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ORIGINAL PAPER / OBSTETRICS

Group B *streptococcus* colonization status and antibiotic use during labour — a single-centre observational study

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ABSTRACT

Objectives: Group B *streptococcus* (GBS) colonization among pregnant women is the leading cause of neonatal infection. Intrapartum antibiotic prophylaxis (IAP) is the most effective method to reduce the incidents of neonatal sepsis. We describe compliance with GBS management and the implementation of IAP in the context of the long-term effect of antibiotics.

Material and methods: The study was conducted among 249 childbearing women hospitalized between January 2022 and February 2022 at University Clinical Center in Gdansk, Poland. The data were obtained from the questionnaire and medical records. We analyzed maternal colonization with GBS, compliance with GBS screening and treatment guidelines, risk factors contributing to GBS colonization, IAP administration, and neonatal congenital infection occurrence.

Results: Of all patients, 240 (96.4%) were screened for GBS, 215 (89.6%) between 35–37 weeks of gestation. Fifty (20%) were GBS-positive, 184 (74%) negative, 15 (6%) had unknown GBS status.

There were no significant differences between the GBS-positive and GBS-negative groups in maternal age, mode of delivery, gestational age at birth, maternal comorbidities, parity, GBS status in previous pregnancies, and the development of infection among infants of both groups, regardless of IAP administration. Of all the studied women, 158 (63.5%) received antibiotics, 91 (36.5%) did not.
The study showed the low positive and the high negative predictive value of the antenatal GBS screening test.
Conclusions: We found that compliance with the universal GBS screening is widespread. The management of women with absent or only partial screening test requires assessing the risk factors before administering IAP.
Keywords: group B *streptococcus*; *streptococcus agalactiae*; screening; intrapartum antibiotic therapy; neonatal microbiota

INTRODUCTION

The human body is the environment for a large community of microbes. They create the microbiota that affects the human organism in the context of health and disease. Bacterial colonization of a newborn starts during delivery and advances rapidly following initial exposure to maternal rectal, vaginal, skin and breast milk microbiota. The profile of a newborn's microbiota is influenced by various factors, including antibiotic exposure during pregnancy or birth, delivery type and perinatal infection [1–3].

Nowadays, up to 50% of neonates delivered in industrialized countries are exposed to intrapartum antibiotic prophylaxis (IAP). The primary cause of antibiotic exposure in the perinatal period is maternal colonization of the genitourinary and gastrointestinal tract with group B *streptococcus* (GBS) [4–6]. Group B *streptococcus*, also known as *streptococcus agalactiae*, is the leading cause of infection in newborns, occurring with either early onset, from birth to the 6th day [early onset disease (EOD)], or late, from the 7th to 89th day of life [late-onset disease (LOD)] [7, 8]. Vertical transmission before or during labour is estimated to occur in 40–60% of maternal carriers, whereas, in the absence of IAP, 1 to 2% of their neonates will develop GBS EOD [9]. The prevalence of vaginal or rectal GBS colonization in pregnant women in Poland is estimated at 3.3–20% and 11–35% worldwide, making it the leading cause of early-onset neonatal sepsis and meningitis [10–12]. The Center for Disease Control and Prevention (CDC) initially issued pregnancy-specific guidelines for screening and treating GBS in 1996. Since then, GBS screening guidelines have been revised in response to concerns about antibiotic overuse and microbial resistance. Based on these

recommendations, Polish Gynecologic Society (PTG; Polskie Towarzystwo Ginekologiczne) has issued guidelines in Poland. It is recommended to perform universal GBS screening at 35–37 weeks of gestation with subsequent IAP for those with positive swabs [12–14]. The aim of IAP is to prevent the transmission of pathogenic bacteria from the mother to the infant. Moreover, IAP is widely used for caesarean section surgical prophylaxis. Preventive efforts to identify and treat GBS have decreased maternal GBS disease and neonatal GBS EOD frequency. However, a concern about the negative impact of IAP has been raised. Children born to mothers who received IAP showed a lower abundance of Actinobacteria and were more frequently colonized by Firmicutes and Proteobacteria. This alteration of infant microbiota is essential in the pathogenesis of numerous diseases like allergies, asthma, obesity, inflammatory bowel disease and neurologic complications later in life [15, 16].

Objective

Our study aims to describe compliance with GBS management in an era of universal screening in the context of the implementation of IAP. We also evaluated the risk factors contributing to GBS colonization. Since intrapartum administration of antibiotics seems to have a profound impact on infant gut colonization, insufficient adherence to guidelines may lead to the excessive administration of antibiotics in some patients.

There is a gap in the literature on how adherence to the recommendations affects the intrapartum antibiotic regimen. Therefore, we assessed the implementation of these guidelines in the context of the long-term effect of antibiotic treatment in our cohort.

MATERIAL AND METHODS

This study was conducted among mothers who gave birth between January 2nd, 2022 and February 28th, 2022, hospitalized in the postpartum ward of the Department of Neonatology, at the single tertiary perinatal care centre. The data on the subjects and their babies were obtained through the questionnaire and their medical records during their hospital stay. Mothers were asked to complete a questionnaire regarding pregnancy course, GBS carriage, mode of delivery, previous obstetric history, parity, and maternal smoking. The survey was anonymous in the Polish language. It consisted of 33 closed single- and multiple-choice questions. All questionnaires were gathered in written, paper form. Only entirely filled-in questionaries were enrolled on the analysis. The mothers were first asked to express their written consent to participate in the study. We excluded five mothers because of language

barriers, three questionnaires lacked significant data, and three women did not give their consent. Results from 249 questionnaires were included.

As a part of hospital routine, GBS colonization was assessed based on the result of a screening test performed at 35–37 weeks of gestation according to the CDC and PTG procedures in all women presenting for delivery. On admission to the hospital, according to the local hospital protocol, during a vaginal examination, endocervical samples were collected for routine microbiological investigations for genital tract infections and analyzed using culture methods in the Clinical Microbiology Laboratory. This test was extended to a GBS culture.

Newborns suspected of infection were admitted to the Neonatal Intermediate Care Unit (NIMCU) or Neonatal Intensive Care Unit (NICU). They were also tested for bacterial colonization by taking microbiological swabs from the external ear, oral cavity and rectum, and blood culture before administering antibiotics.

IAP administration

Following recommendations and hospital protocol, all pregnant women admitted for a delivery who were screened positive for GBS were eligible to obtain IAP. In case of unknown GBS screening result at the time of delivery onset, women were also administered IAP. When only vaginal or rectal culture was known, women were qualified for IAP regardless of the culture result. Women with either preterm labour and membranes rupture ≥ 6 h or a fever of ≥ 38.0ºC were also treated with IAP regardless of the GBS status. Patients undergoing cesarean birth (regardless of GBS colonization status) were administered one dose of prophylactic antibiotics before the incision to reduce the risk of postoperative infections. Group B *streptococcus* positive women delivering by elective surgery were not given IAP.

According to the hospital antibiotic policy, the drug of first choice for IAP was ampicillin; unless the patient was allergic to it or the bacteria was resistant to ampicillin, a different IAP was administered. As the pre-incision antibiotic prophylaxis for all cesarean deliveries, cefazolin was administered. Intrapartum antibiotic prophylaxis was defined as adequate when the initial dose was given at least four hours before birth. If a mother presented to the delivery earlier, IAP administration was continued until birth.

The following information was analyzed: whether GBS screening was performed, gestational age (GA) at testing, specimen collection site: rectovaginal swab, only vaginal or only rectal swab, has there ever been a urine culture, and whether GBS status was known at the time of delivery, IAP administration and the accordance of the result of hospital

endocervical culture with screening GBS test. We also analyzed maternal age at delivery, self-reported GBS status, a history of GBS carriage in a previous pregnancy, GA at delivery, mode of delivery, body mass index (BMI), and any comorbidities present before and during pregnancy.

The following neonatal data were assessed: GA at birth, birth weight, and congenital infection occurrence.

Microbiological testing

Cervical or vaginal microbiological swabs are secured with a Stuart transport medium. Within 1–3 hours of acquisition, culture on the following solid media is performed: non-elective Columbia agar with 5% ovine blood, MacConkey agar (MAC) — a selective and differentiating agar that only grows gram-negative bacterial species, Sabouraud dextrose agar (SDA) — selective medium for funghi isolation, GBS agar — a selective medium for Streptococcus agalactiae isolation and Mycoplasma selective agar (OXOIDTM). The cultures are incubated in definite conditions. Columbia and GBS agar are incubated at 36.0ºC in a 5% CO_2 atmosphere for 18–24 hours. MacConkey and Sabouraud agar incubates in aerobic conditions. After the incubation, bacterial growth on the agar surface is assessed (on a solid medium), followed by bacterial and yeast species identification using MALDI-TOF mass spectrometry. For some species (*e.g. E. coli, K. pneumoniae, S. agalactiae, S. haemolyticus*, *E. faecalis* and others), *in vitro* susceptibility to antibiotics is determined (antibiogram) with the use of disk diffusion method and Mueller-Hinton II dehydrated medium (concordant with the EUCAST recommendations).

Statistical analyses

The data was collected using the Excel sheet. Statistical significance of differences between categorical variables was calculated using Fisher's exact test (for 2 × 2 categorical comparisons) or Pearson's Chi-squared independence test. The use of Fisher's exact test was motivated by low observation counts in some contingency tables. For GA and BMI, means (M) were compared with Welch's t-test with unequal variances correction. All analyses were conducted in Python (version 3.9) using the following packages: Pandas (version 1.5), Pingouin (v.0.5), SciPy (v.1.1) and Seaborn (v.0.12). In all cases, the statistical significance threshold (alpha) was set at 0.05.

RESULTS

We enrolled 249 mother-infant dyads. Cohort characteristics are presented in Table 1. Of the 249 women, 240 (96.4%) were screened antenatally for GBS. Of them, 215 (89.6%) were cultured between 35–37 weeks of gestation, 22 (9.2%) at a different time, 3 (1.2%) did not respond to this question. Among full-term women presenting to labour and delivery, 97.4% (224/230) have been screened for GBS. Out of 19 preterm deliveries, 16 women were tested for GBS, and in 15, the result was known before the delivery. Concerning the sampling site, 186 (74.7%) patients were tested by rectovaginal swab (in this group, one patient was screened only by urine culture), the remaining group of 54 (21.7%) had only vaginal culture performed (53 patients), one had only rectal swab, five had urine culture additionally.
Of the 249 subjects, 50 (20%) tested positive for GBS, 184 (74%) negative, 15 (6%) had unknown GBS status, including untested women and cases of missing or conflicting documentation.

There were no statistically significant differences between the GBS-positive and GBS-negative groups in maternal age, mode of delivery, GA at birth, maternal comorbidities, parity, GBS status in previous pregnancies, newborns' state after birth or maternal smoking. Although maternal BMI was higher in the GBS-positive group, the differences were insignificant (Tab. 2).

We observed discrepancies between the screening test result and the swab taken upon admission to the hospital. Of the 50 GBS-positive women at screening, 16 (32.0%) confirmed positive, while 33 (66.0%) occurred GBS-negative, and one (2.0%) was not swabbed at the hospital. Of the 184 prenatally GBS-negative women, 174 (94.6%) were still negative, and 7 (3.8%) tested positive for GBS, three (1.6%) were not tested at the hospital. Among 15 women with unknown antenatal GBS test, one (6.7%) occurred GBS-positive, 12 (80.0%) negative, and two (13.3%) were not tested at the hospital.

The positive predictive value of the GBS screening test (calculated against the ground truth value assumed to be given by the hospital test) was 0.32 [95% confidence interval (CI) 0.19–0.45], the negative predictive value was 0.99 (95% CI 0.98–1.00). The sensitivity and specificity of the GBS screening test were 0.94 (95% CI 0.83–1.00) and 0.84 (95% CI 0.79–0.89), respectively. Patients with unknown screening or hospital test results were excluded from this analysis.

Of all the studied women, 158 (63.5%) received antibiotics, while 91 (36.5%) did not. In the group of patients receiving antibiotics, 74 (46.8%) obtained pre-incision prophylaxis during the cesarean delivery. Intrapartum antibiotic prophylaxis because of a positive GBS screening was used in 35 (22.2%), in 24 (15.2%) due to incorrect specimen collection, vaginal

culture only, and in 10 (6.3%) due to unknown GBS status. Premature rupture of membranes (PROM) ≥ 6 hours (8 women) or ≥ 18 hours (4) or other reasons (3) were prompted to antibiotics administration in 15 (9.4%) women.

Of the 50 women with a positive GBS screening test, 35 (70%) received antibiotic prophylaxis, 11 (22%) obtained prophylaxis before cesarean delivery, four (8%) remained without IAP.

The timing of IAP administration in 35 GBS-positive women and 84 patients who underwent antibiotic prophylaxis for various reasons (incorrect sampling, unknown GBS status, PROM or other reasons) is shown in Figure 1.

Of the 249 women ever tested, 58 (23.3%) had a positive GBS culture, including the results of tests performed on admission to the hospital.

There were 20 (8%) cases of infection among neonates. Infants born to mothers from the GBS-positive group did not develop infections significantly more often than infants born to mothers from the GBS-negative group (10.4% vs 14.7%). There were no significant differences in the development of infection signs among infants of both groups, regardless of the use of IAP. Positive blood culture was not recorded in any case of neonatal infection (Tab. 3).

DISCUSSION

Strategies of intrapartum antibiotic prophylaxis have been successfully applied to decrease the frequency of GBS EOD in neonates. In high-income countries, relevant recognition of cases and routine prenatal and perinatal surveillance is noted [12, 17, 18]. However, approximately 11–30% of pregnant women carry GBS at any time, and there is the threat of passing the infection from the mother to the infant during the delivery. In our study, the prevalence of maternal GBS colonization was 23.3%, consistent with the previous reports [19]. We did not find significant differences in maternal and newborns' characteristics between the GBS-positive and GBS-negative groups. Maternal BMI was slightly higher in the GBS-positive group. Similar association was found in a cohort of American women [20].

According to recommendations, the majority of our patients were screened prenatally for GBS, and most of them were tested timely. It had positive clinical implications concerning intrapartum antibiotics administration.

The specimen collection site strongly affects diagnostic sensitivity. Rectovaginal sampling increases the number of GBS-positive women detected compared to the solely vaginal sample [12, 21]. In our study, strict adherence to screening protocol regarding

specimen collection site occurred in 75% of all patients. Based on previous reports, it has been demonstrated that incorrect specimen collection — most typically single culture from the vagina, was the most commonly identified error [12, 22]. A similar trend was observed in our study, as a quarter of all patients had only a vaginal swab.

Most scientific societies recommend universal screening and applying IAP to all GBS-positive women. However, uncertainties exist in managing women presenting to the delivery with the unknown result of prenatal GBS culture or with negative, though only vaginal culture taken. The question remains if these patients require IAP. In our cohort, these women were administered IAP, while most probably would not have had an affected child even without IAP. Remarkably, we showed that congenital infection occurred in one-fifth of newborns regardless of antibiotic prophylaxis implementation. Regarding the potential impact of widespread use of IAP for the mother and baby, antibiotic administration upon risk-based assessment appears more appropriate in GBS-negative women with only vaginal culture results. According to recommendations, IAP should be offered to women with unknown GBS culture status when the following risk factors for GBS EOD exist: preterm labour, preterm prelabour rupture of membranes (PPROM) or PROM ≥ 18 hours at term or maternal intrapartum fever ≥ 38°C. Therefore, for women at term without risk factors, either a rapid intrapartum test or a known history of GBS colonization in a previous pregnancy may be used to assess the indications for IAP [12, 14, 23]. Intrapartum antibiotics are delivered at a critical time in the development of the infant's microbiome [24, 25]. Strict antibiotic stewardship is a key to minimalize their adverse effects on the mother and babies, such as longer hospital stay, antimicrobial resistance or altered gastrointestinal bacterial colonization [26–28].

What is even more important, the use of IAP is rising due to increasing rates of cesarean sections [29]. We noticed a similar trend in our study.

Because many infants are exposed to antibiotics antenatally, identifying mother-infant pairs who would benefit from intrapartum prophylaxis becomes an essential challenge of perinatal care. Especially since GBS colonization in pregnant women can be temporary and antenatal GBS culture screening will not strictly indicate women requiring IAP. Up to 10–33% of patients with a positive GBS culture at 35–37 weeks were GBS-negative at delivery. On the other hand, approximately 4% of women colonized at delivery had a negative culture at 35–37 weeks and therefore did not receive IAP [30]. Although different samples were compared in our study, *i.e.* rectovaginal swab and cervical swab, we noted similar discrepancies between antenatal culture and swabs collected on admission to the hospital. Our

cohort also included women GBS-negative in prenatal screening and GBS-positive at the delivery who were not offered IAP.

Rectovaginal culture for GBS remains the gold standard [12, 14]. Nevertheless, the results are obtained after 48–72 hours and have a low predictive value of the positive result. These values varied between 43–67%, while negative predictive values ranged between 80-100% [30]. We confirmed the high negative predictive value of prenatal culture, which may have clinical implications and will allow us to avoid unnecessary treatment in a proportion of patients.

Gaps in current maternal screening and treatment protocols need efforts to target better women who require IAP. Therefore, the culture-based method may be enhanced by applying rapid identification methods such as intrapartum real-time rapid polymerase chain reaction (PCR) assay or nucleic acid amplification test (NAAT) [12, 19]. The updated CDC guidelines recommend rapid testing. Moreover, American College of Obstetricians and Gynecologists (ACOG) recommends updating universal GBS screening guidelines and performing it between 36 0/7–37 6/7 weeks of gestation. This recommendation serves to prevent infection in the potentially at-risk neonates and avoid the administration of ineffective antibiotics to women at term whose babies are not at that risk of infection.

Limitations of the study

Our results are based on an observational study design, so covariate factors could bias our findings. Despite the relatively high number of enrolled mother-baby diads, some subgroups were scarce. Therefore, the findings of the study should be further investigated, preferably in a multicenter, prospective study.

CONCLUSIONS

We found that compliance with the universal GBS screening approach is widespread. It is accepted by health care providers and pregnant women. Complete implementation of this strategy needs periodical training of providers about standard practices, especially concerning appropriate specimen collection.

The majority of patients presenting to the hospital have a valid result of antenatal GBS screening. Nonetheless, a group of GBS-positive women are admitted too late to receive complete antibiotic prophylaxis.

Adherence to GBS screening and treatment guidelines helps to avoid antibiotic over- and misuse, which may contribute to reducing the adverse effects of antimicrobial agents on the neonatal gut microbiota.

Particular emphasis should be placed on patients with incorrectly collected or unknown GBS screening test results. Their management should include a thorough analysis of risk factors followed by rapid intrapartum GBS tests.

Article information and declarations

Data availability statement

Data available on request from the authors.

Ethics statement

The study protocol was approved by the Bioethical Committee affiliated with the Medical University of Gdańsk (no. NKBBN/518/2021).

Author contributions

Iwona Janczewska: Study conception and design, acquisition of data, analysis and interpretation of data; drafting the article; final approval of the version to be published. Agreement to be accountable for all aspects of work ensuring integrity and accuracy. Corresponding author.

Joanna M. Jassem-Bobowicz: Study conception and design, acquisition of data, analysis and interpretation of data; drafting the article; final approval of the version to be published. Agreement to be accountable for all aspects of work ensuring integrity and accuracy.

Katarzyna Hinca: Acquisition of data, analysis of data; drafting the article; final approval of the version to be published. Agreement to be accountable for all aspects of work ensuring integrity and accuracy.

Katarzyna Stefanska: Study design, interpretation of data; revising the article critically for important intellectual content; final approval of the version to be published. Agreement to be accountable for all aspects of work ensuring integrity and accuracy.

Iwona Domzalska-Popadiuk: Study conception, revising the article critically for important intellectual content; final approval of the version to be published. Agreement to be accountable for all aspects of work ensuring integrity and accuracy.

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Conflict of interest

The authors declare no conflict of interest.

Supplementary material

None.

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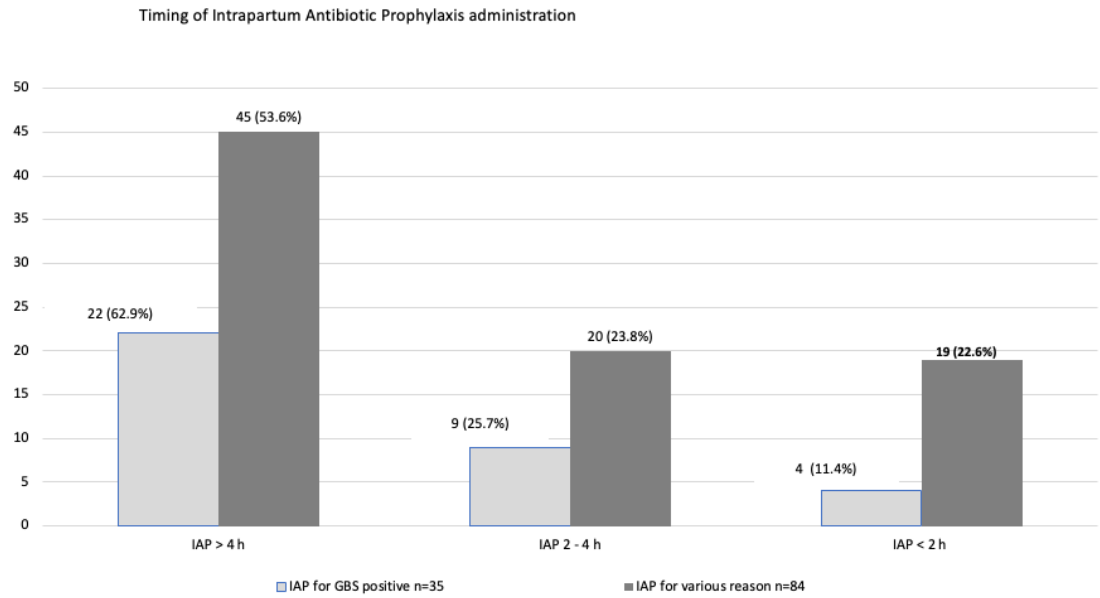

Timing of intrapartum antibiotic prophylaxis administration

Table 1. Cohort characteristics

Maternal and neonatal characteristics	
Maternal age at delivery [years]	31.03 ± 4.7
BMI before pregnancy [kg/m^2]	23.73 ± 4.9
BMI at delivery [kg/m^2]	28.6 ± 4.9
Vaginal delivery	154 (62)
Scheduled CD	50 (20.0)
Emergency CD	45 (18.0)
Full term births	230 (92.4)
Preterm births	19 (7.6)
GA at birth [weeks]	39.03 ± 1.7
GA at preterm birth [weeks]	35.3 ± 1.2
Newborns' weight at birth [kg]	3388.3 ± 488.2
Newborns' head circumference [cm]	34.24 ± 1.5
Female	126 (50.6)
Male	123 (49.4)
Apgar Score 8–10 points	237 (95.2)
Apgar Score 0–7 points	12 (4.8)

Data are presented as mean ± standard deviation (SD) or No. (%); BMI — maternal body mass index; CD — cesarean delivery; GA — gestational age

Table 2. Analysis of variables in relation to maternal group B *streptococcus* (GBS) status

Variables	**GBS (+)**	**GBS (–)**	**p value***

Mother's age at delivery	30.18 ± 4.52	31.28 ± 4.79	0.112
Gestational age at birth	39.19 ± 1.38	38.98 ± 1.80	0.359
Apgar score 0–7 points	3 (25)	9 (75)	1.0
Apgar score 8–10 points	55 (23.2)	182 (76.8)	
Emergency CD	13 (28.9)	32 (71.1)	0.618
Scheduled CD	11 (22.0)	39 (78.0)	
Vaginal delivery	34 (22.1)	120 (77.9)	
Preterm labour — no	57 (24.8)	173 (75.2)	0.085
Preterm labour — yes	1 (5.3)	18 (94.7)	
Hypertension during pregnancy — yes	50 (22.3)	174 (77.7)	0.395
Hypertension during pregnancy — no	6 (31.6)	13 (68.4)	
Gestational diabetes mellitus — yes	47 (23.4)	154 (76.6)	0.843
Gestational diabetes mellitus — no	9 (21.4)	33 (78.6)	
Pregestational diabetes mellitus — yes	54 (22.8)	183 (77.2)	0.624
Pregestational diabetes mellitus — no	2 (33.3)	4 (66.7)	
Hypothyroidism — yes	35 (23.0)	117 (77.0)	0.99
Hypothyroidism — no	21 (23.1)	70 (76.9)	
Body mass index before pregnancy (kg/m^2)	24.44 ± 5.31	23.51 ± 4.85	0.235
Parity — multiparous	23 (19.2)	97 (80.8)	0.177
Parity — primiparous	35 (27.2)	94 (72.8)	
GBS status in previous pregnancies positive	5 (31.3)	11 (68.75)	0.303
GBS status in previous pregnancies negative	13 (18.1)	59 (81.9)	
Never smoking	38 (23.2)	126 (76.8)	0.338
Smoking now	3 (50.0)	3 (50.0)	
Quit smoking before pregnancy	14 (24.2)	44 (75.8)	
Quit smoking during pregnancy	3 (14.3)	18 (85.7)	

Data are presented as mean ± standard deviation (SD) or No. (%); *P values for Fisher’s exact test (categorical comparisons) or Welch’s t-test (mean comparisons); CD — cesarean delivery

Table 3. Infection in neonates in relation to the maternal group B *streptococcus* (GBS) status and intrapartum antibiotic prophylaxis

Maternal GBS status, Reasons for IAP	**Infection in neonates**	**p value**

	None	Yes, GBS positive ear swab culture	Yes, other than GBS	
GBS-positive group				
IAP for GBS positive	32 (91.4)	0 (0.0)	3 (8.6)	0.216
IAP for GBS unknown	1 (100.0)	0 (0.0)	0 (0.0)	
IAP for incorrect sampling (only vaginal swab)	1 (100.0)	0 (0.0)	0 (0.0)	
Pre-incision prophylaxis during CD	11 (100.0)	0 (0.0)	0 (0.0)	
No IAP	7 (70.0)	2 (20.0)	1 (10)	
	52 (89.6)	2 (3.4)	4 (7.0)	
GBS-negative or unknown or incorrect sampling (only vaginal swab) group				
IAP for GBS unknown	8 (88.9)	0 (0.0)	1 (11.1)	0.939
IAP for incorrect sampling (only vaginal swab)	22 (95.6)	0 (0.0)	1 (4.4)	
PROM or other reasons	14 (93.3)	0 (0.0)	1 (6.7)	
Pre-incision prophylaxis during CD	59 (93.6)	0 (0.0)	4 (6.4)	
No IAP	74 (91.4)	0 (0.0)	7 (8.6)	
	177 (92.7)	0	14 (7.3)	

Data are presented as No. (%); IAP — intrapartum antibiotic prophylaxis; CD — cesarean delivery; PROM — premature rupture of membranes