International Journal of Medicine, 3 (1) (2015) 8-11

International Journal of Medicine

Journal home page: www.sciencepubco.com/index.php/IJM
doi: 10.14419/ijm.v3i1.3910
Review Paper

Group A, G and C β-hemolytic Streptococci

Shobha K L [1]*, Kusumakshi [2], Vishnu Prasad [3], Ramachandra L [4]

[1] *Dept of Microbiology, MMMC, Manipal University, Manipal*
[2] *Dept of MLT, SOAHS, Manipal University, Manipal*
[3] *Dept of Microbiology, KMC, Manipal University, Manipal*
[4] *Dept of Surgery, KMC,Manipal University, Manipal*
**Corresponding author E-mail: shobha.kl@manipal.edu*

Abstract

Group A Streptococcus (GAS) is the most common causative agent of sore throat, pharyngitis, skin infections, rheumatic fever (RF), rheumatoid heart disease (RHD) and glomerulonephritis in young adults. Group G and C streptococcal species are also known to cause complications like acute rheumatic fever and rheumatic heart disease. Isolation of these from the throat could be a warning signal so that the further complications can be prevented. Estimation of prevalence could help clinicians to make informed decisions regarding diagnostic testing of children with symptoms of sore throat and pharyngitis. M protein both GAS and GGS/GCS share in many virulence factors that contribute to virulence, some of which act as collagen binding adhesins that facilitate acute infection. Both GAS and GGS/GCS can cause similar spectrum of disease symptoms. The sequenced M Protein provides a view into the genetic elements responsible for diversity in the species. emm types historically associated with RF are rarely seen in India. The epidemiologic picture of streptococci in India shows some of the serotypes are more common with in a population in different geographical area.

Keywords: *Group A C And G Streptococcus; Pharyngitis; M Protein; Emm Genes.*

1. Introduction

Group A Streptococci (GAS) are the most common causative agents of sore throat, pharyngitis, skin infections and post infection complications like Rheumatic fever (RF), Rheumatoid heart disease (RHD) and glomerulonephritis in young adults (Asrat D et al.2011). In India and other developing countries rheumatic fever and RHD is one of the major public health problems contributes to significant cardiac morbidity and mortality (Chopra P et al.2007). Pharyngeal carriage of GAS vary according to the geographical and seasonal variations and indoor air pollution in healthy school children (Nandi S et al. 2001).
Several species of Streptococci can carry Group G and C antigens, including Streptococcus dysgalactiae subspequisimilis, S. canis, S. dysgalactiae subsp dysgalactiae, S. equi subsp equi, S equi sub sp.zooedemicus and S. anginoses(Shimomura Y et al.2011). Streptococcus dysgalactae subsp equisimilis (SDSE) consist of both Lancefield G and C antigens(Takahashi T et al.2011). Group G and C Streptococci (GGS/GCS) are most commonly considered as commensals (Rouff KL et al.1988). SDSE typically colonizes the oropharynx and skin of the humans and closely related to GAS, a significant human pathogen(McMillan DJ et al.2010). Recovery of Group G and C Streptococcus from the throats has been reported to exceed that of GAS in regions where Streptococcal disease is endemic (Mcdonald M et al.2006; Bramhachari P V et al.2010).

2. Morphology of β hemolytic streptococci

Group A Streptococci is β hemolytic Gram Positive organism (Cunningham MW.et al.2000), similar to GAS, Group G and C Streptococci (SDSE)are β hemolytic Gram positive bacterium (McMillan DJ et al. 2010) and tend to have large colonies and a hyaluronic acid capsule (Mcdonald M et al.2006).

3. Pathogenicity of β hemolytic streptococci

Extensive reviews have been written about the pathogenesis of RF and RHD. M protein is a major virulence factor of Streptococci plays an important role in the pathogenesis of RF and RHD (Guilherme L et al., 2006). The sequenced M Protein provide a view into the genetic elements responsible for diversity in the species (Smoot JC et al, 2002). emm types historically associated with RF are rarely seen in India(Smoot JC et al. 2005). Epidemiological Study done in North India for the prevalence of pharyngitis and impetigo reports that the most prevalent of emm types of GAS that cause pharyngitis differ from those included in M protein based vaccine (Kumar R et al . 2009). Furthermore, association of MHC Class II molecules are noticed with multiple valvular lesions in RHD patients (Guilherme L et al. 2006). Including M protein both GAS and GGS/GCS share in many virulence factors that contribute to virulence(Mcdonald M et al .2006) some of which act as collagen binding adhesins that facilitate acute infection (Reissmann S et al,2010). Both GAS and GGS/GCS can cause similar spectrum of disease symptoms(Brandt CM et al.2009;Mark R et al.2005)
Reports says that Mouse antibodies to GGS/GCS M protein react with human cardiac myosin (Haidan A et al.,2000) and antibodies to streptolysin O and hyaluronic acid increase after infection with GGS/GCS(Williams GS.2003). There is also some evidence to suggest that theses organism may play a role in the pathogenesis of acute rheumatic fever (ARF) and Streptococcal glomerulone-

phritis(Reid H et al 1985;Haidan A et al.2000). Australian GGS strains have been shown to cross react with human heart muscle myosin, which has reported to indicate a potential to elicit an autoimmune response that may trigger acute rheumatic fever(HaidanA et al,2000). Carditis is the most serious manifestation of ARF, Resulting in chronic valvular lesions (Stollerman G, 1997). Auto antibody responses against the heart and cardiac myosin have been associated with rheumatic carditis and may cross react with valvular endothelium and initiate disease(Tb M et al, 2008).

Streptococcus equisimilis (GCS) produces extracellular enzymes streptokinase and Streptolysin O (SLO). The nucleotide sequence of open reading frames of SLO genes in GGS and GCS are almost identical to GAS(Efstratiou A.1997). The species are also known for lateral genetic transfer(Sriprakash KS et al, 1996). The horizontal gene transfer and gene rearrangement are of particular significance in light of the fact that the regulatory genes involved in the controls of these pathogenicity factors (rofA) have also been identified in SDSE (Towers RJ et al.2004). Molecular markers are essential to distinguish these species and delineate their epidemiology more precisely since it is difficult to distinguish GAS and GGS/GCS on a morphologic basis, as both species are usually large colony forming with similar hemolytic patterns(McMillan DJ et al. 2010). Genome wide comparison with GAS indicates that GGS/GCS is closely related to GAS. Recently, the presence of GAS virulence genes encoding streptolysin S and glyceraldehyde - 3- phosphate dehydrogenase has been reported in human GGS/GCS (Mg R et al .2010).

4. Prevalence of streptococci in India

There are some studies done in India to know the scenario of Streptococcal throat colonization of school age group children where the Vellore region of India had high incidence of group C and G Streptococcal infection (Brahmadathan KN et al. 1989). Pharyngeal carriage of β hemolytic Streptococci were found in school age children of Orathur, Tamil Nadu and two of them had Rheumatic heart disease. Pharyngeal carriage of group A was common in these population with 0.6% of prevalent rheumatic heart disease which emphasizes the need for active surveillance (Menon T et al. 2004). Both Group A and G were found in school children of Salem where Group G (43.2%) was predominant followed by group A (28.8%) out of 21.6% of β hemolytic streptococci.(Navaneeth B V et al. 2001). Throat swabs collected from the patients with acute pharyngitis in Tamil Nadu reports presence of β hemolytic streptococci where once again Group C (59.7%) was predominant followed by Group G (25%) and Group a (15.3%) of total 124 β hemolytic streptococcal strains. Presence of superantigens in non emm typable group G and C streptococci were observed; so these strains may emerge as potential human pathogens which could lead to late complications of streptococcal infection(Anand T et al. 2012). 16.3% of β hemolytic streptococci, a very high carriage rate were seen in asymptomatic children of different locations in Chennai out of which 8.4% were GAS. Even high carriage of β hemolytic streptococci is a serious threat to the community. Carriers are the important source of infection in the community especially in crowded area as well as in their families (Lioyd C et al. 2006). Another study done in Chennai reported 36% of GAS, 9% of GCS and 1% of GGS in school age children of slum area (Kalpana S et al. 2012).

GGS and GAS are the most predominant β hemolytic streptococci found in healthy school children at Mangalore Region of Karnataka State. The prevalence of GAS was 5% and GGS was 6% among 300 school children. The isolation rates were high for both Group A and G in winter season (Pavanchand, N et al. 2014). Similar study done around the rural village, B G Nagara, Mandya District of Karnataka reported about 44 pharyngeal carriers of β hemolytic streptococci out of which 86.36% were group A, 11.36% were group C and 2.27% were group G (Vijaya D et al. 2013). A total of 60 GAS isolates were recovered from throat cultures obtained from healthy school age children in Bangalore; emm typing confirmed the regional difference existing among these isolates with in the same country. Due to this heterogeneity the concept of multivalent GAS vaccine appears to be impracticable in India (Lakshmana Gowda K et al. 2010). Cross sectional study conducted in 7 government schools of Ramnagar, Belgaum city, Karnataka reports 30.7% beta hemolytic streptococci in 300 children and prevalence of GAS was 30.7%. Out of 300 children 87 were symptomatic and 39.1% β hemolytic streptococci were found in these children (Kushwaha N et al. 2014). Throat swabs collected from 7 Municipal school of Mumbai showed High Group G and C streptococcal carriers than Group A streptococci. The GGS/GCS carriage rate was 11% and GAS carriage rate was 1.5%. 21 different emm types were identified in GGS/GCS and 15 different emm types were found in GAS (Bramhachari P V et al. 2010).

One of the study done in AIIMS, New Delhi, says 64 isolates of GGS and 5 isolates of GCS out of 529 β hemolytic streptococci were found in respiratory samples received in the clinical bacteriology laboratory during the year 1996-2000 (Mathur P et al.2004). In the rural communities of Haryana, Northern India streptococcal pharyngitis was found to be more common than impetigo and the prevalent GAS emm types differ from those included in the multivalent vaccines (Kumar R et al. 2012). The study done to estimate the incidence and risk factors of group A streptococcus sore throat among school aged children living in periurban slum area of Chandigarh, North India reported the incidence of GAS sore throat was 0.95 episodes per child year. Incidence were related to age, season and indoor air pollution and were higher in winter and rainy season (Nandi S et al.2001). Studies done on throat carriage of β hemolytic streptococci during the year 1972-90 in rural and urban school children around Delhi showed12.2%-64.3% depending upon the season and number of swabs taken, where group A was found to be most predominant serogroup. Study says there was no difference between the distribution of β hemolytic streptococcus carriers among urban and rural school children (Prakash K et al.1992).

5. Detection of β hemolytic streptococci

The majority of streptococcal infections are caused by β hemolytic Streptococci (Olender A et al. 2012). Acurate identification and typing is an important part of epidemiological study as well as pathogenetic studies (Kumar R et al.2009). Direct examination of specimens or Microscopy provides the most rapid identification of microbial infection and the infection is confirmed by isolating and identifying the microorganisms using artificial culture medium (Washington JA,1996). Beta hemolytic Streptococci are identified by the hemolytic pattern around the colony and colony morphology on sheep blood agar (Baron EJ.2001, Hussain Z et al. 1984). Recovery of GAS increases on SXT-BA (Sulfamethoxazole and trimethoprim) when compared with conventional sheep blood agar (Gunn BA et al. 1977). For the rapid detection of Group C beta hemolytic streptococci latex agglutination test is used directly on throat swabs where the results are very specific but poorly sensitive (Hayden GF et al.1992). Bacitracin is used to identify GAS but 5%of other beta hemolytic streptococci show resistance to bacitracin; PYR reaction is more specific for GAS(Hussain Z et al. 1984). Only bacitracin cannot be used to identify GAS due to the existence of bacitracin resistant strains (Olender A et al. 2012). Direct plate Phadebact procedure is a rapid and reliable test to identify β hemolytic Streptococci where sufficient colonies are available (Slifkin M et al.1978).

Early typing methods for these organisms were based on bacteriocicns and Bacteriophage typing (Vereanu A et al. 1979). Serological typing of T protein is used only for epidemiological studies and not for the virulence whereas typing of M protein is relevant in studying virulence features (Efstratiou A.1997). Serogrouping based on specific cell wall associated carbohydrates was first done by Rebecca C Lancefield in 1933 (Lancefield BRC,1932). The Lancefield system of serogrouping the strepto-

cocci are still useful in the identification of streptococci but it cannot be used for the accurate identification of specific β hemolytic species (Facklam R et al. 2002). The use of series of four physiologic tests i.e β-D glucoronidase, Pyrolidonl arylamodase and esculin hydrolysis, Hippurate hydrolysis and Voges-Proskaer test can be used for routine processing of β hemolytic Streptococci which are sufficiently rapid, more accurate and less costly compared to serologic methods (Kirby R et al. 1995). Analysis of 16S RNA sequences is one of the most powerful tools used to identify these species. Biochemical methods or API system can also be used for identifying these organisms (Brandt CM et al. 1999). Biotyping may be a useful alternative method in laboratories unable to do molecular typing (Ambu M et al.2005).

Morbidity and mortality due to streptococcal late consequences remain very high in India (Burden D.2010). All these studies done to find the prevalence of streptococci are important for regular surveillance to prevent the streptococcal infection. The epidemiologic picture of streptococci in India shows some of the serotypes are more common with in a population in different geographical area (Brandt ER et al. 2000). Group A, G and C streptococcal species are known to cause complications like acute rheumatic fever and rheumatic heart disease. Isolation of these from the throat could be a warning signal so that the further complications can be prevented. Estimation of prevalence could help clinicians to make informed decisions regarding diagnostic testing of children with symptoms of sore throat and pharyngitis. Poor Income and hygiene conditions, overcrowding may play a significant role in spreading the infection. Awareness should be given or education should be given to the population about healthy life style as a measure of prevention. The spread could be prevented by regular screening of carriers and appropriate treatment.

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