



STREPTOCOCCUS GROUP B IN FEMALE GENITAL TRACT AND IS IMPACT ON NEWBORNS

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| Article history: | Abstract: |
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| <p>Received: 10th August 2021 Accepted: 11th September 2021 Published: 30th October 2021</p> | <p>Streptococcus agalactiae, GBS, or group B streptococcus, is a gram-positive Streptococcus found in the human vagina and rectum. On a woman's vaginal or rectal mucosa, GBS can replicate quickly, repeatedly, or continuously. Worldwide, There are 0.38 incidences of systemic invasive GBS per 1000 pregnant women, with a death rate of 0.2%. GBS affects around 13,604 Chinese people each year, with 1141 GBS-related newborn deaths occurring each year. When a pregnant woman transmits GBS to her unborn child, the baby is at risk of developing the disease at an early or late stage. This makes GBS a prevalent cause of neonatal infection and death. Pregnant women between 36 and 37 weeks gestational age should be screened for GBS, and those with positive results should be treated with intrapartum antibiotic prophylaxis (IAP). This recommendation was made by the American College of Obstetricians and Gynecologists in 2019.</p> <p>The GBS virus infects around 21 million pregnant women every year, and it is also responsible for 35% of neonatal fatalities. This means that identifying GBS infections throughout pregnancy and after birth is critical.</p> |

Keywords: Group B Streptococcus , Pregnant Women, Newborn Deaths, Infectiongbs

INTRODUCTION:

It was first isolated in 1930 by Rebecca Lancefield in milk and cows infected with bovine mastitis. Lancefield discovered it in the vaginal canals of women who had no visible symptoms. However, it wasn't until 1938 that its human pathogenicity was discovered, when three reports of deadly postpartum infection were reported. In the 1960s, when the incidence of infection in adults and neonates rose, the human prevalence was determined. (Lancefield et al., 1933) ,(Lancefield et al., 1935)

It has recently emerged as the most common cause of invasive newborn infection, as well as a dangerous pathogen for immune-compromised individuals, pregnant women, elderly patients, diabetes, neuropathy, cancer, and liver fibrosis. (Rosa et al., 2017) .

CHARACTERS AND VIRULENCE FACTORS :

Infected newborns are more likely to suffer and die from Streptococcus agalactiae than healthy newborns. One of the most common causes of neonatal sepsis and meningitis, as well as unfavorable pregnancy outcomes like stillbirth and miscarriage, is widely recognized around the world.(Chukwu et al., 2015). It is a Gram-positive, β -hemolytic opportunistic bacterium (Anna et al., 2017)In healthy females, it was observed to colonize the genital and GI tracts. One of the leading causes of invasive neonatal illness is mother-to-child transmission of GBS. (Brzychczy et al., 2012)It is also a leading cause of infections in the elderly and immunocompromised patients. GBS is divided into 13 serotypes based on capsular polysaccharide (CPS) antigens. Among the 13 variants, 9 are clinically significant: Ia, Ib, II, III, IV, V, VI, VII, and VIII. (Arabestani et al., 2017).

Except for the Lancefield group B cell-wall specific polysaccharide antigen, only Streptococcus species possess it. GBS can be broken down further. into 10 Type-specific capsular polysaccharides enable the identification of several serotypes (Ia, Ib, and II through IX). (El Aila et al., 2017)(Slotved et al., 2007)

There are essential virulence factors with antiphagocytic functions in the capsular polysaccharides of GBS isolates, and these polysaccharides are exploited in the development of novel multivalent GBS vaccines. The CPS has been employed in the detection of serotypes. The prevalence of GBS may shift over time due to changes in factors such as age at first sexual experience or parity.(Shrestha et al.,2020)

GBS VIRULENCE FACTORS THAT ENHANCE VAGINAL COLONIZATION:

The female rectovaginal tract is the principal host niche where GBS survives as an asymptomatic colonizer. Many of the same tactics used by GBS to colonize the vaginal area, including adhering to host surfaces and undermining immune defenses, are used by GBS to colonize the vaginal area. In addition, it promotes disease transmission and harms vulnerable host niches, such as neonates. Specific virulence traits have evolved in some GBS strains throughout time, increasing their ability to disseminate and evade the immune system while also causing tissue damage. GBS modulates the expression of virulence factors at the cellular level via signal transduction systems, which perceive and adapt to different host environments and thereby promote survival outside the lower genital tract. This section begins with a brief introduction to GBS's known signal transduction systems and then lists particular elements that GBS uses to enhance vaginal colonization and spread. (Armistead et al., 2019).

ADHESIONS:

Adherence to epithelial cells via surface-associated adhesions is a significant mechanism used by GBS to colonize the lower genital tract. Among these are fibrinogen-binding proteins (Fbs), the immunogenic bacterial adhesin (SfbA), the hypervirulent GBS adhesin (HvgA), laminin-binding proteins (Lmb), C5a peptidase, and pili, as well as plasminogen-binding surface proteins (PbsP) (BibA). These adhesions can bind GBS to extracellular matrix components (ECM). Cell invasion and immunological evasion are two more functions of GBS adhesins. GBS must contact host cells via adhesins to create a niche in the digestive and vaginal tracts. mucosa, as well as penetration into additional host compartments. GBS's ability to overcome host barriers is strengthened when it binds to surfaces, which is most likely why the improved ability of GBS to bind host cells boosts its pathogenic potential. (Rosenau et al., 2007).

CERVICAL MUCUS PLUG COMPOSITION:

When a woman is pregnant, a thick plug of mucus called a cervical mucus plug (CMP) develops in the cervical canal. Some people's CMPs contain proinflammatory cytokines and antimicrobial molecules such as secretory leukoprotease inhibitor 1, while others have antimicrobial substances such as lysozyme, lactoferrin, and calprotectin (Becher et al., 2009). The CMP's role in defending against harmful bacteria is still unclear, although a study of 60 human CMPs indicated that proteins linked with the CMP activated leukocytes in whole blood, boosting GBS mortality. Except for CMPs still containing antibiotics provided after Caesarean section and before CMP collection, the concentration of antimicrobial components was insufficient to kill several strains of GBS. These findings demonstrate that GBS has devised strategies to neutralize the antibacterial effects of CMPs. GBS may use CMP resistance to boost vaginal colonization during pregnancy, a disease with specific immunological traits that have been linked to the virus. Resistance to antimicrobials in the CMP may contribute to GBS crossing the cervix, however, the mechanisms by which GBS bind to and ascend the CMP are still unknown. (Vornhagen et al., 2018).

TRANSMISSION:

At this time, the method of transmission of this bacterium is unknown. It is found in the female reproductive system and digestive system, and it is not disseminated by water or food. This infection affects a large number of people, but the transmission of the pathogen to the fetus poses the greatest danger. The majority of pregnant women do not display signs of the condition because germs are present in the vaginal and rectum at the time of birth, but they travel and have an impact on newborn children during pregnancy. At the time of birth, they can infect newborns and cause serious diseases. According to a 20-40% study in the United Kingdom, roughly 319,000 neonates were infected in 2015, resulting in 90,000,000 deaths worldwide. Newborn head injuries, premature births, infections, and the birth of a dead fetus have all been associated with the bacterium. (Nanduri et al., 2019). A study in Ethiopia carried by Gizachew et al., 2020 showed that 88 confirmed transmissions of the bacteria at birth within 30 minutes after birth by taking 385 swabs of the ear and nose for newborns, the presence of bacteria was found in 385/62 and 16.1% of all newborns. The time to collect samples is very important. (Gizachew et al., 2020) It is preferable to take vaginal and rectal scans together for pregnant women for more than five weeks before birth and to recommend that all pregnant women must be screened for the colonization of GBS 35 to 37 weeks of pregnancy, According to ACOG, the first time this information was made public was in 1996. The CDC and the American Academy of Pediatrics also announced similar findings (AAP). When there is an infection, the mother's protective antibiotics must be taken during labor to avoid transmission to the newborn (John et al., 2020).

THE SIGNS AND SYMPTOMS OF GBS BACTERIA VARY BY AGE AND INCLUDE:

- 1-Non-pregnant women: symptoms are fever, headaches, difficulty in breathing and coughing in case of pneumonia, skin pain and swelling in case of cellular tissue inflammation, and burning sensation during urination.
- 2- Pregnant women: abdominal swelling, fever, and tenderness of the uterus.
- 3- Newborns (first week): low blood pressure, shortness of breath, bacteremia
- 4-Infants between the ages of one week and a few months suffer from inactivity and seizures, fever, anorexia, irritation, blue-colored skin. Meningitis, pneumonia (Hanna *et al.*, 2020).

In neonatal medicine, two types of clinical conditions affect newborns and become more severe during the first three months of birth. The first is GBS infection during the first week of life, Early-onset disease EOD(occurring 0-

6 days after birth) usually, during the first 24 hours of birth, which is 60-79%, the patterns (Ia, Ib, II, IIim, V) are responsible for the infection. It has caused serious problems such as meningitis, pneumonia, sepsis and very few children die even with treatment. (ROSE *et al.*, 2017).

The second Late-onset disease LOD is a GBS infection that appears after birth (7-90 days), symptoms appear in the form of bacterial inflammation, and serotype IIII that can be obtained from the most common community or hospital (Edwards *et al.*, 2015).

Newborn babies with GBS may suffer from long-term complications such as developmental disorders, deafness, and especially children with meningitis. Despite good care in the United States for newborn babies, 4-9% of children with GBS die. Adult GBS infection can be fatal in case of severe infection such as pneumonia and blood embolism, with approximately 1 in 20 non-pregnant women dying for GBS (Votava *et al.*, 2001). The study proved. Taking scans of the vaginal recto vaginal leads to increased access to GBS bacteria (EI Alia *et al.*, 2010).

MATERIALS AND METHODS

Samples are taken from the vaginal and anal area using sterile scans to detect GBS bacteria in pregnant women between 35-37 weeks of pregnancy. Carrier communities such as Todd-Hewitt broth, supported by 8mg/ml of Gentamycin, nalidixic acid, use 15 µg/ml and sheep blood, As well as the carrier medium (Stuart, Amies), the carrier medium can be saved at fridge temperature for 4 days in case of late bacterial diagnosis. The sample is striking on Bacterial Selective media such as Neomycin and Nalidixic Acid medium (NNA) (Dunne *et al.*, 1999) It contains the blood of sheep, nalidixic acid, and the antibiotic Neomycin, as well as the medium (CAN) Columbia agar, which has 5% blood Sheep, 10mg/ml colistin, as well as nalidixic acid (15mg/ml) and Central Granada agar shown in the image) (2), on which colonies appear in orange. Also in the middle of chromium Strepto B agar (Wollheim *et al.*, 2017) formed red colonies based on phosphatase production. (Morita *et al.*, 2014)



Fig. 2 Images of *Streptococcus agalactiae* on Granada agar, anaerobic incubation

PCR Serotyping:

Based on type-specific capsular antigens, GBS are divided into ten groups; Ia, Ib, II, III, IV, V, VI, VII, VIII, and IX. Many methods are available to carry out GBS serotyping which include:

- 1-Lancefield precipitation test (the standard method)
- 2-Latex agglutination method (commercial kits that serotypes isolate phenotypically).
- 3-Real-time PCR
- 4-Conventional PCR (recommended and validated).
- 5-Whole-genome sequencing.

Real-time PCR:

A molecular approach that uses real-time PCR assay which targets the CAMP factor (cfb gene: that promotes pathogen entry into host cells and eases its intracellular survival and spread (Kuwait *et al.*, 2013) to detect *S. agalactiae*. the CAMP factor encoding gene (cfb) on GBS pathogenicity . This gene is ubiquitous in GBS strains, hence a CAMP test or PCR search for the gene to distinguish GBS from other Streptococcus species was commonly utilized. (Hensler *et al.*, 2008) This assay is useful for direct detection from clinical samples when culture is not available or negative (Kim *et al.*, 2020). (Mousavi *et al.*, 2016) .

Real-time PCR targets for *Streptococcus agalactiae* :

The table (1) below shows the genetic sequence of bacteria by the Real-Time PCR method (Diaz *et al.*, 2013). Vaccination against GBS is favored by most women but they are at the early stages of development (Philip *et al.*, 2018). Infection control policies like hand hygiene, environmental disinfection can prevent GBS outbreaks and helps neonates who are vulnerable to a quire nosocomial infections (Kim *et al.*, 2020).

GBS real-time PCR assays like Xpert GBS (Cepheid, USA) and Xpert GBS LB are now available (Cepheid, USA). Using the Cepheid Gene Xpert System, which extracts, amplifies, and detects DNA automatically, nations that have been approved by regulatory bodies could use the system outside of laboratories, with simple operation and results in less than an hour. This would make a rapid diagnosis of GBS more practical) Armistead *et al.*, 2020.(.Nearly all GBS have the CAMP factor encoding gene) Choera *et al.*, 2020 (targets this gene. Additionally, Xpert GBS and Xpert GBS LB both use the Gene Xpert System to screen for GBS before and during pregnancy. Following the findings of)Vieira *et al.* 2019), Xpert GBS LB require enrichment before detection, whereas Xpert GBS tests the primary specimen immediately.)Han *et al.*, 2021).

Table (1): Genetic sequence of *S. agalactiae* by Real-time PCR (Kathleen et al., 2016).

| Real-Time PCR Target | Primer/Probe | Sequence (5' – 3') | Gene | Accession No. | Location | Conc. (nM) |
|----------------------------------------------|--------------|------------------------------------------------------|------------|---------------|----------|------------|
| <i>Streptococcus agalactiae</i> ³ | Forward | GGG AAC AGA TTA TGA AAA ACC G | <i>cfb</i> | JQ289578 | 207 | 200 |
| | Reverse | AAG GCT TCT ACA CGA CTA CCA A | | | 311 | 200 |
| | Probe | 5'-FAM-AG ACT TCA TTG CGT GCC AAC CCT GAG AC-3'-BHQ1 | | | 263 | 200 |

About one-quarter of all healthy adult women in the United States are colonized by the Group B Streptococcus (GBS), which is the leading infectious cause of early newborn morbidity and mortality (Baker et al, 2021). This study looked at the clinical performance of the PhenoMatrix (PM) chromogenic detection module (CDM) digital imaging software for the detection of GBS from LIM broth plated the Chromatin ID chromogenic medium containing strepto B (ChromID) as shown in image (2) processed by the WASP program. Examining the PM CDM's outcomes in comparison to results from manual culture review and molecular detection, researchers found that the PM CDM outperformed both of the other methods. After 48 hours, ChromID alone had an 84.5 percent sensitivity and 94.7 percent specificity in comparison to nucleic acid amplification, which required more time. the investigation that goes into great detail (NAAT) Compared to nucleic acid amplification tests, ChromID's sensitivity and specificity were 84.5 percent and 94.7 percent higher after 48 hours. There were no true-positive GBS isolates missed when using PM CDM to detect ChromID GBS with 100 percent sensitivity compared to the composite reference for positivity. a different one of GBS detection methods was evaluated at 48 hours for sensitivity and found to be 98% sensitive for NAAT; ChromID with PM CDM; and ChromID on its own. ChromID with PM CDM had a sensitivity of 96.7 percent when compared to NAAT and ChromID by themselves. ChromID's sensitivity was comparable to molecular detection when used in conjunction with the PM CDM. Eight new positive specimens were discovered by the algorithm because the system was never called a culture-negative that was later proven to be positive by manual reading.

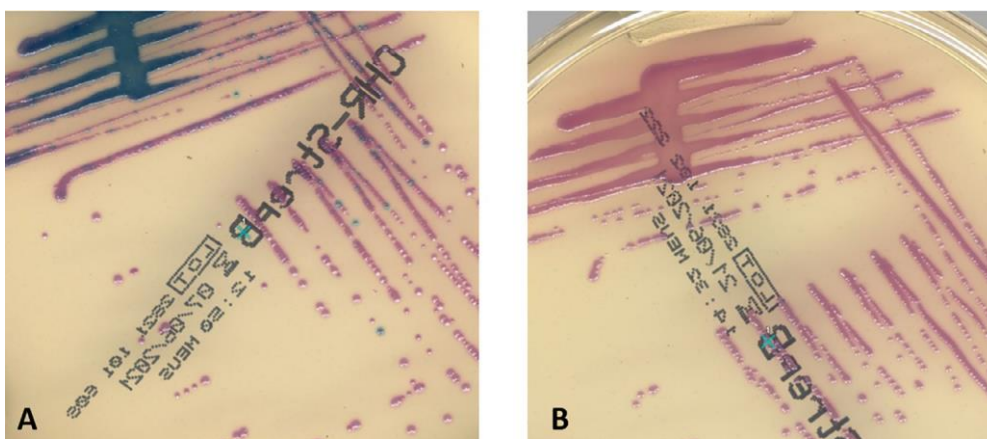


Fig. 2 Images of representative cultures on CHROMagar StrepB medium. (A-B) *Streptococcus agalactiae* – GBS (Foschi et al., 2021)

TRETMENTS :

To prevent the transfer of GBS to the fetus, antibiotic prophylaxis should begin at least four hours before delivery. Prophylaxis with shorter-term antibiotic therapy, however, may provide some benefit. You should start antibiotic prophylaxis for a patient regardless of whether or not labor and delivery are expected within the next four hours.(Verani et al., 2010).

Intravenous treatment is given at birth to prevent newborns from becoming infected with B-group swallows. Penicillin G is administered into the vein in the first dose of 5 million units, During labor, 3 million units are produced every four hours. Ampicillin is substituted for penicillin if the former is unavailable. A 2 g intravenous dose is given first, followed by a 1 g dose every 4 hours throughout labor. And if the patients have hypersensitivity, vascular edema, self-distress, or bad after taking penicillin, they should choose an antigen allergy. Clindamycin (mg 900 in the vein every 8 hours) or Vancomycin (mg 900 in the vein every 8 hours) are advised. It is regarded to be effective prevention of bacterial transmission to the fetus every 12 hours during labor and the commencement of antibiotic prophylaxis no more than 4 hours before birth. (Jisuvei et al., 2020)

For intrapartum prophylaxis, pregnant GBS carriers should take penicillin or ampicillin as a first-line antibiotic, according to the (CDC). Women with penicillin allergies can take erythromycin or clindamycin. Because of their limited

spectrum of activity and ability to reach high intra-amniotic concentrations, they've been studied as potential alternatives to conventional antibiotics. (Shrestha, *et al.*, 2020).

CONCLUSION:

We advise all Mosul maternity facilities to check pregnant women for GBS at 35-37 months of pregnancy because of the importance of these bacteria and their impact on newborns. DNA may be extracted, amplified, and detected automatically using the Xpert System. This makes it possible to quickly diagnose GBS using the Xpert System. Aside from the laboratory, countries where regulatory bodies have approved it could employ this technology outside of the lab because it is easy to use and gives results quickly (in less than an hour).

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