maternal age	GBS vaginorectal culture					
< 35 years	33.95 ± 5.4 years	Positive	263	13.3%	PreTerm NB	107	
		Negative	1449	73.1%		GBS Positive	5 (4.7%)
		Unknown	270	13.6%	At Term NB	1875	
						GBS Positive	257 (13.7%)
>35 years	38.93 ± 2.63 years	Positive	293	14.6%	PreTerm NB	130	
		Negative	1490	74.0%		GBS Positive	10 (7.7%)
		Unknown	230	11.4%	At Term NB	1883	
						GBS Positive	284 (15.1%)

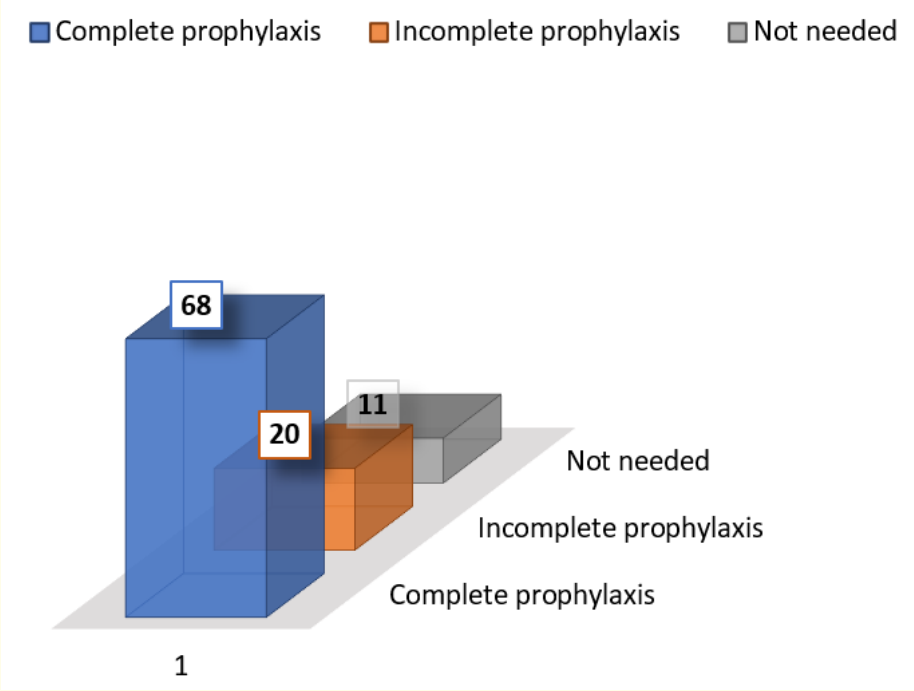
Table 1: *Distribution of GBS vaginorectal culture.*

GBS+ newborn	559		
Infectious risk	100	Preterm NB	8%
		Term NB	92%
ATB Prophylaxis		Complete	68%
		Incomplete	20%
		Not needed	11%

Table 2: *Results of newborns of mothers with GBS.*



Graph 2: *Infectious risk in newborns of mothers with GBS.*



Graph 3: *Percentage of patients with GBS who received complete antibiotic dose prior to delivery.*

Of the 100 NB admitted, 13 (13%) required antibiotic therapy. None of the cases had bacteriological confirmation (0%).

Discussion

Streptococcus agalactiae (Group B Streptococci, GBS) can cause severe neonatal sepsis. The recto-vaginal GBS screening of pregnant women and intrapartum antibiotic prophylaxis (IAP) to positive ones is one of the main preventive options. However, such a strategy has some limitations and there is a need for alternative approaches [1].

The World Health Organization estimates that every year, one million neonatal deaths occur because of neonatal infection. Furthermore, an equal number of stillbirths are thought to be caused by infections [2].

Multiple studies have been conducted to assess the possibility of screening strategies in different geographical areas, as well as their need and benefit over the population. Ji Y., *et al.* performed an optimized hospital strategy for GBS screening implemented in the Inner Mongolian area, which targeted expectant mothers (including those with preterm births) from January 2016 to December 2016 in a population-based cohort. Three common screening strategies were simulated to estimate the availability of the hospital strategy used. Altogether, 9770 eligible women were tested and the rate of GBS carriage was 2.7% (266/9770). In total, 198 of the 266 maternal GBS carriers accepted intrapartum antibiotic prophylaxis (IAP) treatment. Among the 9860 neonates of 9770 mothers, four cases of neonatal early-onset GBS (EOGBS) infection were identified and one case was missed (EOGBS incidence with screening and IAP: 0.5/1000). Risk factors for maternal GBS colonization included preterm birth (between 35 and 37 weeks) [odds ratio (OR) = 1.7 (95 % confidence interval: 1.22 - 2.33)], region of origin, resident areas, maternal age (older than 34 years) [OR = 1.5 (1.06 - 2.09)], prelabour rupture of membranes [OR = 1.8 (1.34 - 2.35)], gestational diabetes mellitus [OR = 1.6 (1.14 - 2.28)] and maternal mild anemia (Hb: 90-110 g dl^{-1}) [OR = 1.5 (1.16 - 2.06)]. This new screening strategy resulted in less antibiotic exposure and least number of cases missed [3].

Rottenstreich M., *et al.* tried to evaluate the maternal group B streptococcal (GBS) colonization rate and EOGBS disease in term deliveries, a decade apart by a retrospective computerized study between 2005 and 2016. A universal GBS culture-based approach gradually replaced the GBS risk-oriented screening. The GBS screening rate constantly increased from 20% in 2005 to 47.5% in 2016. GBS colonization rates significantly decreased, from 50.3% in 2005 to 31.7% in 2016, $P < 0.001$. Overall, EOGBS disease was diagnosed in 37 term neonates (0.25 per 1000 live births.). The rate of EOGBS in neonates decreased dramatically from 0.361 per 1000 deliveries between 2005 and 2009 to 0.19 per 1000 deliveries between 2010 and 2016 ($P < 0.05$). The authors concluded that the universal screening policy was associated with a significant decrease in neonatal EOGBS and therefore should be adopted [4].

In another retrospective cohort study, based on a validated computerized database the years 2005 - 2016 the group of Rottenstreich M., *et al.* analyzed the pregnant women that had records of up to three additional term consecutive deliveries and GBS colonization status.

A total of 8641 primiparas met inclusion criteria; 3972 (46.0%), 993 (11.5%) and 243 (2.8%) had second, third, and fourth consecutive deliveries with recorded GBS status respectively. The overall colonization rate for primiparas was 28.4%. The cumulative rates and cumulative risks of repeated GBS positive colonization at the second, third and fourth term consecutive deliveries were 62.0%, 6.93 (95% CI 5.96 - 8.06), 68.0%, 5.05 (95% CI, 3.67 - 6.93) and 66.1%, 2.96 (95% CI, 1.54 - 5.68), respectively. Notably, after a negative GBS colonization in the first, second, and third repeated deliveries, the rate and cumulative risk of GBS positive in each consecutive delivery was significantly lower: 18.2%, 0.14, (95% CI 0.12 - 0.17), 19.4%, 0.21 (95% CI 0.15 - 0.28) and 21%, 0.26 (95% CI 0.13 - 0.51) for the second, third, and fourth consecutive deliveries, respectively. As conclusion, the authors report that GBS colonization status at the time of first pregnancy is a milestone for the colonization risk in subsequent term deliveries [5].

Group B *Streptococcus* remains the most common culture-confirmed neonatal bacterial infection in the United States and is a significant source of neonatal morbidity globally. Intrapartum antibiotic prophylaxis has reduced the incidence of early-onset neonatal disease without a notable impact on the incidence of late-onset neonatal disease. Penicillin G remains the mainstay of therapy, although reduced penicillin susceptibility has been observed in select isolates. Increased frequency of resistance to non-beta-lactam antibiotics, including clindamycin, erythromycin, and fluoroquinolones, has been observed, with some isolates demonstrating resistance to vancomycin. The development and implementation of strategies to identify hosts, treat judiciously with antimicrobials with the narrowest spectra, and prevent invasive disease, with vaccines, are essential to reduce the burden of group B *Streptococcus* disease [6].

With regard to the treatment and management of patients with positive GBS, multiple studies demonstrate the effectiveness of intrapartum antibiotic treatment and discuss the different patterns and multiple resistances.

Melo SC., *et al.* studied 544 pregnant women, 136 (25%) were positive for GBS based on the combination of the three culture media in the two clinical specimens.

All of the GBS isolates were susceptible to penicillin, vancomycin, and cefotaxime. The authors found that 11 (8.1%) of the GBS isolates were resistant to erythromycin; three (2.2%) of these had a constitutive resistance to clindamycin (cMLSB, macrolide, lincosamide, and streptogramin B). The eight (5.9%) erythromycin-resistant GBS isolates, which showed to be susceptible to clindamycin or intermediately resistant were submitted to the D-zone test. These erythromycin-resistant GBS isolates showed to be positive in the D-zone test, indicating that these isolates were clindamycin-resistant (inducible MLSB phenotype). None of the isolates showed the M phenotype (resistance to erythromycin only). Six isolates (4.4%) were intermediately resistant to chloramphenicol. In the study, a high rate of GBS resistance (82.3%) to tetracycline was detected [7].

Another Spanish study performed in La Rioja through the group of Rojo-Bezares B., *et al.* investigated the antibiotic and heavy-metal resistance mechanisms, virulence genes and clonal relationships of macrolide- and/or lincosamide-resistant (M +/- LR) *Streptococcus agalactiae* (group B *Streptococcus*, GBS) isolates from pregnant women. In total 375 GBS isolates were recovered during 2011. About

three-quarters of isolates were from European nationals and the remainder distributed among 23 other nationalities. Seventy-five (20%) were classified as M +/- LR strains and 28 (37%) of these were resistant to ⩾ 3 classes of antibiotics. Capsular serotypes III (29·3%), V (21·3%) and II (12%) were the most frequent. A wide variety of antibiotic resistance genes were detected in M +/- LR strains; notably, 5·3% harboured the lsa(C) gene associated with cross-resistance, and tet (W) was identified in a single strain. A wide diversity of genetic lineages of macrolide, lincosamide and heavy-metal- resistant GBS strains was observed in an ethnically diverse maternal population [8].

The group of Martin V., *et al.* studied the vaginal microbiota of 30 non-pregnant and 24 pregnant women, including the assessment of GBS colonization to assess the capacity of eradication of the microbiological agent through *Lactobacillus* determinations. Among the *Lactobacillus* isolates, 10 *Lactobacillus salivarius* strains were selected for further characterization. *In vitro* characterization revealed that *L. salivarius* CECT 9145 was the best candidate for GBS eradication. Its efficacy to eradicate GBS from the intestinal and vaginal tracts of pregnant women was evaluated in a pilot trial involving 57 healthy pregnant women. All the volunteers in the probiotic group (n = 25) were GBS-positive and consumed ~9 log10 cfu of *L. salivarius* CECT 9145 daily from week 26 to week 38. At the end of the trial (week 38), 72% and 68% of the women in this group were GBS-negative in the rectal and vaginal samples, respectively. They concluded that L. salivarius CECT 9145 seems to be an efficient method to reduce the number of GBS-positive women during pregnancy, decreasing the number of women receiving IAP during delivery [1].

Da Silva HD., *et al.* performed a review aimed to analyze the evidence of the correlation between universal screening for *Streptococcus agalactiae* colonization in pregnant women and early onset Group B neonatal infection. The meta-analysis revealed a Risk Ratio of 0.37 with a 95% of Confidence Interval, indicating a positive factor for the questioning [9].

Despite the dimensions of the problem, there is a shortage of recent clinical studies that have as fundamental question the association between the universal screening of pregnant women for GBS infection and the reduction of neonatal infection rates [10].

Conclusions

In our centre, the prevalence of mothers with GBS is 13.9%, similar to the global epidemiological data and 77.8% received complete intrapartum antibiotic prophylaxis. Of all the NBs born to mothers carrying SG, 17% required surveillance for infectious risk but only 1% developed overt sepsis.

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