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Epidemiology, Prevention, and Treatment of Group *B Streptococcus* Infections in Newborns and Mothers: A Comprehensive Review

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Abstract: ***The review summarizes recent studies on the epidemiology of Group B Streptococcus GBS infection in mothers and newborns, highlighting the early and late onset of infections in infants. It discusses modern approaches to prevention and treatment, and examines the pathogenicity factors and antibiotic resistance mechanisms of GBS strains. This comprehensive review provides critical insights into the ongoing challenges and advancements in managing GBS infections in neonatal and maternal health.***

Keywords: Group B streptococcus (GBS), infants, pregnant women, infection, prevention, treatment

1. Introduction

For many decades (more than 50 years) active research has been conducted on infection in infants with Group *B streptococcus (GBS*). [1, 2, 3, 4, 5**].** However, neonatal infection caused by this pathogen still persists. The difficulty of controlling this infection is related to the biological properties of GBS, their pronounced toxicity, and their ability to quickly develop antibiotic resistance. However, neonatal infection caused by this pathogen remains relevant at present [3, 5, 6, 7, 8].

Group *B streptococcus* (the main representative is *Streptococcus agalactiae*) is a facultative gram - positive β - hemolytic bacterium that is surrounded by a capsule and forms a coccus chain [1, 3]. It can asymptomatically colonize the human vaginal and gastrointestinal tracts. However, during pregnancy, *GBS* can become a highly invasive and pathogenic agent of ascending infection for the fetus and mother, leading to an unfavorable outcome, mainly preterm birth, stillbirth, and foetal death. [3, 7, 9, 10]. Vaginal colonization of *GBS* has a direct correlation with the vertical transmission of this pathogen to the fetus [3, 7, 9, 11, 12].

The fetus and newborn are very susceptible to *GBS*. This is due to the poor anti - infectious protection of newborns, especially premature newborns, due to the still incomplete immune system development. Bacteria cause sepsis, pneumonia, and meningitis in newborns, which in severe cases lead to serious pathology in the central nervous system and the babys lungs, potentially resulting in disability [3, 4, 5, 6, 7, 9, 13]. Nearly 50 of infants who survive GBS meningitis may have long- term neurological effects [3, 9]. The outcomes of *GBS* infection are developmental delay or neurological abnormality (blindness, deafness, cerebral palsy as assessed by motor or psychomotor measures), seizures, renal dysfunction, pulmonary disorders, immune dysfunction, necrotizing enterocolitis, and malabsorption. [5, 9]. A case of facial cellulitis in a very preterm infant is known. [14]. In the mother, *GBS* infections can lead to chorioamnionitis, postpartum endometritis and sepsis, and urinary tract infection can cause premature labor and miscarriage [3, 7, 15, 16, 17].

The purpose of this review is to synthesize recent findings on the epidemiology, prevention, and treatment of Group B Streptococcus infections in mothers and newborns, and to discuss the implications for clinical practice and future research. This review is significant as it consolidates current knowledge on GBS infections, which remain a leading cause of neonatal morbidity and mortality, and provides updated insights into prevention and treatment strategies.

2. Method

Search strategy and literature selection criteria. This review utilized a comprehensive search strategy to identify relevant studies on GBS infections published between 2014 and 2022, using databases such as PubMed and Google Scholar. The selected studies were analyzed to summarize findings on epidemiology, prevention, and treatment.

To identify recent *GBS* studies that address maternal colonization, ascending and nosocomial fetal infection, a literature search was performed using Google Scholar and PubMed Central. Variants of the terms "pregnancy", "preterm birth", "vaginal colonization", "colonization", "uterus", "infection", "fetus", "vaccine", "epidemiology", "antibiotics" with "group *B streptococcus*" were used. or *Streptococcus agalactiae*. We additionally searched the list of references to articles to identify studies that were foundational to recent work in this area, including papers published prior to 2014.

3. Results

Ep*idemiology*.
A number of phenotypic and genotypic classifications can be used to identify the diversity of *GBS* strains. Information on maternal colonizing strains and neonatal disease strains allows monitoring and optimization of vaccine prevention and treatment, as well as helping to develop new therapies [16].

GBS prevalence varies significantly between pregnant women and newborns in different geographical areas around the world. For example, recto - vaginal colonization of *GBS* in women is 35% in the Caribbean, North America and Europe, and 25% in South Africa. Approximately 20 - 25% of women have been affected by *GBS* infections on average worldwide [16]. The main factors responsible for recto - vaginal *GBS* colonization are premature rupture of membranes, the presence of *GBS* in the intestinal tract, and maternal age over 40 years. Ethnicity, poor hygiene, illiteracy, obesity, and other factors also contribute to *GBS* colonization [18]. It has been established that *GBS* is the leading cause of preterm birth and stillbirth worldwide. So, about 3.5 million cases of preterm birth in one year were associated with *GBS* infection [18].

P. T. Heath, and L. J. Jardine (2014) indicate that one in four women is a carrier of *GBS* vaginally and can infect the amniotic fluid before delivery or infect the baby during delivery, causing sepsis, pneumonia or meningitis [9]. Another systematic review reported that 0.38 out of 1000 pregnant women had invasive *GBS* infections. which could even lead to maternal death. Thus, *GBS* infections remain problematic for the mother, fetus, and newborn [4].

L. Madride et al, (2017) analyzed the incidence of *GBS* infection in infants based on 135 scientific publications [6]. The cumulative incidence of invasive *GBS* infection in neonates was 0.49 per 1000 live births (95% confidence interval [CI], 0.43–0.56). The highest incidence was in Africa (1.12) and the lowest in Asia (0.30). The incidence of early - onset disease caused by *GBS* (*GBS* EOD) was 0.41 (95% CI, 0.36 - 0.47); the incidence of late - onset disease caused by *GBS* (*GBS* LOD) was 0.26 (95% CI, 0.21 - 0.30). Case fatality risk (CFR) was 8.4% (95% CI, 6.6% - 10.2 [6].

C. Plainvert, et al. (2020) conducted molecular capsular typing of 1262 *GBS* isolates. Serotype III accounted for 57% (95% CI, 52% - 62%) of *GBS* EOD cases and 82% (95% CI, 79% - 84%) of *GBS* LOD cases. The hypervirulent strain *GBS* CC17, which includes sequence type (ST) 17, causes 66% (95% CI, 63% - 68) of neonatal *GBS* disease. The frequency of *GBS* CC17 was higher in *GBS* LOD (74%, CI, 71% - 77%) compared with EOD (48%, 95% CI, 43% - 53%; p<0.0001) and in cases of EOD with meningitis according to compared with bacteremia (68%, 95% CI, 59% - 77% vs.41%, 95% CI, 36% - 47%; p<0.0001). The incidence of GBS CC17 increased by 50% over the study period from 53% (95% CI, 40% - 65%) in 2007 to 76% (95% CI, 68% - 82%) in 2019 (p = 0.0001). This increase is related to its prevalence in LOD, which increased from 59% (95% CI, 41% - 75%) to 85% (95% CI, 77% - 91%) of cases during 2007 - 2019 (p= 0.025) [19].

The five serotypes (Ia, Ib, II, III and V) represent approximately 98% of all serotypes identified in maternal colonization and neonatal disease A small proportion of maternal colonization and neonatal disease is associated with the remaining five CPS IV, VI, VII, VIII and IX [16]. Detailed information on the distribution of specific *GBS* serotypes in different countries can be found in the LL L. L. Furfaro review, et al., (2018). [16]. Maternal *GBS* colonization rates in South India are high at 12.9% (95% CI, 9.2% - 17.6%). It has been associated with premature rupture of membranes (2.93, 95% CI - 1.66 - 5.16). There was a positive correlation between anhydrous duration ≤ 4 h and disease in the newborn, as well as between maternal *GBS* colonization and a 1 min Apgar score ≤ 4 [8].

K. M. Puopolo et al., (2022) showed that the incidence of *GBS* EOD (2.70/1000 births) and *GBS* LOD (8.47/1000 births) did not change significantly over time (in 1986 - 2016) in infants born at 22–28 weeks gestation and surviving > 12 hours. The adjusted relative risk of death/NDI was higher among infants with *GBS* EOD than among infants with other infections (adjusted relative risk 1.22 and 1.44, respectively). *GBS* LOD occurred at a significantly later age than non - *GBS* late - onset infection [20].

According to Jjing Huang et al. (2019), 4.4% of newborns out of 976 live births in China in 2017 had a positive *GBS* DNA test.4 infants had early manifestations of *GBS*, including pneumonia in 2 cases and sepsis in 2 cases. *GBS* positivity and anti - *GBS* capsular polysaccharide antibody levels in preterm infants correlate with gestational age [21].

The prevalence of *GBS* among pregnant women in Brazil has ranged from 4.2% to 28.4% over the past 10 years. Serotype Ia was the most common [22].

The rate of maternal *GBS* colonization was about 20% from January 2004 to June 2005, and the rate of neonatal *GBS* infection was one per 1000 live births in Taiwan. Rates are similar from 0.7‰ to 3.7‰ live births in the US and from 0.2‰ to 3.25‰ in Europe before the introduction of universal antenatal screening for *GBS* and intranatal antibiotic prophylaxis. The prevalence of *GBS* in pregnant women remained around 20%, but the incidence of *GBS* EOD decreased by 80% after the start of implantation in 2012. Thus, the effect of prevention is obvious, but the threat of *GBS* infection still exists [3].

An important component of epidemiological research is the study of the genome of pathogens, which will allow not only to identify the chains of infection, but also to determine virulence genes, which will help in the development of vaccines [16, 23].

Neonatal GBS infection.

As mentioned above, two variants of the clinical course of *GBS* infection in newborns are now distinguished: early - onset disease incidence (EOD) and late - onset disease incidence (LOD) [3].

Early onset *GBS* disease (*GBS* EOD) is a disease in which *GBS* is shed from a normally sterile locus within six days of birth. It most often appears 12–24 hours after birth [23]. Babies born before 37 weeks of gestation account for 28% of all cases of *GBS* and have a case fatality rate of 19% compared to 2% for full - term babies. Maternal colonization leads to *GBS* - EOD, so testing and intrapartum antibiotics help reduce the onset of *GBS*. Meningitis was diagnosed in 10% of babies with early onset *GBS* and in 9% of these cases proceeded without bacteremia [23].

According to Nan - Chang Chiu (2019), vertical transmission of *GBS* occurs in utero or during labor through the vagina of a colonized woman. About half of babies born to mothers with *GBS* are colonized with *GBS* [3]. *GBS* - EOD occurs in babies born to screen - negative mothers in about 8% of cases. [23].

Late onset *GBS* disease (*GBS* - LOD) is acquired between 7 days and 3 months (89 days) after birth from breast milk or from environmental and community sources [3]. The mean incidence of late - onset *GBS* did not change from 2006 to 2015. This indicates that maternal colonization at birth is less responsible for the late onset of *GBS* [23]. Contamination of newborns with *GBS* may be associated with caregivers of infants. Bacteremia was found in 93% of infants diagnosed with *GBS* - LOD, and meningitis was diagnosed in 31%. Preterm birth, maternal screening positive for *GBS* at birth and postpartum are strongly associated with *GBS* EOD [23].

Clinical features of *GBS* EOD include tachycardia, tachypnea, and lethargy, which can lead to severe cardiorespiratory failure, persistent neonatal pulmonary hypertension, and perinatal encephalopathy [23].

According to P. T. Heath and L. A. Jardine (2014), *GBS* EOD usually presents with sepsis (69% of cases), pneumonia (26% of cases), respiratory distress syndrome (13% of cases) and rarely meningitis (11% of cases). Symptoms of *GBS* EOD may be non - specific, including temperature instability, poor appetite, excessive crying or irritability, and respiratory problems [9].
GBS LOD most often presents with bacteremia without identified foci of infection, a temperature of 100.4°F (38°C) or higher, lethargy, poor appetite, weak sucking reflex, irritability, tachypnea, grunting, or apnea. Infants with late meningitis may also be irritable, have vomiting, temperature instability, fontanelle protrusion, or seizures. Late onset *GBS* can also develop pneumonia, bone or joint infections, cellulitis, and adenitis [9, 24, 25]. F. Miselli, et al, (2022) note that late - onset infection usually presents with fever or meningitis (about 30%). According to these authors, *GBS* LOD can rarely cause septic arthritis, cellulitis, or osteomyelitis [25]. *GBS* LOD tends to be less fulminant and less likely to be fatal than early - onset infection. Thus, mortality with *GBS* EOD was 14% compared with 4% with *GBS* LOD [24].

The *GBS* LOD assessment includes cultures of blood, urine, and cerebrospinal fluid; clinical and laboratory analysis of cerebrospinal fluid; determination of inflammatory markers. If a bone or joint infection is suspected, x - rays, magnetic resonance imaging, and bone or joint fluid cultures may be required [24].

GBS LOD is characterized by the detection of *GBS* with serotypes Ia, Ib II–IX. Serotypes Ia, Ib, II, III, IV, and V are the most common, with serotype III accounting for the majority (56%) of *GBS* LOD. The incidence of *GBS* LOD is currently estimated at 0.28 to 0.31 per 1, 000 infants in the United States. GBS LOD is characterized by the detection of *GBS* with serotypes Ia, Ib II–IX [25]. These data are consistent with the analysis by L. Madride et al, (2017), who showed a predominance of *GBS* serotype III (61.5%) in different countries of the world, with 97% of cases being caused by serotypes Ia, Ib, II, III and V [6].

Pathogen transmission routes in *GBS* LOD remain poorly understood. Approximately 2/3 of babies receive *GBS* from their mother and 1/3 from the health workers who care for them. In some infants, the development of *GBS* LOD has been associated with massive contamination of breast milk with *GBS*, since in these cases it is not possible to identify a source of *GBS* LOD other than breast milk. In addition, compared with the overall risk, a higher rate of *GBS* LOD recurrence has been reported in infants fed GBS - contaminated breast milk (25% versus 0.5–4.5%). However, *GBS* LOD does not develop in most breastfed babies. Factors contributing to the development of *GBS* LOD are high bacterial inoculum and persistent intestinal colonization, long hospital stays, high hospital overcrowding, high patient - to - nurse ratios, and inadequate disinfection practices.

High maternal *GBS* colonization was noted in Africans, young maternal age, HIV infection, and prematurity. The most important factor is prematurity. In fact, about 40% of all *GBS* LODs currently affect preterm infants before 37 weeks' gestation [25].

For hospitalized neonates, even a single case should be considered as a potential source of nosocomial transmission: retrospective and prospective follow - up should be strengthened to identify a possible cluster [25].

If an infant with *GBS* infection is one of multiple infants, doctors should monitor siblings for signs of infection and treat them if they develop symptoms. Antibiotics should not be given without evidence of GBS disease [24].

It must be kept in mind that persistent mucosal colonization and reduced immunity from primary infection may lead to recurrent *GBS* infection after initial treatment of early - and late - onset GBS disease. [24].

Risk assessment for severe *GBS* infection in infants at 35 weeks' gestation and older can be done in three ways. Antibiotics have previously been recommended for all infants with clinical signs of infection or maternal temperatures above 100.4°F. Newborns with good clinical status, born to mothers with insufficiently effective intrapartum antibiotic therapy, were followed up for 36 - 48 hours. This strategy has led to empiric treatment of many infants at low risk of infection [24].

Multivariate risk assessment (second option) uses the risk factors of the mother and the clinical condition of the infant. Online calculators are available for this assessment, such as the Early Onset Neonatal Sepsis Calculator [26].

The third option recommends giving antibiotics to infants who show signs of illness at birth and during the first 48 hours of life. Babies born to mothers with a birth temperature of 100.4°F or higher should be observed for 36–48 hours [24].

Pathogenicity factors of Streptococcus B and mechanisms of development of GBS infection.

GBS virulence factors affect the ability of a strain to colonize and/or cause severe disease. Important factors in the pathogenicity of *GBS* are capsular polysaccharide, beta - hemolysin, peptidase C5a, adhesins, and immunogenic surface proteins [3, 23, 27, 28]. Hemolysin (β - hemolysin/cytolysin) has a *GBS* (granadaene) pigment in its molecular basis and has a direct cytotoxic effect on many types of host cells [29]. The *GBS* capsule is involved in various mechanisms of evasion of the immune response and contributes to the development of infection [30],

One of the key virulence factors is the sialylated capsular polysaccharide *GBS* (CPS). Ten capsular serotypes are now known (Ia, Ib, II - IX), six of which account for 98% of *GBS* colonization worldwide (Ia, Ib, II - V) [4]. The same serotypes cover more than 99% of all cases, including EOD and LOD [31].

Recto - vaginal *GBS* colonization of a pregnant woman is a major cause of intrauterine ascending neonatal infection. As a rule, the carriage of *GBS* in women is asymptomatic, which makes it difficult to identify it early. In this regard, it is recommended, if possible, a mass (preferably universal) examination of pregnant women for *GBS* carriage [4].

The development of maternal and child GBS infection arises from a large number of virulence factors of bacteria, which vary widely in different strains and can change expression depending on the host niche, on the massive colonization of the mucosa of the birth canal and the fetus. An important factor in the development of infection is a violation of the interaction in the host - pathogen system, in which the balance between colonization of the vaginal tract by the pathogen and local immune defense changes. The result is ascending invasion of the pathogen into the uterus and colonization of the fetus. Infection of the fetus with strains of *GBS* and other infectious agents can also occur during childbirth [4, 7, 28, 32].

When studying the mechanism of maternal infection with *GBS* strains, membranous vesicles of *GBS* (*GBS* MVs) were found. *GBS* colonies in the vagina secrete MVs that travel to the upper genital tract and can cause extensive collagen degradation and tissue destruction in the fetal sacs, leading to fetal injury and preterm birth [7, 28, 33, 34, 35].

It has been established in mice that *GBS* MVs can cause preterm labor and fetal injury when administered prenatally [33] and exacerbate morbidity and mortality in GBS - infected mice [29]. *GBS* MVs are filled with virulence factors such as, nucleic acids, specific lipids, hyaluronate lyase, C5a peptidase and sialidase *GBS* MVs [33, 35].

GBS MVs can penetrate into cell lines: HeLa, human lung epithelial cell line (A549), human keratinocyte cell line (HaCaT), differentiated macrophage - like cells (dTHP - 1) and mouse dendritic DC2.4GBS (A549 [34]. The effect of *GBS* MVs on several cell types explains the pleiotropic manifestations of *GBS* infection [36].

N. K. Kurian, and D. Modi (2022) studied in detail several factors that determine the virulence of *GBS* strains and their ability to induce preterm birth. These are MVs, β - hemolysin, hyaluronidase, and Cas9. These factors activate inflammation at the fetal - maternal border and contribute to the stimulation of preterm labor. This inflammation may be caused by the activation of NLRP3 - mediated inflammasome pathways, including activation of Toll - like receptors, which recognize conserved microorganism structures and activate a cellular immune response. The increased secretion of IL - 1β and IL - 18 observed in human macrophages treated with *GBS* pigment (β - hemolysin) can induce inflammasome activation. It was also found that fetal damage by hemolytic *GBS* pigment can also occur in a manner independent of NLRP3 - inflammasome [7].

Genetic studies of GBS strains

The study of the genome of three strains of group *B strept*ococcus (serotypes Ia, III and V) made it possible to establish where the classical virulence genes are mapped. This provided insight into the metabolism and regulation of the microorganism and how these genes affect its virulence. These research results open up an opportunity to search for new means of preventing group *B streptococcus* infection in infants [23].

A study was conducted on the prevalence of various *GBS* capsular genotypes among at - risk pregnant women in Brazil. *GBS* capsular genotypes occurred with the following frequency: Ia– in 35.5%, Ib 6.5%, II 11.6%, III 10.2%, IV 1%, V 34.1%, VIII 0.3 %. Two isolates (0.7%) were not genotyped by the method used. No statistically significant correlation was found between gestational age, demographics, and capsular genotype distribution. According to the authors, the inclusion of capsular genotypes Ia and V in future vaccines will cover 69.6% of capsular genotypes in this population. [37].

The development of *GBS* vaccines is challenging because capsular polysaccharide vaccines have low immunogenicity in vivo. L. S. Thoma and L. C. Cook (2022) believe that the addition of a protein conjugate will improve immunogenicity and strain coverage among *GBS* serotypes. The authors investigated the role of the *BvaP* protein in vaginal *GBS* colonization. *BvaP* was previously identified as the gene (determining the synthesis of the corresponding protein) with the highest expression in the transcriptome of the *GBS A909 strain.* The absence of *BvaP* was then found to affect the ability of *GBS* to attach to extracellular matrix components and human vaginal epithelial cells, and the ability of the *ΔbvaP* mutant to colonize the vaginal tract in a mouse model was significantly reduced. Morphological changes in bacterial shape, chain length and clustering were also observed in the knockout mutant strain. Given its high level of expression in vivo, its high degree of conservatism among *GBS* strains, and its role in vaginal colonization, *BvaP* may be a suitable target for *GBS* vaccination and/or drug therapy [28].

Li Zhang et al, (2021) conducted a genetic study of 54 invasive *GBS* strains isolated from neonates and pregnant women with invasive *GBS* disease. The most common sequence type of the hypervirulent *GBS* clone in infants was

ST10 (72.2%, P<0.05), followed by *ST23* and *ST19*. The *ST10* strain was also the leading sequence type in the colonization of pregnant women (44.4%, P<0.05). All isolates carried at least one pilus islet. The most common pilus islet was *PI - 1+PI - 2a* (85.2%, P < 0.05), followed by *PI - 2a* and *PI - 2b*, which was especially common in infections in the infant [27].

GBS can be classified genetically using multilocus sequence typing. Among the global sample of strains, four main types of sequences were found: *ST - 1*, *ST - 17*, *ST19* and *ST23*. Of these, *ST - 1* and *ST - 19* were associated with asymptomatic carriers, *ST - 23* was common in both asymptomatic carriers and patients with invasive diseases. Strains of *ST - 17* serotype III have been associated with neonatal invasive infections [38]. A study of invasive isolates from Taiwan showed that *ST - 1* and *ST - 17* cause disease in the mother and newborn [39]. *ST - 17* strains have been found worldwide and are associated with increased susceptibility to neonatal meningitis and antibiotic resistance [40].

Risk factors for neonatal infection caused by Streptococcus B

According to Jjing Huang et al (2019), premature rupture of fetal membranes and amniotic fluid shedding >18 hours and chorioamnionitis may increase the risk of *GBS* colonization in preterm infants **[**21].

As mentioned by T. C. Bank and, A. Sciscione (2022), the percentage of infants at ≥35 weeks gestation and with suspected intrauterine infection (including *GBS*) who were admitted to the neonatal intensive care unit with a diagnosis of maternal chorioamnionitis ranged from 6.0 to 91.7% with considerable variation between hospitals [32].

J. Raymond et al, (2007) considered viral infection as a risk factor for *GBS* infection in newborns. They examined 5 newborn infants with late - onset *GBS* infection between 5 and 12.5 months of age.2 infants had meningitis and 3 infants had septicemia. Viral infection was proven in 4 infants and suspected in one infant who had rash and pharyngitis. The authors believe that viral infection may provoke late - onset disease in colonized infants with *GBS* [41].

Antibiotic therapy for GBS infection

Ampicillin with aminoglycoside is recommended in infants under seven days of age. Broader - spectrum therapy should be prescribed if there is concern about resistance to ampicillin, especially in infants with very low birth weight. Ampicillin and ceftazidime are recommended for infants 8 to 28 days old, and ceftriaxone is recommended for infants 29 to 90 days old in the absence of signs of meningitis or severe disease. Vancomycin may be added if there is evidence of meningitis or in patients in critical condition [24]. Probiotics are prescribed for gastrointestinal dysbiosis prophylaxis [25, 42].

Antibiotic therapy should be based on antibiotic sensitivity analysis of the pathogen. This is important because there is a worldwide increase in multidrug - resistant strains of *GBS* [5, 7, 1725].

Sensitivity analysis of 1, 262 *GBS* isolates to antibiotics, which was performed in France between 2007 and 2019, showed that all isolates were sensitive to penicillin, amoxicillin and vancomycin. Resistance to tetracyclines did not change during the study period and involved 91% (95% CI, 89 - 92%) of strains and was due to the genetic determinant *tet (M*) in 92% of cases. Only 3 isolates (0.2%) (95% CI, 0.1% - 0.7%) showed high levels of resistance to gentamicin. High levels of amikacin resistance increased from 0% (95% CI, 0% - 7%) in 2007 to 18% (95% CI, 12% - 26%) in 2019 (p<0.0001). Resistance to erythromycin increased from 22% (95% CI, 13% - 34%) to 30% (95% CI, 23% - 38%; p= 0.019). Resistance to erythromycin was mainly the result of ribosome modifications that confer cross - resistance to lincosamides and are encoded by the genetic determinants *erm* (*B*) (64%), *erm* (*A/TR*) (13%), or *erm* (*T*) (1%). These cases were 22% the result of a leakage mechanism encoded by the genetic determinant "*me f*" [19]. The same authors report the emergence of an *MDR CC17 GBS* subline that shows resistance to tetracyclines, macrolides, and lincosamides at the same time.

The highest rates of resistance of *GBS* strains in Brazil were to tetracyclines, and high rates were also to clindamycin and erythromycin [22, 43].

Lakshmi M Warrier et al (2022) noted high clindamycin resistance in 20% of the GBS strains in South India. All maternal GBS isolates were sensitive to ampicillin, cefotaxime, penicillin and vancomycin [8].

Back in the late 1970s and early 1980s, the concept of early antibiotic administration to low birth weight infants was recommended based on the effectiveness of such antibiotic policies [1, 2]. In subsequent years, as in the present, this approach has been maintained and demonstrated to be effective [5, 8, 19, 43].

Strict adherence to recommendations for cardiopulmonary resuscitation in patients with severe *GBS* infection is advisable. First - line measures include prompt administration of fluids in severe sepsis and septic shock; inotropes (dopamine, dobutamine, adrenaline) should be administered within 1 hour of the start of treatment, if there is no response to volume filling [25].

Life - threatening infections require immediate and aggressive use of antimicrobials. For empirical therapy of late - onset sepsis in infants 8 to 28 days old, ampicillin plus gentamicin is recommended. If meningitis is suspected, ampicillin plus cefotaxime should be used, with a higher recommended dosage of ampicillin. When *GBS* infection is confirmed, penicillin G (or ampicillin as an acceptable alternative) is recommended. Despite some reports of penicillin - resistant *GBS* strains, beta - lactams remain the antibiotic of choice. Based on expert opinion, intravenous antibiotics for 10–14 days are recommended for undiagnosed sepsis (without a detected lesion) and uncomplicated meningitis, but longer courses (eg, 4 weeks for ventriculitis) may be required for meningitis complication. For septic arthritis or osteomyelitis, three to four weeks is recommended [25].

As noted in their review of VN. Raabe and AN. Shane (2019), penicillin G remains the mainstay of invasive disease treatment. Generally, *GBS* is susceptible to other beta - lactam antibiotics, including ampicillin; cephalosporins of the first, second and third generation; and carbapenems, however, the level of activity of these drugs is different. Alternative treatments include clindamycin, erythromycin, fluoroquinolones, and vancomycin in patients with severe allergy to beta - lactam antibiotics. A number of studies have shown resistance in clinical *GBS* isolates to clindamycin, erythromycin and fluoroquinolones, and resistance to vancomycin has also been reported [44].

Human milk oligosaccharides (HMOs) against group B streptococci

Human milk oligosaccharides show antimicrobial activity against *GBS*, and *GB*S - specific IgA in milk and colostrum are associated with both increased *GBS* clearance and reduced risk of *GBS* LOG in infants **[**25]. HMOs make up 8 to 20% of human milk and have a prebiotic effect on the infant's gut [45].

The question of the possible use of HMOs for the sanitation of the maternal birth canal and the prevention of intrauterine *GBS* infection is currently being considered. A study was conducted using the mouse vaginal *GBS* colonization model [46]. The authors found that HMOs concentrations similar to those in colostrum and breast milk inhibit the growth of wild - type *GBS* and have bacteriostatic activity against these strains. L. M. Lyon and K. S. Doran (2022) report that HMOs can sensitize *GBS* to intracellular antibiotics and show synergy with conventional antibiotics, altering their biofilm structures. HMOs do not affect the protective microbiota of the vagina, in particular the growth of *Lactobacillus spp*. [45]. These studies open the possibility of using new natural medicines to reduce *GBS* colonization and improve neonatal health.

Probiotics to protect against GBS infection

The vaginal microbiome is malleable, so treatment and prevention may include drugs based on the protective microflora of the vagina and gut (*Lactobacillus spp., Bifidobacterium spp.)* [47]. Clinical trials of oral probiotics *Lactobacillus spp. (L.)* (NCT01577108) in humans showed that administration of *L. rhamnosus GR - 1* and *L. reuteri RC - 14* during the third trimester of pregnancy reduced the incidence of rectovaginal *GBS* colonization at delivery [48, 49].

J. M. Cajulao, and L. Chen (2021) showed that *Lactobacillus rhamnosus* reduces the cytotoxic effects of group *B streptococcus* on *HeLa cells* [50]. The *L. salivarius CECT9145* probiotic also reduced rectovaginal *GBS* colonization during pregnancy [51].

Positive clinical effect was obtained when using the complex drug Bifilis (VIGEL). One dose of the drug contains live *Bifidobacterium bifidum I* (at least 10^7) and lysozyme hydrochloride (10±1 mg). The drug is administered as oral lyophilisate and/or suppositories intrarectally and intravaginally [42].

Screening and prevention

Prevention of *GBS* infection in infants and their mothers includes universal screening for *GBS* infection in pregnant women, if possible, and preventive treatment of the infection in the mother and infant [5, 42, 52]. The rather high incidence of contamination of the rectum and birth canal of women (according to the authors in different countries, this figure varied in different years from 4.2% to 28.4%) is the rationale for this [9, 21, 22, 53]. According to Janek L, et al (2004), prophylactic intrauterine antibacterial therapy given to pregnant women with penicillin or clindamycin in the presence of a history of allergy has completely eliminated the infection of infants with group *B streptococcus*. In the control group of newborns whose mothers did not receive prophylaxis, the incidence of *GBS* disease in newborns reached 7.5 per 1, 000 newborns. The incidence of invasive neonatal *GBS* was 2.6 per 1, 000 newborns [53].

The American Academy of Pediatrics (AAP) and the American College of Obstetricians and Gynecologists (ACOG) recommend intrapartum antibiotic prophylaxis for the following categories of patients: 1) all women at delivery who have positive antenatal vaginal - rectal cultures for *GBS* colonization; 2) women with *GBS* - induced bacteriuria during pregnancy, 3) women with preterm birth or premature rupture of membranes before 37 weeks' gestation 4) *GBS* screening should be performed between week 36 and the end of week 37, 5) women at 37 weeks' gestation or later who have not been screened for *GBS* if they develop a temperature of 100.4° F (38° C) or higher or have ruptured membranes and have not delivered within 18 hours or longer.6) Women in labor with unknown *GBS* status in this pregnancy, but with colonization of *GBS* in a previous pregnancy, and 7) newborns before 35 weeks of gestation should receive empirical antibiotic therapy if the effect of intrapartum antibiotics, intrapartum fever in the mother, or signs of illness in the newborn [24].

Penicillin, ampicillin, or cefazolin are recommended for prophylaxis, and clindamycin and vancomycin are reserved for cases of severe maternal allergy to penicillin. Special consideration should be given to infants born at less than or equal to 35 weeks' gestation in assessing the risk of *GBS* [54]. Cefazolin and vancomycin are also recommended for intrapartum antibiotic prophylaxis in women with penicillin allergy with low risk of anaphylaxis. Erythromycin is not recommended because *GBS* is becoming increasingly resistant to macrolide antibiotics. Vancomycin is recommended for women with clindamycin - resistant *GBS* isolates with penicillin allergy and high risk of anaphylaxis [24]. Application of these recommendations reduced the incidence of *GBS* infection in newborns from 0.37 cases per 1, 000 live births in 2006 to 0.25 cases per 1, 000 live births in 2015. Among newborns with a gestational age of 37 weeks or older, there were fewer than 2 cases per 10, 000 live births in 2015 [55]. Vaginal - rectal culture is not required if antenatal urine culture has already confirmed *GBS* colonization. Hospital PCR tests are not recommended to determine maternal colonization because of varying sensitivity to antibiotics or lack of this information [24].

Dotters - Katz, Sarah K. et al (2022) recommend the following approach to the prevention of neonatal *GBS*

infection. Screening for *GBS* should be performed between week 36 and the end of week 37. However, prophylactic antibacterial treatment should be given to patients with *GBS* in urine ahead of time regardless of the number of colonies in culture. *GBS* - positive patients with premature and preterm fetal rupture after 34 weeks are not candidates for a wait - and - see approach because of the higher rate of neonatal infectious complications in this population [56]. Screening of pregnant women for carriage of group B streptococcus in the intestines and birth canal is mandatory in a number of countries (USA, France, Germany). Screening is selective when at risk in the UK and Sweden.

The question of the possible use of *Lactobacillus spp*. to colonize and protect the vaginal tract from bacterial pathogens, including *GBS*, for the prevention of neonatal *GBS* disease. In an in vitro experimental study using *HeLa cells*, it was found that *GBS* causes detachment of *HeLa cells* and destruction of the F - active fibers of these cells, reduces the length and number of microvilli on the surface of *HeLa cells*, as well as the size of secreted vesicles. *Lactobacillus rhamnosus* partially inhibits *GBS* - dependent destruction of microvilli and vesicles and protects cells against *GBS* colonization [50].

One of the most promising and effective methods of preventing *GBS* infection in newborns and their mothers is the use of vaccines against this bacterial pathogen. Group *B Streptococcus* vaccines (*GBS* vaccines) under development should contain the most common capsule genotypes that are identified in the target population. Epidemiological studies on *GBS* carriage among pregnant women are needed in low - and middle - income countries to inform a vaccination strategy against the development of neonatal *GBS* sepsis [3, 37]. Introduction of *GBS* vaccine to mothers in low - and middle - income countries could be of significant benefit in reducing the incidence of *GBS* in early life [5, 15].

The trivalent Novartis/GSK vaccine (Novartis/GSK GBS3) consists of a *GBS* Ia/Ib/III conjugate. It is considered safe for pregnant women, causes the synthesis of high titers of maternal antibodies that are transmitted to infants through the placenta. [57]. However, this vaccine does not include all clinically relevant serotypes and may result in the selection of non - vaccine strains. Patients known to be simultaneously infected with multiple *GBS* serotypes [58]. Promising is a hexavalent CPS conjugate vaccine derived from serotypes Ia, Ib, II, III, IV and V [13]. This Pfizer *GBS*6 vaccine was well tolerated in healthy adults and induced high antibody titers in preliminary studies. [5].

4. Conclusion

GBS infection remains a significant challenge in neonatal and maternal health. Despite advances in prevention and treatment, the infection continues to pose risks due to antibiotic resistance and virulence factors. This review highlights the need for ongoing research to develop effective vaccines and improve prophylactic measures, aiming to reduce the incidence and impact of GBS infections.

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