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The Epidemiology Of Streptococcus Pyogenes Associated With Characterisation, Pathogenesis, Diagnosis And Treatment- A Review

Nilotpal Banerjee[1], Anupal Chowdhury[2], Sabina Yeasmin[3]
Spandan Hospital, A Unit Of Spandan Advance Medicare Pvt. Ltd., India[1]
Future Institute Of Technology, Garia, West Bengal[2]
Phd, Department Of Polymer Science & Technology, University Of Calcutta, India[3]
Corresponding Author: Sabina Yeasmin*

Abstract
A potential wide range of human infections causes by Group A streptococci ubiquitous bacteria. Human host adapted Streptococcus pyogenes(Group A Streptococcus; GAS) that result in various asymptomatic infection like pharyngitis, pyoderma, scarlet fever and invasive diseases. Gas adopted both innate and adoptive immune responses to infection. It display a wide range of gas infection which allow colonization, dissemination, and transmission of diseases inside the host. GAS classified as gram – positive cocci which causes a range of diseases. A special type of surface M protein present on the surface as GAS. For the presence of M protein GAS can be classified in 100 subtypes. Infections due to GAS result in acute pharyngitis, impetigo, erysipelas, dental damage and cellulitis. Streptococcal toxic shock syndrome and necrotizing fasciitis are two most invasive diseases. Acute rheumatic fever and post- streptococcal glomerular nephritis are two acute infection causes by GAS infection. This activity reviews the evaluation and treatment of Group A Strep infections and highlights the role of the interprofessional team in evaluating and treating patients with this condition.

Keywords:*Streptococcus pyogenes; sepsis; GAS capsule; M protein; S protein; diagnosis; oral infection*

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I. Introduction:

Streptococcus pyogenes (Group A Streptococcus; GAS) is a host adapted bacterial pathogen that causes human infections such as pharyngitis, impetigo, septicaemia, necrotizing fasciitis and streptococcal toxic shock-like syndrome (STSS). Gas infections can lead to rheumatic fever that can result also in rheumatic heart disease (RHD) [1]. Gas can be classified on the basis of presence of M protein on the surface of the bacteria [2,3]. In Asia and United Kingdom scarlet fever spreads due to multiple clone of GAS [4-7]. GAS can gain both innate and adaptive immune system by colonizing in specific area of sore and throat. It can alsodisemminate in a new host. By investing new host defence mechanisms GAS can also employ some virulence strategies. Host cell pyroptosis also invade by Gasdermin A (GSDMA) by the GAS protease streptococcal pyrogenic exotoxin B (Spe B) [8,9]. Mucosal-associated invariant T cells (MAIT cells) identify by the patient affected with STSS and a primary contributors associated with different disease [10].

Due to lack of invention of GAS vaccine some normal antibiotics in nature use to treat GAS infection. After prolong use of penicillin in less amount GAS become antibiotic resistance. GAS also shows resistance towards β-lactam antibiotics [11-15]. WHO also developed a GAS research technology to preferred product characteristics [16].GAS population and vaccine antigen coverage can also discovered by large scale genomics [17]. New GAS vaccine produced against vaccine antigen M protein [18]. A primate model of GAS pharyngitis has use to measure GAS vaccine efficacy [19]. Controlled human infection model (CHIM) of GAS pharyngitis provide a future opportunity of vaccine efficacy in human host [20].

Gas causing different diseases

Gas is a common human pathogen causes a broad spectrum of diseases. Diseases like sinusitis, meningitis, endocarditis, pneumonia, peritonitis and osteomyelitis infection can be spread by GAS infection. GAS is a invasive bacteria that can causes half of millions of death annually [21]. GAS infection causes significant amount of death more than 100 million over the year, 0.1% spread as pharyngitis among the children [22]. In low and middle income country this GAS diseases spread in rapid rate.In Australia and New Zealand where there is less economy GAS spread rapidly [23]. As it spread rapidly its impact can be poorly understood when it spread worldwide. Figure 1 represent different diseases by GAS infection.

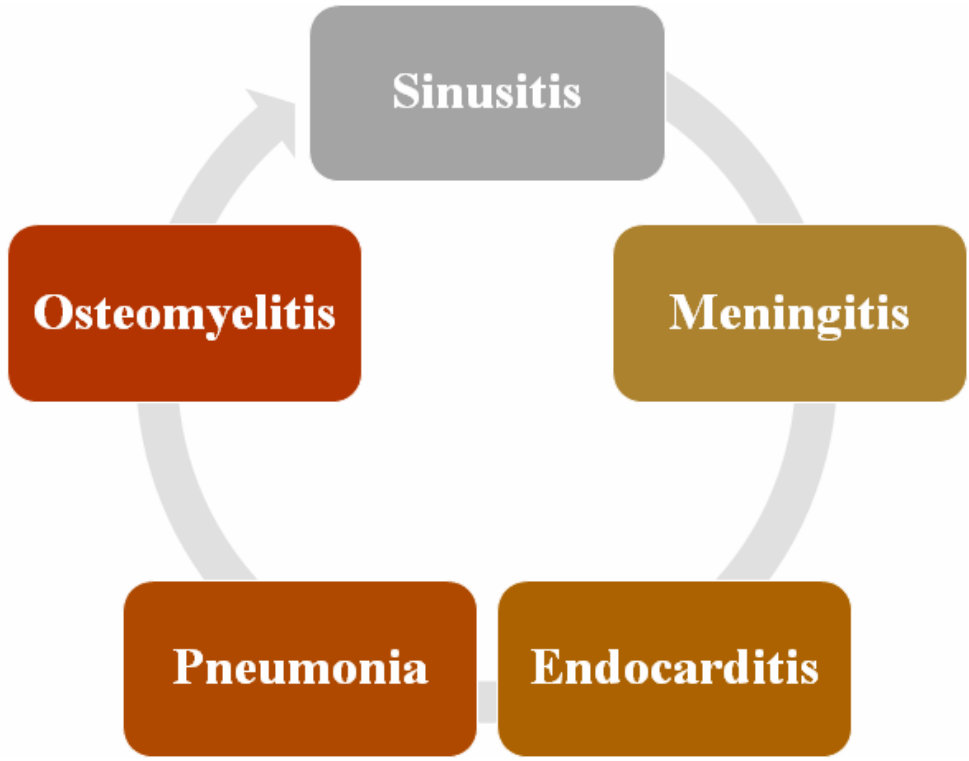

Figure 1: Different diseases caused by group- A Streptococcus (GAS infection)

A long spread of GAS causes rheumatic heart disease (RHD) that can be raises awareness among the people [24,25]. Rheumatic heart disease (RHD) is a large public health program spread among high income countries like United States and Israel [26]. From different scientific reports it is clear that skin infection can also causes immune sequelae [27,28].

Scarlet fever is a one type of fever disappeared at the end of twentieth century, again it appeared in China, Hong Kong, South Korea, Singapore and United Kingdom [4,5, 29-31]. Scarlet fever can also be detected in different geographical areas [32,33]. GAS diseases become dangerous when it is invasive [34]. In vulnerable populations GAS can spread rapidly in invasive manners [4,35-37]. GAS epidemiology can also closely monitor different population. It should be noted that improved healthcare system can also increase the detection of disease.

GAS infection spread by the following mechanisms

Both host and bacterial factors causes complex and multifactorial GAS infection in human. GAS secreted a large number of virulence factors associated with cell-wall protein. This cellular components created immune reponse was focused in a review [1]. Here in this review we focus on some key virulence factors help on the colonization of epithelial tissues in advance area.

Surface bound protein that act as virulence factors

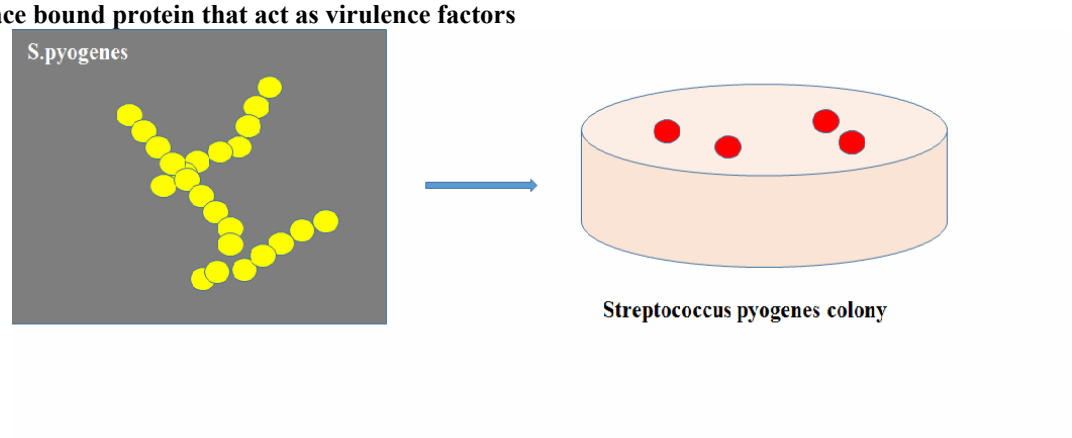

Figure 2: *S.pyogenes* structure observed under FESEM and in open eye in a petriplate

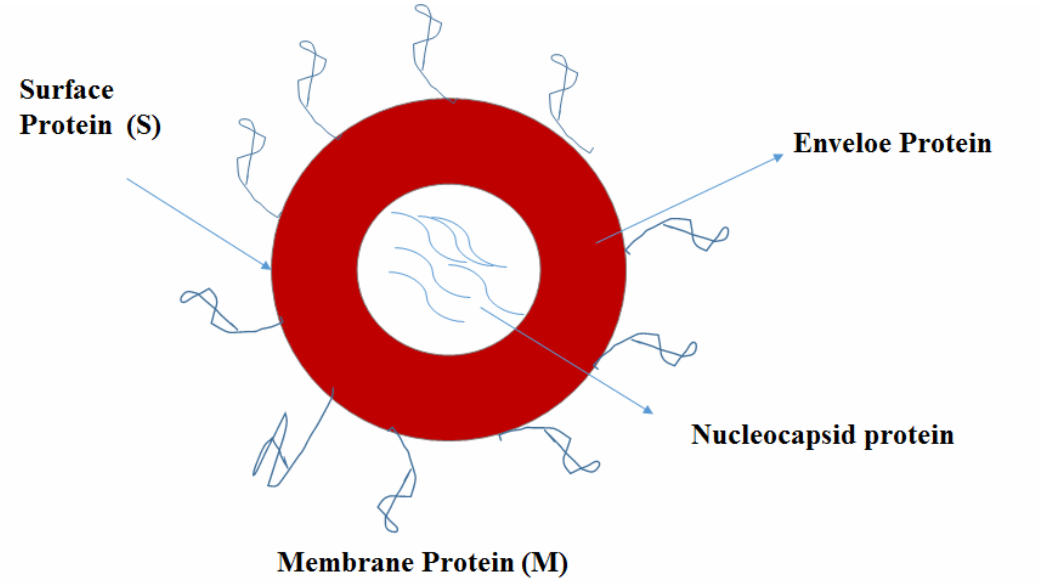

Figure 3: Different protein like M protein, S protein and others are present on the surface of group-A Streptococcus (GAS)

M protein

M protein (emm) present on the surface of GAS encoded by the gene present on the 5' end of the GAS. More than 220 emm genotypes have been identified [2]. M protein [Figure2 and Figure3] extends from bacterial cell wall. It is a dimeric coiled-coil fibrillar proteins [38]. The carboxy terminal is made up of a covalent bond attached to M protein. N terminal contains antigenic diversity [39]. M protein can directly bind to the host components, plasminogen and fibrinogen present on the Streptococcal surface. After binding it creates innate and adaptive immune responses [1]. NLRP3 inflammasome machinery inserted inside the macrophages and programmed cell death occur. This lead to secretion of two proinflammatory cytokines interleukin-1β (IL-1β) and interleukin 18 (IL-18) [40,41]. Host colonization are also influenced by M protein. Colonization occur by adhesive interaction of MCP or CD 46 (membrane cofactor protein) and cell-surface glycan [42,43,44,45].

Hyaluronic acid capsule

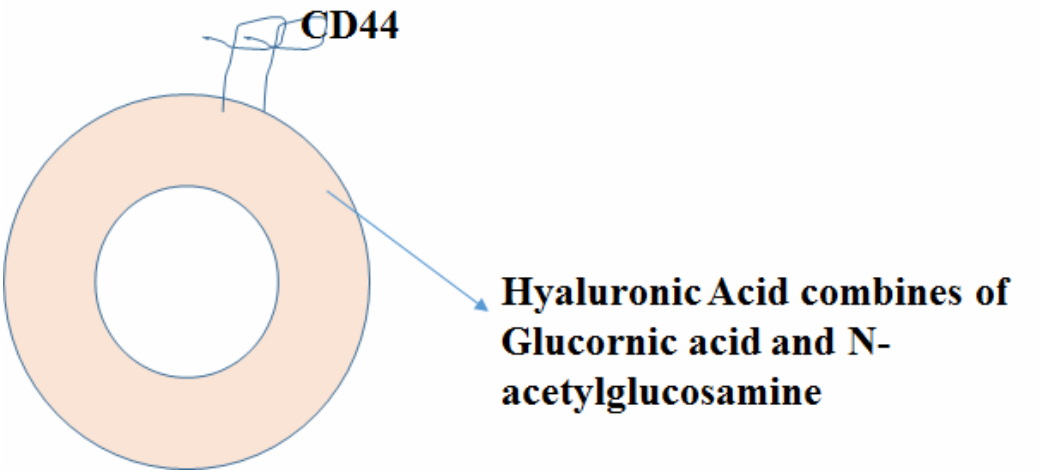

Figure 4: Hyaluronic acid present on the surface of GAS (group-A streptococcus)

Glucornic acid and N-acetyl glucosamine are two repeating disaccharide unit present in hyaluronic acid capsule [Figure4] of GAS. It determines the colony morphology. The hyaluronic acid present in the GAS capsule have similar properties with hyaluronic acid present in the human. Some extracellular matrices we found in connective and epithelial tissues. The main function of this GAS capsule was helping the pathogen in camouflage. CD44 is a primary glycoprotein bound on the human cell surface [46]. GAS capsule adhere on the surface of human pharynx and skin [47]. When CD44 bind on the surface of GAS capsule it penetrates on the inner layer of tissues [47]. This lead to phagocytic killing of the cells [48]. From different emm types loss of

capsule production has been reported for both invasive and non-invasive strains. ABC capsule gene operon (emm4, emm22 and emm89) or mutation inactivating genes like has AB genes (emm28 and emm87) [49-52].

S protein

A new type of molecular mimicry has recently described in a highly conserved surface-associated protein (S protein, Figure 2 and Figure3) was shown to selectively bind RBC (red blood cells) membranes [53]. If S protein present in the membrane surface it prevents phagocytic killing. It creates a link between haemolytic activity of the pathogen and immune camouflage strategy. This help in blood survival and dissemination.

Other extracellular growth products

The interaction of streptococcal products with mammalian blood and tissue is widely discussed in different journal. Streptolysin S (oxygen-stable cytolysin) and Streptolysin O (oxygen labile cytolysin) are two cytolysin present in GAS.Hyaluronidase can digest hyaluronic acid present in the capsule. Fibrin present in the cell wall digested by Streptokinase. A-D Streptodormases help in initiation of deoxyribonuclease activity whereas B and D possess ribonuclease activity [54]. There are 3 types of pyrogenic exotoxins present in *S pyogenes*. T cells also stimulate binding to class II MHC molecules. When *S pyogenes* is lysogenized by certain bacteriophages, other streptokinase's (A or C) are produced. All bacterial chromosomes are encoded by streptokinase's B. Carbohydrate surface antigens present on the surface of Group B Streptococci. It also associated with anti phagocytosisneuroaminidase that help in pathogenesis.

Pathogenesis

Streptococcus pyogenes have a wide range of pathogenic potential. A clear scheme has been drawn for the *S. pyogenes* pathogenesis. We can found *S.pyogenes* in the human nasopharyngeal flora. If this microbes invade the microbial flora and take entry in blood causes several diseases. *S. pyogenes* causes infection on the upper respiratory tract or on the skin. If we collect it from the pharynx and respiratory tract it do not primarily causes skin infection. If the microbe invade the lower and upper respiratory tract result in the infection of middle ear, sinusitis etc. Meningitis occur by direct infection from the middle ear. When microbes increases in the blood stream causes bacteremia and it result in infection of bones (osteomyelitis) or joints (arthritis) [55,56,57].

Pharyngitis and tonsillitis are causes by GAS infection. *S. pyogenes* infection can lead to sinusitis, otitis, mastiditis, pneumonia, empyema, joint or bone infections, myositis, meningitis and endocarditis [58,59]. Skin infection may be superficial or deep. When Streptococcal infection become complicated it give rise to scarlet fever. Antibiotic therapy can decreases disease risk like pharyngitis and rash. Nowadays *S. pyogenes* infection is increasing day by day. If it is not reported as national diseases in clearing houses in US then absolute number of infected patient are also not calculated. There has been no more change in susceptibility of *S. pyogenes* to commonly used antibiotics.

Diagnosis

Diagnosis is dependent on what type of infection you have.
Your provider will offer tests to confirm a diagnosis:

1) Presence of *S.pyogenes* in blood culture report for an infection in Figure 5.
2) A rapid culture test with a swab taken saliva from your throat and looks for bacteria under microscope.
3) Biopsy is done by collecting some tissue sample.
4) A imaging test like an MRI, CT scan or ultrasound to look at the damage underneath your skin caused by the infection [60].

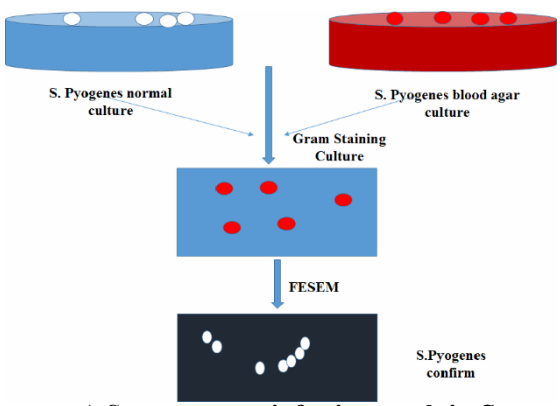

Figure 5: Diagnosis of group-A Streptococcus infection result in *S.pyogenes* confirm structure

Treatment

Antibiotics (Penicillin, amoxicillin, azithromycin) generally use for the treatment of Group A streptococcal infections.

But no vaccine available for Group A Streptococcal infections [60]

Oral Infection

Oral and maxillofacial region are infected by *S. pyogenes*. Most oral infections are adontogenic, occurring through the root apex of the tooth or the periodontal pocket. Edentulous patients have lower

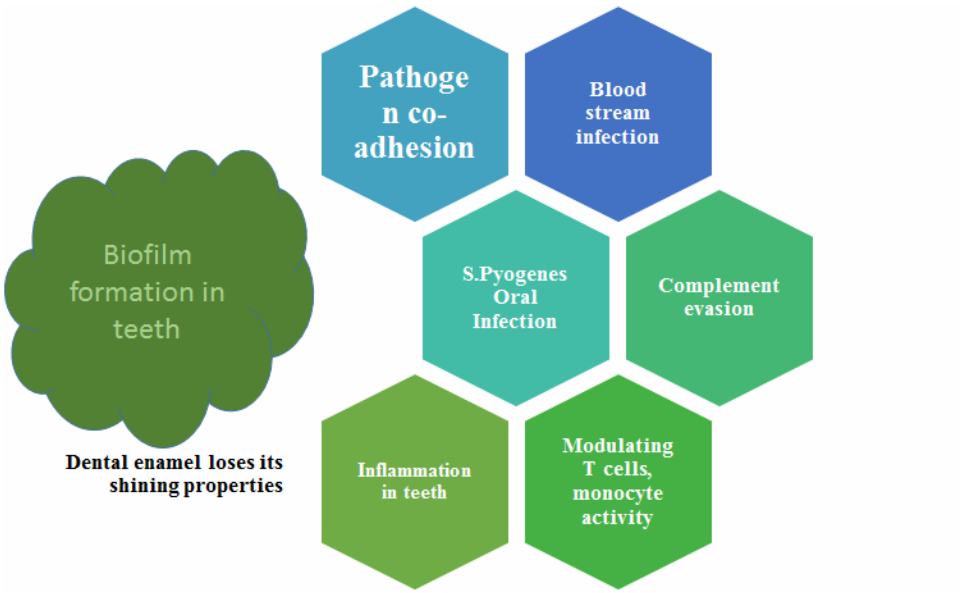

Figure 6: Oral infection causes step wise after *S.pyogenes* infection

Risk of oral bacterial infection. In many reports it was reported that systemic infections caused by oral infection. In few cases oral infections spread in edentulous patients. We study a case history in a 89-year-old Japanese woman [61]. Oral and maxillofacial cellulitis disease (Figure 6) followed by sepsis for *S. pyogenes* infection. It is detected in the wound of left macular and blood sample [61,62]. *S. pyogenes* causes severe oral infection as a part of neck and throat infection. *S.pyogenes* derived from the sinusitis and leaked to the oral cavity might have caused systemic infection through wounding of the oral mucosa [62,63].

II. Conclusion:

GAS is a pathogenic aerobic bacteria. It causes infection through air. Both research and public health laboratories are the key of pathogenic GAS populations. Although the epidemiology of GAS infection occur in some developed countries over the last century. GAS transmissions chains and provide a framework to assess the impact of future prevention of GAS infection. M protein, S protein, hyaluronic acids are some substances present on the extracellular matrix. This reaction occur by binding of CD44 on this surface. Diagnosis done by standard method. Some antibiotics are also use for the treatment of GAS infection. At last oral infection also studied by standard method.

Conflict of Interest: There is no conflict of interest.

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