8 Pathogenesis, Virulence Factors, and Antibiotic Resistance of Group B Streptococcus

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Contents

Abstract

Streptococcus is an important genus in the gram-positive coccus, belonging to family Streptococcaceae. The members of the genus *Streptococcus* are biomedically relevant owing to their widespread pathogenic profile causing severe healthcare issues such as pharyngitis, pneumoniae, neonatal meningitis, sepsis, endocarditis, bacteremia, and urinary tract infections (UTIs). The diversified species of genus *Streptococcus* are basically categorized based on the inherent hemolytic properties,

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i.e., either facilitating the oxidation of iron in hemoglobin within the red blood cells (Alpha-hemolytic) or complete rupturing of red blood cells (beta-hemolytic). The beta-hemolytic group of *Streptococci* are further classified into several serotypes using Lancefield grouping system which is based on the presence or absence of specific carbohydrate moieties on the bacterial cell wall. Among the different serotypes, Lancefield group A (Group A Streptococcus) and Lancefield group B (Group B Streptococcus) are critically important in the medical settings based on their ability to cause life-threatening diseases in the immunocompromised individuals. Among the different species of genus *Streptococcus*, the most clinically relevant species are *Streptococcus pneumoniae* and *S. viridians* (belonging to Alpha-hemolytic group of *Streptococcus*). Apart from Alpha-hemolytic Streptococcus, Lancefield groups A and B (also known as "group A strep" and "group B strep") are also considered to be highly relevant in clinical and biomedical setup. Group B Streptococcus is an opportunistic pathogenic bacteria causing severe neonatal sepsis, meningitis, bacteremia, urinary tract infections, endometritis, maternal bacteremia, and other associated diseases. The disease severity and chronic infection profile of GBS could be attributed to the presence of specific virulence determinants such as pore-forming toxins and capsular polysaccharides. The epidemiological profile of GBS gained considerable attention owing to its ability to exhibit resistance against conventional antibiotic treatment by forming recalcitrant biofilms. In the fight against GBS infection, specific antibiotics like penicillin and vancomycin, high throughput therapeutic strategy like intrapartum antibiotic prophylaxis (IAP), and public awareness programmes are considered to be effective in controlling the bacterial infections. In addition, novel drug molecules from natural sources could also be utilized as prolific arsenal against GBS infections. Despite the development in the therapeutic strategies to control GBS infections, the mortality and morbidity caused by GBS infections remain an uphill challenge for the scientific community. In this context, it is imperative to quest for novel strategies in preventing the GBS infections and that could be implemented through public awareness programmes and prenatal screening workshops apart from conventional therapeutic approach.

Keywords
Group B Streptococcus · Pathogenesis · Antibiotic resistance · Biofilm · Maternal immunization

8.1 Introduction

Since the discovery of antibiotics to treat microbial infections, an array of antibiotics belonging to different classes have been discovered and are effectively used as an arsenal against microbial infections and related health consequences. Though there is a marked development in the field of finding novel antibiotics form last half-decade;

the evolutionary changes in the microbial spectrum also emerge as lethal challenge to the available antibiotics in the form of resistance. The incidence of resistance to conventional antibiotics becomes more prominent from last few decades, thereby microbial infections remain a significant public threat both at sociological and economical levels (Rajagopal 2009). The advent of the resistance to antibiotics has also put a significant burden to the developing countries as well as under-developed countries. Among the pathogenic bacteria causing severe public health issues and showed resistance towards the conventional antibiotics, the emergence of Streptococcal infections also gained considerable attentions due to their detrimental effects on human health such as meningitis, cellulitis, pneumonia, pericarditis, pharyngitis, and urinary tract infections (UTIs). A majority of the *Streptococcus* sp. are found to be commensal microorganisms owing to their ability to inhabit oral cavity and nasopharynx of human beings without affecting their physiological functions. However, the Streptococcal sp. also have the inherent ability to cause various chronic diseases and lethal infections in the form of superficial or systemic infection and in most cases without symptomatic infections and hence they are generally considered as opportunistic pathogens (Nobbs et al. 2015).

8.2 Grouping and Classification of Genus *Streptococcus*

The genus Streptococcus belongs to the Phylum Firmicutes and can be classified on the basis of their differential hemolytic activity, antigenic composition, growth characteristics, genetic features as well as biochemical characteristics. On the basis of hemolytic properties, the genus Streptococcus was differentiated into alpha-hemolytic, beta-hemolytic, and gamma-hemolytic types. According to the antigenic properties shown, the beta-hemolytic streptococci were grouped into different classes such as A-H and K-V. Among these groups, five groups such as A, B, C, D, and G have gained considerable attention based on their inherent potential to cause infections and disease conditions. Group B streptococci (GBS) are further sub-categorized into type I a/c, and III based on the presence of specific surface proteins as antigenic markers.

8.2.1 Group A Streptococcus (GAS)

Among the pathogenic *Streptococcus* sp., Group A Streptococcus (GAS) are known for their ability to induce severe infections such as pharyngeal and skin infections, necrotizing fasciitis, and toxic shock syndrome in humans. One of the interesting features of GAS colonization and subsequent infections is the involvement of highly complex regulatory network. The unique characteristic of this regulatory network is its differential regulation mechanisms under different environmental circumstances promoting diversity in the routes and manifestations of infection pathways in the hosts (Shelburne et al. 2008).

8.2.2 Group B Streptococcus (GBS)

Group B Streptococcus (GBS) is a beta-hemolytic group of catalase negative facultative anaerobe. The GBS has the inherent ability to colonize the oropharynx, gastrointestinal, and genitourinary tract in 10–30% of humans without any sorts of symptoms. The GBS is known for its ability to cause severe invasive neonatal infections such as neonatal bacteremia, sepsis, pneumonia, and meningitis. Apart from neonatal infections, GBS also tend to colonize adult human beings especially pregnant women with severe invasive infections such as endometritis, urinary tract infections, and occasionally, maternal bacteremia. The unique ability of GBS to cause severe infections could also be attributed due to their efficacy in infecting non-pregnant individuals in the form of sepsis and meningitis leading to increased mortality and morbidity (Rosa-Fraile and Spellerberg 2017; Skolnik et al. 2017). As per recent trends, GBS remains one of the most common causal agents for inducing severe neonatal sepsis and meningitis in the immunocompromised patients (Zimmermann et al. 2017). The lethality and severity of GBS infections could be observed from their ability to cause serious diseases not only neonates but also in pregnant women as well as non-pregnant immunocompromised individuals. In majority of cases, the GBS infections occur in the genital tract or placenta in pregnant women and lead to severe miscarriages and stillbirth issues. In addition, the immunocompromised individuals with diabetes, cancer, cirrhosis, HIV infection, and age factors could be instrumental in the onset of GBS infections (Chen et al. 2013).

8.2.3 Group B Streptococcus: An Overview

Streptococcus agalactiae (Group B Streptococcus, GBS) is an opportunistic pathogen colonizing the gastrointestinal and genitourinary tracts of health individual causing severe asymptomatic health issues. Apart from that, GBS also accounts for the leading cause of invasive neonatal infections (Lopez et al. 2018). The GBS has the inherent property of colonizing the genitourinary tract of 15–35% pregnant women who can transmit the pathogen to their neonate during childbirth and contribute to early onset disease (EOD) leading to severe sepsis and meningitis (Medugu et al. 2017). In addition to neonatal meningitis and sepsis, GBS is also associated with severe life-threatening syndromes such as necrotizing fasciitis and toxic shock syndrome (Lupo et al. 2014). The GBS colonization of the lower genital tract or vagina or rectum in pregnant women leads to asymptomatic bacteriuria, severe urinary tract infections, chorioamnionitis, postpartum endometritis, and bacteremia (Cho et al. 2019). Group B streptococcal infection in elderly individuals is strongly linked to congestive heart failure, neurologic illness, urinary tract infection, pneumonia, and soft tissue infection as the most common manifestations of infection.

Apart from human infections, GBS (*S. agalactiae*) also has the ability to infect other mammalian hosts as well as other vertebrates such as reptiles, amphibians, and fish in particular Tilapia (*Oreochromis niloticus*). The GBS infections in fish cause severe streptococcosis. The fish streptococcosis can be characterized by septicemia,

exophthalmia, and meningoencephalitis and put significant impact on the development of pisciculture sectors worldwide (Chideroli et al. 2017; Zhang et al. 2018). The diversified clinical manifestations by GBS in the immunocompromised individuals could be attributed to the presence of highly specific regulatory network which has the potential to induce efficient adaptability of bacteria under different environmental conditions. The highly complex regulatory network also allows the GBS to express specific virulence determinants thereby promoting the colonization and invasion of epithelial barriers of the host cells. These virulence phenotypes also allow GBS to develop resistance to severe stress conditions by bypassing the host immune mechanisms thereby contributing to the pathogenesis of infection (Otaguiri et al. 2013).

8.3 Pathophysiology of GBS

8.3.1 Epidemiological Characteristics of GBS Infections

The epidemiological severity of GBS infections in the neonatal period and up to 90 days post-birth has provided a greatest impact on human health. The GBS infections in neonates could be categorized into two types such as early onset (EO) and late onset (LO) disease. Among these, early onset GBS disease (infection presenting in the first 6 days of life) accounts for approximately 60–70% of all GBS disease. GBS serotypes Ia, II, III, and V are responsible for most EO disease and invasive infections (Lopez et al. 2018). The pre-requisite factors for the early onset GBS disease are maternal carriage of GBS in the gastrointestinal and/or genital tracts. In majority of cases, early onset GBS disease has the inherent property of causing the disease severity through pneumonia and sepsis. The early onset disease is vertically acquired from the mother through ascending infections from lower genital tract (Kwatra et al. 2016). Despite the high throughput development in the intensive supportive care, diagnostic approaches and therapeutic advances, these early onset GBS infections remain associated with high mortality and morbidity owing to its asymptomatic properties (Melin 2011).

The process of neonatal infection (early onset disease) by GBS is highly complex and assisted by both host and bacterial virulence factors. The first stage in the pathogenesis of GBS-EOD includes the establishment of colonization in the vaginal mucosa of the pregnant woman by successful adherence to the vaginal epithelial cells and increased tolerance to host immune system. The second stage involves the invasion across host epithelial barriers and progression of bacterial colonization into the amniotic cavity followed by rapid proliferation in the skin or mucous membranes of the fetus or to enter the fetal lung through aspiration of infected amniotic fluid. The third important step is the ability of GBS to replicate within the alveoli of the neonate, adhere to pulmonary epithelium, and avoid clearance by pulmonary macrophages after birth. The invasion into the pulmonary epithelial and endothelial cells by GBS significantly allows the GBS progression into the blood stream causing severe septicemia followed by meningitis and osteomyelitis. The disease progression efficacy shows the inherent potential of GBS to bypass the host's natural

immune defenses to adhere, to invade and to progress through several cell barriers (Melin 2011; Cools and Melin 2017) (Fig. 8.1). Meanwhile, the late onset GBS disease (onset between days 7 and 89 of life) is primarily caused predominantly by serotype III and is acquired perinatally, nosocomially or from community sources. In majority of cases, late onset GBS disease (50%) has the inherent property of causing the disease severity through septicemia and meningitis (Doare and Heath 2013; Joubrel et al. 2015; Kobayashi et al. 2016).

During the infection process, GBS utilizes prolific strategies to colonize the vagina of pregnant women. These strategies include the binding to the host surfaces and subverting the host immune defense mechanisms. These strategies also significantly promote the dissemination and colonization efficacy of GBS under severe stress conditions not only in pregnant women but also in the new born babies. Apart from colonization strategies, GBS strains also have the inherent potential of causing disease severity and chronic infections owing to the evolutionary acquisition of specified virulence factors. These factors not only enhance the dissemination and disease progression cycle but also allow the GBS to evade the host immune tolerance. At the cellular level, GBS regulates the expression of specific virulence determinants through highly complex, species-specific signal transduction regulatory network system. This regulatory system has the potential to sense host environments followed by adequate response to enhance the survival in the vulnerable

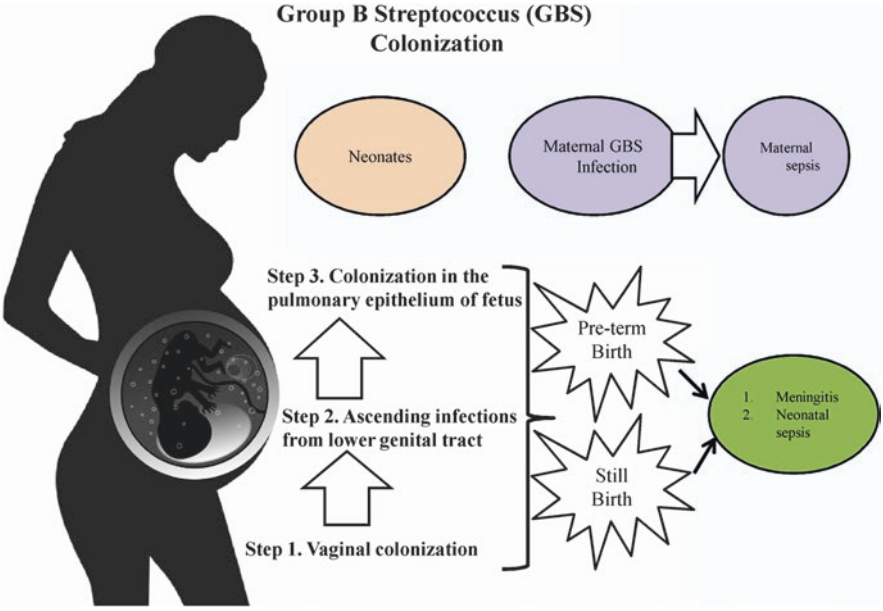

Fig. 8.1 Schematic representation of maternal GBS colonization into the neonates through ascending infections followed by proliferation in the pulmonary epithelium leading to severe meningitis and neonatal sepsis in neonates. Maternal GBS infection also causes maternal sepsis

environmental setup in the host environments outside the lower genital tract for efficient progression of infection process (Armistead et al. 2019).

8.3.2 Virulence Factors Associated with GBS Infections

In pathogenic microorganisms, one of the important factors that plays crucial role in maintaining the pathophysiology is the ability of pathogenic microorganisms to produce a myriad of virulence factors. The production and secretion of virulence factors have enabled the pathogenic microorganisms to invoke healthcare related issues and ability to cause disease. Like other pathogenic counterparts, GBS produces an array of virulence determinants that critically emphasize the pathogenicity of GBS. The important virulence determinants encoded by GBS are pore-forming toxins and the sialic acid-rich capsular polysaccharide (CPS). Apart from pore-forming toxins and CPS, other important virulence determinants in GBS infections are adhesion factors (that facilitate the binding to cells or extracellular matrix), evasion factors (that modulate the neutrophil recruitment and prevent complement binding), and other virulence factors that showed resistance to antimicrobial peptides and other conventional therapeutics (Chen et al. 2013).

The role of pore-forming toxins in GBS is to facilitate the host invasion followed by their survival and systemic dissemination. Two highly characterized pore-forming toxins such as β-hemolysin/cytolysin (β-H/C) and Christie Atkins Munch Peterson (CAMP) factor were reported in GBS. The pore-forming toxin, β-H/C not only promotes GBS invasion of host cell barriers such as the epithelial and endothelial cells of the lung and the blood–brain barrier (BBB) but also promotes immune evasion by inducing host inflammatory responses and enhanced resistance to reactive oxygen species (ROS). The expression of pore-forming toxin, β-H/C is generally regulated by the hyperpigmentation phenomenon which enables GBS to be hyperhemolytic thereby promoting invasive properties and severe pathogenesis (Lupo et al. 2014). Meanwhile, the other pore-forming toxin, i.e., CAMP factor plays a crucial role in increasing the bacterial pathogenesis by inducing septicemia and increased lethality by promoting cell lysis through targeting the susceptible target membranes (Rajagopal 2009).

Apart from pore-forming toxins, sialic acid-rich capsular polysaccharides (CPS) are important determinants of bacterial pathogenicity in GBS infections. The GBS CPSs comprise of various arrangements of monosaccharide building blocks containing glucose, galactose, and/or N-acetylglucosamine. In addition, the presence of sialic acid residue on the branching terminus of each repeating monosaccharide unit characteristically determines unique features of GBS in evading host immune system. The GBS CPSs have the inherent property to evade host recognition, complement factor decomposition, and phagocytosis owing to the presence of sialic acid and remain one of the important constituents in the GBS pathogenesis. The presence of sialic acid residue not only inhibit the complement cascade by accelerated dissociation of C3 convertase but also significantly modulate the phagocytosis and oxidative burst from neutrophils and monocytes, thereby enhancing bacterial survival (Chen et al. 2013). In GBS, ten capsular serotypes such as Ia, Ib, and II–IX have been

reported. During the host infection, GBS utilizes typical CPS for adherence and invasion into the host tissue (Baker 2013; Vornhagen et al. 2017). Among the identified serotypes, type III strains are particularly important in imparting pathogenicity owing to its inherent ability in invading the brain microvascular endothelial cells as compared to its other GBS serotype counterparts (Baker 2013).

The most prevalent virulence factors found in the GBS isolates are *cyl*(E) (encoding cytolysin–hemolysin), followed by *scp*(B) (encoding an invasion with C5a peptidase activity), *rib* (Alp family surface protein Rib resistant to protease effect), and *bca* (encoding beta subunit of the C protein) with a frequency of 90.5, 75.6, 62.1, and 43.4%, respectively. These virulence genes are exclusively found in the GBS isolates isolated from human (Emaneini et al. 2016a). In addition, the virulence factors *pep*(B) (encoding oligopeptidase protein) and *bib*(A) (encoding bacterial immunogenic adhesin) are found to be observed only in neonatal isolates. The virulence factors which are observed to be prevalent in neonatal isolates are *bca* (encoding beta subunit of the C protein) and *scp*(B) (encoding an invasin). The virulence factor, i.e., *fbs*(B) (encoding fibrinogen-binding protein mediating invasivity) has been observed frequently in colonizing and pathogenic isolates as compared to neonatal isolates (Carvalho-Castro et al. 2017; Lopez et al. 2018).

In GBS related infections, the secretion of GBS hyaluronidase significantly promotes the immune evasion process by degrading the pro-inflammatory hyaluronan fragments into hyaluronan disaccharides which in turn block toll-like receptor, TLR2/4 signaling pathway (Kolar et al. 2015). Two-component systems (TCSs) also found to be crucial in inducing pathogenicity in GBS infections by virtue of their ability to detect the environmental changes and other stress conditions.

8.3.3 Antibiotic Resistance Profile of GBS

The pathogenic bacteria have the inherent ability to exhibit chronic pathogenicity by producing an array of virulence determinants as well as recalcitrant biofilms. Biofilms are defined as sessile microbial communities in which the pathogenic bacteria are embedded within a self-produced extracellular polymer matrix. The polymeric matrix is considered to generate a safe microenvironment for the embedded microbial communities from stress conditions such as extreme pH, antimicrobial therapeutics, host immunity and thereby promoting persistent colonization and infection (Boonyayatra et al. 2016; Nie et al. 2018). One of the important members of Group B Streptococcus is *S. agalactiae* which is known for its contagious pathogenicity owing to its ability to form highly resistant biofilm architecture. The inherent ability of *S. agalactiae* to form biofilms can be correlated with enhanced pathogenicity and tolerance to the conventional antibiotics. The microcolonies residing within the biofilm architecture enabled the residing *Streptococcal* microcolonies to modulate the pathophysiological responses on treatment with conventional therapeutics thereby blocking the entry of therapeutic drugs into the bacterial system, thereby minimizing the efficacy of the administered drugs (Ebrahimi et al. 2013).

No doubt the presence of capsular polysaccharides in GBS enhances the bacterial pathogenicity and associated health ailments. In addition to capsular polysaccharides, GBS also contains elaborate surface-anchored pili which enable GBS during colonization in the host cells by promoting bacterial adhesion, invasion into host cells, mitigating host immune responses, and biofilm formation (Xia et al. 2015; Khodaei et al. 2018; Perichon et al. 2019). The epidemiological prospects of surface adhesins and pili enable GBS adaptation to stress conditions and increases host specificity. In GBS, three pilus islands such as (PI)-1, PI-2a, and PI-2b were identified. Each PI encodes for three structural proteins such as a backbone protein (BP), two ancillary proteins (AP), and two pilus-specific class C sortase enzymes. The ancillary proteins allow the initiation of bacterial adherence to various host tissues. Meanwhile, the backbone proteins strictly facilitate the invasion efficacy and paracellular translocation of host cells. The role of class C sortase enzymes is to recognize LPXTG amino acid motifs on structural proteins and facilitate covalent attachment. The pili island, PI-2a is found to be crucial for biofilm formation and thus enable GBS for antibiotic resistance. Meanwhile, PI-2b promotes the intracellular survival of GBS in macrophages (Springman et al. 2014).

As per recent trends, *S. agalactiae* (GBS) exhibited immense resistance profile against aminoglycosides group of antibiotics including sulphazotrim (sulfamethoxazole with trimethoprim), tetracycline, ampicillin as well as fluoroquinolones group of antibiotics (Chideroli et al. 2017). The resistance pattern shown by GBS against conventional antibiotics, especially tetracycline could be attributed to the presence of specific virulence genes such as *scpB*, *hlyB*, and *bca* which are significantly correlated with the presence of tetracycline resistant *tetM* gene (Rato et al. 2013; Emaneini et al. 2016b). Apart from tetracycline resistance, the GBS isolated from neonates from clinical setup shown to exhibit multidrug resistance (MDR) to other traditional antibiotics such as erythromycin and clindamycin (Wang et al. 2015).

S. agalactiae adhesion to host cells constitutes an important step in colonization and frequently involves components of the extracellular matrix (ECM) such as fibronectin, fibrinogen, collagen, and laminin. The cell-wall-anchored (CWA) proteins often bind with ECM and cellular receptors and initiate the progression of chronic infections (Chuzeville et al. 2015). During GBS infections, genes encoding putative surface proteins and in particular an antigen I/II have been identified on integrative and conjugative elements (ICEs) found in *S. agalactiae*. The presence of this antigen as putative surface protein enables GBS in cell-cell aggregation and biofilm formation.

8.3.4 Therapeutic Strategies to Control GBS Infections

The prevalence of GBS infections in the neonates and the critical role of breast milk in imparting severity in the GBS infections suggested the scientific community to develop maternal immunization programme to combat GBS infections. From therapeutic perspectives, maternal immunization programme which includes the development of maternal vaccines remains instrumental in the fight against GBS infections. Till date,

three generations of maternal vaccines such as native polysaccharide vaccines (first generation maternal vaccines), glycoconjugate vaccines (second generation maternal vaccines), and vaccine design with high throughput technological applications (third generation vaccines) have been developed as an arsenal against GBS infections (Chen et al. 2013). The maternal vaccination programme in the pregnant women not only prevent invasive GBS related diseases in the neonates but also significantly reduce the recto-vaginal colonization in the pregnant women, who themselves are at increased risk for developing invasive GBS disease (Madhi and Dangor 2017).

As it is evident from earlier studies that maternal colonization is one of the primary risk factors in the onset of GBS disease and associated health risks, the development of intrapartum antibiotic prophylaxis (IAP) could be considered as promising in reducing the risks associated with GBS infections. The emergence of IAP strategy has been recommended for both GBS colonized women as well as women with premature rupture of membranes, prolonged membrane rupture, fever, and preterm birth owing to its ability in reducing as much as 80% of GBS early onset disease in USA. Apart from prophylaxis strategy, prenatal screening in pregnant women is considered to be influential in reducing the incidence of GBS neonatal disease in the developed countries. However, due to limiting factors such as resources limitations and under-developed infrastructure in the developing and low-income countries, the prenatal screening settings and IAP strategy have not been implemented in these countries (Sadaka et al. 2018). Based on the promising aspects shown by prophylaxis strategy, it is important to develop this strategy in developing countries as well as low-income countries in the fight against GBS related health issues (Medugu et al. 2017).

Owing to the susceptibility shown by GBS towards penicillin, its prophylactic use could be instrumental in the fight against GBS related infections by significantly reducing the incidence of early onset diseases in neonatal individuals (Boswihi et al. 2012). The synergistic activity of gentamicin with penicillin could be explored as an alternative therapeutic approach in minimizing the severity of GBS infections (Ruppen et al. 2017). In addition, gentamicin in combination with benzylpenicillin and/or rifampicin also proved to be effective in combating GBS associated biofilm dynamics (Moreno et al. 2017). However, vancomycin could also be used as a therapeutic strategy for initial treatment of GBS infection in particular cases where the individuals showed allergic reactions to the penicillin treatment.

Apart from conventional therapeutics, the prophylactic use of naturally derived compounds (plant-derived and microbial-derived compounds) could also considered to be promising arsenal against GBS associated infections. In this context, plant-derived eugenol and mycosynthesized silver nanoparticles (AgNPs) showed synergistic activity in controlling the GBS infections. In addition, the use of eugenol in the treatment against GBS infection has a promising aspect in disrupting the biofilm forming ability of GBS and thus increases the sensitivity of GBS towards conventional antibiotics. The therapeutic efficacy of eugenol and other natural-derived drug candidates could be utilized as a promising alternative to advanced IAP-based therapeutics (Biasi-Garbin et al. 2015). Additionally, breast milk and colostrum contain antimicrobial and immunomodulatory components which have the inherent property to impair translocation of infectious pathogens including GBS. These substances not only compensate directly

for deficiency in the neonatal immune system but also enhance the survival of defense agents such as secretory IgA (SIgA), lactoferrin, lysozyme, IFN-γ. In addition, these substances also prevent inflammation or enhance specific-antibody production, such as PAF-acetylhydrolase, antioxidants, interleukins, transforming growth factor (TGF), secretory leukocyte protease inhibitors (SLPIs) and defensin1 (Doare and Kampmann 2014). Recently, human milk oligosaccharides (HMOs) are also considered as alternative approach in controlling the pathogenic profile of GBS by significantly attenuating the biofilm formation and disruption of biofilm architecture of GBS thereby increasing the susceptibility of GBS to conventional therapeutics for the complete eradication of GBS infections (Ackerman et al. 2017).

8.4 Current Trends and Future Perspectives

Owing to the severity of GBS infections in neonates, it is important to take necessary measures to counteract the GBS related infections. Beyond therapeutics and development of GBS vaccines, it is highly important to generate public awareness by educating the public about the severity of GBS infections and by conducting frequent prenatal screening to promote prevention of neonatal GBS infections which could provide new avenues in the prevention of neonatal GBS infections (Burns and Plumb 2013). With the advancement in high throughput technologies and molecular techniques, it is imperative to utilize the arsenal of molecular typing of GBS isolates in order to understand the variability and epidemiology of GBS and thereby provide novel avenues to the scientific community for the development of effective control and eradication programmes in the fight against GBS infections (Reyes et al. 2017). As the capsular polysaccharides played key role as virulence factors and are important targets for the development of vaccine strategies and drug development in the process of fighting against GBS infections (Campisi et al. 2016; Jiang et al. 2016).

8.5 Conclusion

The beta-hemolytic group of gram-positive *S. agalactiae* (Group B Streptococcus, GBS) is often encountered as a part of the normal flora and considered as commensal microorganism colonizing the gastro-intestinal and the genital tract of healthy women. However, GBS could reach the new born through the birth canal and cause sepsis and/or meningitis and hence observed to be opportunistic pathogen. Apart from neonatal sepsis and meningitis, GBS is also associated with severe chronic infections such as UTIs, bacteremia, endocarditis, and other related health issues. The severity of chronic infections caused by GBS could be attributed to the diversity of virulence determinants such as pore-forming toxins and capsular polysaccharides. In addition to capsular polysaccharides, other surface associated factors like pili islands could be instrumental in inducing bacterial resistance phenomenon by its inherent ability to form persistent biofilms. As per recent trends, IAP therapeutics and conventional antimicrobial therapy are observed to be instrumental in controlling GBS infections. However, associated

resistance could limit their widespread applications. In this context, it is imperative to develop effective strategies to counteract GBS infections related health issues. One of the primary strategies to prevent GBS infections is to generate public awareness through prenatal screening which could be advantageous in the fight against GBS infections.

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