GROUP B STREPTOCOCCAL AND PREMATURE BIRTHS: A NARRATIVE REVIEW

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ABSTRACT

INTRODUCTION: Premature births are those that occur before 37 weeks of gestational age. A clinical condition that remains problematic for obstetrics, mainly because of the high neonatal mortality it causes. Although most children survive, they are at risk of increased damage to neurological development and respiratory and gastrointestinal complications. Microorganisms, such as Streptococcus agalactiae (Group B Streptococcal - GBS), have been associated with prematurity. This comprehensive review aims to present data on the association between GBS and prematurity.

METHODOLOGY: The keywords Group B Streptococcal, prematurity, and Intrapartum antibiotic therapy were used in PubMed, Cochrane, SciELO and LILACS. Besides, using the inclusion criteria: GBS colonization in gestation, intrapartum antibiotic prophylaxis, premature births implications on childhood, and the exclusion criteria: GBS infection in non-pregnant women, premature births without GBS colonization resulted in 68 studies.

RESULTS: Premature rupture of ovular membranes (PROM) occurs in 1-3% of pregnancies, being an important cause of perinatal morbidity and mortality and being associated with 30-40% of premature births. Infection caused by group B streptococcal, has been indicated as an important risk factor of premature birth, especially in patients with premature amniorrhexis of the ovular membranes.

DISCUSSION: Preventive prophylaxis measures for pregnant women, such as intrapartum medication, resulted in a significant decrease in early newborn disease by GBS. In addition, penicillin was and remains as the antimicrobial of choice due to the fact that it has a narrower microbicidal spectrum than the ampicillin, and so it reduces the likelihood of the development of bacterial resistance. However, few studies with cause and effect relationship between the variables and a not systematic review were limitations.

CONCLUSION: GBS has been associated with increased risk of preterm delivery due to PROM. Also, antibiotic therapy for vaginal infection by bacteria reduced preterm birth with low weight in some populations.

KEYWORDS: Group B Streptococcal; Prematurity; Antibiotic Prophylaxis.
Microbial invasion of amniotic fluid has been indicated as an important risk factor of premature birth with intact membranes, especially in patients with premature amniorrhesis of ovular membranes. It is worth noting that vaginal bacterial infection was associated with increased risk of 1 to 4 times of premature birth with low birth weight. In addition, massive colonization was associated with an increased risk of 1 to 5 times of the same clinical condition mentioned.

Microorganisms, such as *Streptococcal agalactiae* (Lancefield group B streptococcal - GBS), *Escherichia coli*, *Gardnerella vaginalis*, *Neisseria gonorrhoeae*, and enterococci, have been associated with prematurity and prematurity rupture of the membrane. GBS has been associated with an increased risk of preterm delivery due to premature rupture of the membrane and not of preterm delivery with intact membranes. In addition, antibiotic therapy for vaginal infection by bacteria reduced preterm birth with low weight in some populations. Thus, considering that this comprehensive review aims to present data on the association between GBS and prematurity, the centrality of this study is on the first clinical condition. The objective is to summarize the key aspects of the association between GBS and premature births, as well as the conventional treatment of pregnant women colonized with the microorganism.

### METHODOLOGY

Using the keywords *Group B Streptococcal*, *prematurity*, and *Intrapartum antibiotic therapy* in a period from January 1, 1973 to December 31, 2021, with no language restriction applied, we founded 134 articles on the following databases: PubMed (n=52); the Cochrane databases (n=3), SciELO (n=31) and LILACS (n=48). The inclusion criteria was: GBS colonization in pregnant women, intrapartum antibiotic prophylaxis, premature births implications on childhood. After analysis, 66 studies were eliminated due to the exclusion criteria: GBS infection in non-pregnant or postpartum women, premature births without GBS colonization or with intact ovular membranes, by induction or cesarean section. After this, a total of 68 studies were primarily selected for this review. The references of the selected studies were also checked, and twelve more relevant articles were included. The PRISMA diagram can be found in Figure 1.

![PRISMA Diagram](source)

**FIGURE 1. Methodology for articles selection.**

**Source:** Elaborated by the authors.

### RESULTS

**PREMATURE RUPTURE OF OVULAR MEMBRANES IN THE ETIOLOGY OF PREMATURITY**

Premature rupture of ovular membranes (PROM) is characterized by the loss of amniotic fluid until 1 hour before the beginning of labor regardless of gestational age. PROM occurs in 1-3% of pregnancies, being an important cause of perinatal morbidity and mortality and being associated with 30-40% of premature births and 20% of perinatal deaths in this period. This cause of perinatal morbidity and mortality is typically due to a short latency period, increased potential for perinatal infection, and compression of the umbilical cord.

The latency period is the time between the PROM and the beginning of labor contractions, being inversely proportional to the gestational age, and it is divided into 4 stages: 1) 12 hours to 2 days; 2) from 3 to 7 days, 3) from 8 to 14 days, and 4) above 14 days. It is important to bring an existing classification based on the gestational age criteria: 1) above 37 weeks: PROM at term, 2) below 37 weeks: preterm PROM, with the category subdivided into: 2.1) below 24 weeks: pre-viable PROM to the extent that it relates to the worst fetal prognosis due to significant possibility of impairment of fetal maturation.
and risk of infection. 2.2) 24 to 34 weeks: early PROM, and 2.3) 34 to 37 weeks: PROM close to term.

PROM has a multifactorial etiology. In addition to the previous history of PROM, in previous pregnancy and antepartum bleeding, several risk factors for PROM have been emphasized by the literature with all of them leading to impaired integrity of the amniotic membranes, such as: 1) invasive procedures, (amniocenteses); 2)uterine overdistension (polymyohamnios, twinning, and multiple pregnancies); 3) mechanical factors, (uterine contraction and fetal movement); 4) alteration of cervical integrity (cervical cerclage and incompetence); 5) factors intrinsic to the membranes (Ehlers-Danlos syndrome, alpha-1-antitrypsin deficiency, and collagen malformation); 6) alteration of the tissue oxygenation (smoking); 7) alcoholism and use of illicit drugs; 8) living conditions, such as stress; 9) occupational conditions (work in a standing position); 10) low body mass index; 11) short interval between pregnancies; 12) young and more advanced maternal age; 13) increased bacterial immunological activity of amniotic fluid; and 14) presence of infection, mainly of genital origin.

PROM has been significantly associated with premature labor, given that one of its main consequences is prematurity leading to neonatal complications, such as: necrotizing enterocolitis, respiratory distress syndrome, and intraventricular hemorrhage. Furthermore, bacterial infection has been implicated in prematurity after premature amniorrhexis. Infection of the amniotic fluid by microorganisms has been indicated as an important risk factor of premature birth. It is important to point out that the incidence of chorioamnionitis in PROM is 15-25%, which can progress to complications such as conditions of endometritis, septic shock, and fetal sepsis. Regarding fetal sepsis, it can occur even before clinical manifestation of the pregnant woman's infectious condition, and neonatal sepsis appears to be less severe when the latency period is longer than 4 weeks compared to conditions in which the latency phase is short.

PROM is considered a relevant public health problem, justifying the objective of giving the necessary care to reduce the maternal and fetal morbidity and mortality it triggers. In this context of care, the diagnosis is fundamentally of a clinical nature with confirmation through genital examination with the use of a sterile speculum that allows the amniotic fluid to escape through the external orifice of the uterine cervix. From the diagnosis of PROM, the pregnant woman must be hospitalized for maternal-fetal surveillance and assessment of the presence of an infectious condition, and the following conducts must be observed: 1) measurement of vital signs every 6 hours; 2) observation of the presence of tachycardia and fever; 3) culture for GBS and specular examination; 4) blood count, erythrocyte sedimentation rate, C-Reactive Protein, urine culture with antibiogram, and urine analysis every 48 hours; and 5) obstetric ultrasound to assess gestational age, estimate weight, and amniotic fluid.

In relation to the culture for GBS, a study using 309 pregnant women, including 46 with positive culture for GBS, investigated the microorganism in vaginal secretions and from swabs from the anorectal region. Regarding the vaginal culture of the 46 pregnant women, only 38 (82.6%) were positive while the other 8 pregnant women presented false-negative results (17.4%). Meanwhile, the anorectal culture, of the same 46 pregnant women, showed only 20 (43.5%) positive results and the other 26 (56.5%) were considered false-negative. The conclusion that can be drawn from the experiment is that only 12 study participants were positive in both cultures. Thus, the study recommends collecting secretions from both the vagina and the anorectal area. Furthermore, another study found that there was a significant difference (p <0.0001) when it is compared the state of both anorectal and vaginal carrier to the state of vaginal carrier only, confirming the importance of collecting both anorectal and vaginal culture.

**GROUP B STREPTOCOCCAL INFECTION AS A RISK FACTOR OF PREMATURE RUPTURE OF UMBILICAL MEMBRANES**

The infectious condition has been indicated by the literature as one of the main risk factors to PROM in the same extent that about 32-35% of the cases have positive amniotic fluid culture. Infections related to PROM are mainly caused by: GBS, Gardnerella vaginalis, Neisseria gonorrhoeae, Escherichia coli, and enterococcus. GBS, the object of this study, colonizes the genitourinary and gastrointestinal tract in 10-30% of pregnant women and is the primary reservoir for GBS. Regarding the predisposing factors behind this colonization, it is important to highlight that the lactobacilli of the vaginal microbiota as well as the lactic acid they produce are considered a primary microbiological barrier against infection by genital pathogens. In addition, these microorganisms are well known for producing antimicrobial compounds, such as lactocidine, acidoline, lactam B, and hydrogen peroxide. According to a cohort and case-control study, deficiency in lactobacilli in the vaginal microbiota may allow colonization by GBS.

In many industrialized countries in the 1970s, GBS infections became the main cause of early newborn disease (occurring up to 7 days of age) with sepsis and meningitis from vertical transmission generally occurring during labor or after the rupture of membranes. In that decade, the neonatal mortality rate from infections caused by GBS was reported to be around 50%. Colonization by GBS during pregnancy remains the main risk factor of serious neonatal infection by this microorganism with its significant risks of infant morbidity and mortality despite the great progress in its prevention.
There is a consensus in the literature that approximately 50-60% of women colonized with GBS will transmit the bacteria to their newborns\(^2\). Infectious processes triggered in newborns from these clinical conditions, in the first 3 days of life, remain among the main causes of infectious infant death in the United States and can result in lifelong sequelae among survivors\(^5\).

The virulence of the pathogen is mainly determined by the ability to evade phagocytosis, mediated by the polysaccharide capsule. The capsule interferes in the phagocytosis until the patient develops specific antibodies\(^2\). Antibodies directed to type-specific capsular antigens passively protect laboratory animals from bacterial vicissitudes\(^2\), which partially explains the predilection of the microorganism for newborns\(^3\), mainly premature ones\(^1,2,4,10,15,18,19,25\). This is because in these children, low titers of protective type-specific maternal antibodies were transferred through the placenta\(^2\) leading to a higher risk of contracting the disease\(^3\). And, because physiologically, they have low levels of complement proteins\(^2\). In relation to the latter, the classic and alternative pathways of the complement system are necessary to kill the GBS, particularly types Ia, III, and V\(^2\). As a result, there is a greater likelihood of systemic spread of the microorganism in premature colonized children and in children with physiologically low levels of the complement system or in children in which the receptors for the complement (or for the Fc fragment of IgG antibodies) are not exposed in neutrophils\(^2\).

In addition to the greater immunological susceptibility of premature newborns to infection by GBS\(^1,4,7,10,12,16,17,18,20,22,23,25,33,49\), genital colonization by these bacteria has been related to the increased risk of premature birth\(^1,5,12,13,14,15,17,19,23\). The mechanism which bacterial vaginal infection is associated with preterm birth and premature rupture of ovular membranes, occurs from the cumulative interaction between microorganisms and the individual\(^1,5,13,15,16,17,18,23\). Pathogens, such as GBS and E. coli, adhere to the chorioamniotic membrane producing enzymes (proteases, collagenases, elastases, and phospholipases), weakening the fetal membrane, activating prostaglandins, and prematurely rupturing the fetal membrane\(^1,5,13,14,16,17,18,23,33,57\). In addition to being produced by the bacteria that causes chorioamnionitis, phospholipases A2 and C are present in the fetal membrane and are released from bacterial invasion. Thus, the activation of prostaglandins F2α and E2 occurs stimulating contractions. Moreover, leukotrienes and thromboxanes also act causing local necrosis. This set of localized reactions weakens the chorioamniotic membrane increasing the risk of premature rupture and preterm delivery\(^1,5,18\). Thus, babies can be infected by GBS through the aforementioned vertical transmission through the aspiration of amniotic fluid infected after rupture of the fetal membrane or during the passage through the vaginal canal\(^1,6,16,17,20,22,23\). Several studies in the 1980s, reported increased association between PROM, newborns with LBW, and early-onset neonatal disease by GBS\(^4,5,6\). In an important cohort study\(^4\) of 13,646 pregnant women, conducted as part of the Study of Vaginal Infections and Prematurity, the researchers were able to identify that women heavily colonized with GBS from 23 to 26 weeks of gestation were more likely to give birth to a premature baby with LBW. Consequently, GBS became associated with prematurity\(^1,11,12,14,15,17,19-22\). and the literature started to report premature rupture of membranes before 37 weeks occurring in 30-40% of preterm births\(^3\).

**DISCUSSION**

**THE IMPLEMENTATION OF INTRAPARTUM ANTIBIOTIC THERAPY FOR THE TREATMENT OF PROM BY INFECTIONS CAUSED BY GBS**

Clinical trials in the 1980s showed that early-onset GBS disease can be prevented by antibiotic therapy during labor in mothers colonized by such microorganisms\(^1,2,6,8,9\). Thereafter, preventive prophylaxis measures for pregnant women, such as intrapartum medication, to reduce the vertical transmission of invasive GBS diseases resulted in a significant decrease in early newborn disease by the pathogen\(^2,8\). During the 1990s, in the USA less than 10% of neonatal cases were fatal with mortality being significantly more likely among preterm children\(^9\). As a result of intrapartum antibiotic therapy and advances in neonatal care, the high neonatal mortality rates from the 1970s dropped to about 4% in the 2000s\(^3,7,8,9\). Thus, in addition to postnatal antibiotic therapy after premature labor from premature rupture of membrane, intrapartum antibiotic therapies have been shown to be very effective in reducing neonatal colonization by GBS as demonstrated by several clinical trials\(^9\).

The result was that clinical and public health authorities in the USA, Canada, and Australia began to draft guidelines on intrapartum prophylaxis. In 1996, The Centers for Disease Control and Prevention (CDC) recommended that all pregnant women should be screened for GBS between 35 and 37 weeks of gestation. The authorities recommended two approaches to health professionals. One was the screening approach, which consists of testing pregnant women between 35 to 37 weeks of gestation to check if they are GBS carriers administering chemoprophylaxis if positive\(^6,9\). The other one was the risk-based approach, which the criterion was women who presented at the time of labor clinical risk factors for the transmission of the disease\(^6,9\). Pregnant women are considered to be at high risk for having a baby with invasive disease by group B streptococcal, if they have previously had a child with the disease or if risk factors are present at the time of birth. These factors are: 1) intrapartum temperature of at least 38°C; 2) membrane rupture at least 18 hours before delivery, and 3) positive vaginal or rectal culture for the microorganism from 35 to 37 weeks of gestation\(^2,20,22,63,64\). Intrapartum fever and history of a previous delivery due to group B streptococcal disease were the factors associated with an increased risk of early-onset disease\(^6\). The CDC started to recommend intrapartum antibiotic
prophylaxis for women identified from the risk-based approach between the rupture of the membrane and/or premature delivery\textsuperscript{20,22,63,64}. Penicillin was and remains as the antimicrobial of choice due to the fact that it has a narrower microbial spectrum than the ampicillin, and so it reduces the likelihood of the development of bacterial resistance\textsuperscript{20,65}. Intravenous penicillin G is recommended at least four hours before delivery. Once resistance to erythromycin and clindamycin has been reported\textsuperscript{66}, cefazolin is used in women allergic to penicillin and at low risk of anaphylaxis\textsuperscript{30,65}. If already at risk of anaphylaxis, clindamycin is used if the strain is susceptible\textsuperscript{69}. Another alternative in this situation is the use of vancomycin\textsuperscript{30}. It is important to point out is that a study\textsuperscript{41} identified that erythromycin for women with PROM is associated with a series of health benefits for the newborn. The results showed that this widely available antibiotic has effects in reducing major neonatal diseases and can, therefore, have a substantial health benefit on the long-term regarding respiratory and neurological function of many kids. In terms of therapeutic limitation, the combination of amoxicillin and clavulanic acid cannot be routinely recommended for PROM due to its association with neonatal necrotizing enterocolitis supposedly for its ability to select \textit{Clostridium difficile}. Another equally important observation is that the CDC algorithm for prophylaxis of GBS for women at risk of premature birth that covers those with PROM includes the prescription of intravenous penicillin for at least 48 hours. At the doctor’s discretion, antibiotic prophylaxis may be continued beyond this period. On this matter, later, a study\textsuperscript{21} that aimed to determine the length of time required to eradicate group B streptococcal from the lower genital tract in pregnant women with PROM concluded that a 3-day antibiotic prophylaxis regimen appears to be adequate to eradicate the GBS of the genital tract of patients with PROM. A 1995 GBS disease review study done in four areas in North America, suggested that the strategies recommended by the CDC would reduce the incidence of early-onset GBS disease about 41% using the risk-based prevention or 78% using the screening for all pregnant women between 35 and 37 weeks of gestation\textsuperscript{67}. After the publication of the aforementioned guidelines, an additional reduction in invasive GBS diseases was reported\textsuperscript{20,22,50}. An important study analyzed the effect of preventive measures of prophylaxis of pregnant women, and found that the rates of fatal cases were at that time much lower when compared to those of the 1970s\textsuperscript{20}. The decline was attributed to the faster diagnosis and immediate treatment of symptomatic babies given that the mortality rate was decreasing in both full-term and preterm children. The decrease of early onset of the disease in the newborn by GBS was accompanied by a significant increase in the proportion of hospitals that adopted prevention policies. Only 14% of hospitals had an GBS policy in 1994 compared with 46% in 1997\textsuperscript{20}. A multicenter case-control study ratified the relevance of the risk-based strategy for chemoprophylaxis as a potentially capable instrument of preventing a number of cases of infection by GBS. This study confirmed that the rupture of membranes for more than 18 hours is an important risk factor for the increase in the incidence of early-onset GBS disease\textsuperscript{68}. Thus, during the 1990s candidates for intrapartum chemoprophylaxis were identified according to a screening-based or risk-based strategy. This approach led to a 65% reduction in the incidence of early-onset GBS disease: from 1.7 cases per 1000 live births in 1993 to 0.6 cases per 1000 live births in 1998\textsuperscript{49}. In general, these preventive measures of prophylaxis of pregnant women, whether the risk-based approach or screening approach, were recommended in order to reduce the chance of early neonatal sepsis in newborns by GBS\textsuperscript{20,22,30}. In 2002, the CDC updated the guidelines and the screening approach proved to be about 50% more effective than the risk-based approach in preventing perinatal disease by GBS\textsuperscript{64}. The protective effect of screening resulted from two main factors. First, it enabled the identification of women colonized with group B streptococcal who do not have clinical risk factors—about 30-50% of cases with early-onset sepsis due to GBS develop in babies born to women without risk factors\textsuperscript{18,64}. Second, the screening achieved a greater degree of coverage of the vulnerable population than the risk-based approach\textsuperscript{64}. Successful adoption of screening recommendations is likely to have contributed to the documented decline of 27% in the incidence of early-onset GBS disease from 1999-2001 to 2003-2005. The recommendation for universal prenatal screening for GBS was a relevant policy change that posed challenges to its implementation. All multi-state surveillance sites quickly adopted universal screening after the guidelines were published. The understanding underlying the implementation and adherence to such prophylactic policies was that the feasibility of decreasing the incidence of early-onset group B streptococcal disease would depend in part on the ability to reduce the number of missed prevention opportunities\textsuperscript{49}. Consequently, preventive measures against GBS significantly increased the use of intrapartum antimicrobial agents\textsuperscript{20,22,30}. In line with this optimistic perspective of preventing neonatal GBS infection, a study\textsuperscript{64} suggests that the identification of the absence of a significant association between group B streptococcal bacteriuria and early onset disease should not be considered evidence that such bacteriuria is no longer an important indication of prophylaxis, but of successful prevention considering that 82% of women with bacteriuria received intrapartum prophylaxis. This finding is in line, for example, with the Cochrane meta-analysis\textsuperscript{69} which showed that the administration of antibiotics after PROM was associated with a delay in delivery and a reduction in neonatal infection. It is important to mention that in this research 82% of all women with group B streptococcal bacteriuria also received intrapartum antibiotics. This is also a possibility of interpretation for the findings of retrospective studies such as the research\textsuperscript{28} that did not identify an association between GBS bacteriuria during pregnancy and...
the increased risk of early-onset disease. The results showed that patients with GBS did not have a higher incidence of chorioamnionitis when using prolonged antibiotic therapy, which is an indicator of eradication of the microorganism as well as other microbial infections in the genital tract, reducing the rate of endometrial infection. However, the conclusion of the study problematizes the issue, also considering the possibilities of not having a significant difference in the rate of chorioamnionitis between patients with positive and negative GBS cultures or a possible development of resistance by other pathogens. Results of research like this, subject to controversy, suggest that the absence of a complete consensus on topics related to GBS remains until now. It was even argued for the lack of significant difference in the rate of premature labor caused by PROM between patients with positive and negative GBS cultures. Other studies, argued that it would not be completely clear whether the treatment of pregnant women with bacterial vaginosis would decrease the risk of preterm delivery, and so it is required a large, randomized, well-controlled clinical trial of treatment for bacterial vaginosis in pregnancy. There was still a claim that data on the relative effectiveness of both the risk-based approach and screening recommended to health professionals by the authorities would be lacking. However, even with such questions, typical of the dynamism of the construction of scientific knowledge, it is undeniable that a large set of research in the area progressively argued that the administration of these antibiotics leads to an increase in the pregnancy latency, postponing very premature childbirth and reducing the resulting mortality. Regarding the reduction of neonatal death, it is justified because this strategy guarantees high levels of protective antibodies in the child’s circulatory system at the time of birth.

**INTRAPARTUM ANTIBIOTIC THERAPY FOR GBS AS A TRIGGER FOR INCREASING BACTERIAL RESISTANCE**

Therefore, despite the aforementioned optimistic perspective, dissident voices regarding GBS as an important risk factor of preterm delivery caused by PROM have taken place. Issues have arisen in relation to how effective is risk reduction of preterm delivery from intrapartum antibiotic therapy and in relation to the relative effectiveness of both the risk-based approach and screening recommended by the authorities. In addition, intrapartum prophylaxis has always been seen as a provisional strategy for preventing perinatal disease by GBS. In part due to concerns about the potential emergence of resistance from GBS to highly effective first-line β-lactam therapies. But also because of concerns that exposures to intrapartum antibiotics could increase the risk of sepsis due to non-GBS pathogens. A review study pointed out that no widespread increase in the incidence of neonatal sepsis by other pathogens resistant to penicillin had been identified in the context of prophylactic programs whether intrapartum or postnatal carried out until then. However, the episodes of resistant infections after the use of prophylactic antibiotics that were already being reported were regarded as an issue that deserved further attention in order to characterize the adverse effects of antimicrobial prophylaxis. In this context, since 1996 several studies have come to demonstrate that the resulting widespread use of intrapartum antibiotics for GBS infections brought risks of infections by Gram-negative bacteria, such as that caused by Escherichia coli, particularly among preterm children, and it is of significant severity with risk of death.

In this direction, the literature started to report the wide use of intrapartum antibiotics for GBS infections causing its reduction but also an increase in episodes of resistant infections by E. coli. The results of a study demonstrated that in 1.142 E. coli isolates from urinary tract infections the rate of ampicillin resistance was reported to be 37.7%. Ampicillin belongs to the group of aminopenicillins. Aminopenicillins are semi-synthetic penicillin that expand the spectrum of action of the penicillin which shows useful activity against some Gram-negative bacteria. Another study suggests that compared to beta-lactamase inhibitor and carbapenem-based regimens, empirical therapy with cephalosporins or fluoroquinolones is associated to a higher mortality rate due to sepsis caused by a new strain of E coli (9% vs 35%, respectively). Still results from another research indicated that E. coli strains were becoming more resistant to antibiotics. Furthermore, new strains of E. coli that produces beta-lactamase of extended spectrum were emerging.

Therefore, according to some studies, undeniably, the increased use of prenatal antibiotics prolonged pregnancy significantly during conservative management of PROM and caused significant reductions in early neonatal sepsis caused by GBS.

However, the effects on the spectrum of bacteria involved in early neonatal sepsis and their susceptibility to antibiotics would not be clear to the extent that the literature on the subject presented conflicting research results. In a retrospective study at a single center, the researchers found a possible association between the use of intrapartum antibiotic therapy and infection with aminopenicillin-resistant Escherichia coli (AR-E. Coli). Other research also found this possible association. A study identified that prenatal exposure to ampicillin was an independent risk factor of early-onset sepsis caused by ampicillin-resistant E. coli. From these findings, there have been growing concerns that such use could increase the risk of infections by pathogens other than GBS. A growing concern that the widespread use of intrapartum antibiotic therapy may lead to an increase in Gram-negative bacterial infections due to the AR-E. coli resistance which has been associated with the use of prenatal antibiotics to treat PROM. These concerns are reasonable as we consider, for example, that the screening rate for group B streptococcal before...
childbirth increased from 48.1% in 1998–1999 to 85.0% in 2003–2004, and therefore the percentage of children exposed to intrapartum antibiotics increased from 26.8-31.7% \(^\text{49}\). In this sense, the authorities became interested in a possible change in the distribution of pathogens that cause neonatal sepsis \(^\text{50}\). Results of a study \(^\text{65}\), on the one hand, confirmed previous findings \(^\text{76}\) on a regional basis with 50% of \(E.\ coli\) strains showing resistance to aminopenicillins. The researchers indicate that amoxicillin-resistant \(E.\ coli\) infections were significantly associated with the use of prenatal antibiotics, especially in premature babies born after the administration of such antibiotic therapy for PROM \(^\text{73}\). From this aspect, \(E.\ coli\) would present itself as the main cause of early-onset neonatal sepsis not related to GBS \(^\text{50}\). However, they argued that the occurrence of an increase in cases of neonatal sepsis of early onset caused by non-GBS pathogens seems to be relative rather than absolute. In addition, the literature has shown that although premature babies have a higher incidence of group B streptococcal disease with early onset than full-term babies, in some study populations 74.4% of cases of group B streptococcal disease (189 of 254) occurred in babies born at term \(^\text{49}\). Findings like these are linked to the growing concerns previously mentioned, especially when at the same time there is a high rate of preterm children infected with \(E.\ coli\) (81%) \(^\text{50}\). In line with other findings, \(^\text{49}\) results of a survey \(^\text{69}\) indicate that in the studied population the majority of children with GBS were at term (73%) while the majority with \(E.\ coli\) were preterm (81%). Furthermore, these results indicate that the latter requires more intensive care (93%) than the children with GBS (66%). For the researchers, this would indicate that GBS remains the most frequent pathogen in full-term children, and \(E.\ coli\) the most important pathogen in preterm children. On the one hand, this study helps to settle the concern about the significance of high rates of \(E.\ coli\) infection in preterm children related to the development of resistance due to the widespread use of prophylactic antibiotics. But, on the other hand, although some researchers reported higher mortality for children infected with Gram-negative bacteria, this study concludes, in line with other findings \(^\text{65}\), that the results indicate that the policy on intrapartum prophylaxis for GBS is not associated with an excessive risk of infection by resistant pathogens.

The main limitations of the present article were few studies available with a cause and effect relationship between colonization by GBS. And prematurity, such as control cases and cohorts, and the fact that it is not a systematic review.

**CONCLUSION**

As a corollary of the narrative review made, the data from the American College of Obstetricians and Gynecologists (ACOG) (2020) \(^\text{42}\) that indicates that in the absence of intrapartum antibiotic prophylaxis in women with high-risk pregnancies 1-2% of these newborns will develop early-onset disease caused by GBS, are plausible. It is reasonable that the main obstetric measures necessary for effective prevention of early onset GBS disease continue to include universal prenatal screening by vaginal-rectal culture, correct collection and processing of specimens, appropriate implementation of intrapartum antibiotic prophylaxis, and coordination with pediatric care providers. The ACOG \(^\text{52}\) now recommends universal screening for GBS at between 36 and 37 weeks and six days of gestation. All women whose vaginal and rectal cultures at 36 and 37 weeks and six days of gestation are positive for GBS should receive appropriate intrapartum antibiotic prophylaxis unless a cesarean delivery is performed with intact membranes. It is important to note that although a shorter duration of the recommended intrapartum antibiotics is less effective than 4 or more hours of prophylaxis, 2 hours of exposure to the antibiotic have already shown to reduce the GBS vaginal colony count and decrease the frequency of a clinical diagnosis of neonatal sepsis. However, obstetric interventions when necessary should not be delayed just to provide 4 hours of antibiotic administration before birth \(^\text{42}\).

Although the present study reinforces the importance of screening and preventing GBS infection for neonatal morbidity and mortality, the development of new studies that establish a cause and effect relationship is necessary to better elucidate the subject.

**CONFLICTS OF INTERESTS**

The authors have no conflict of interests to declare.

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