



ALARMING OF MULTI DRUG RESISTANT STREPTOCOCCUS VIRIDIANS IN OROFACIAL INFECTIONS AND VARIOUS SYSTEMIC DISEASES – A SILENT KILLER

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ABSTRACT

Most species of *Streptococcus viridians* group bacteria are part of normal flora that are found in different tracts such as respiratory, gastrointestinal and urogenital regions of human body. Since discrimination between species of *Viridians Streptococci* group (VGS) remains difficult, patient management in identifying the target bacteria was unclear. Moreover dental history is overlooked during many hospital medical evaluations, which can be a clue for diagnosing the underlying pathogen and its virulence. Transient bacteremia and subsequent hematogenous seeding of VGS bacteria after dental procedures should be suspected on patient's immune status, medical, dental and social history. *Viridians Streptococci* group of organisms has become more virulent showing increased resistance compared to last decades. *Viridians streptococci* isolated from in clinical samples often is considered a contamination and therefore many seems to be present in routine diagnostic practices and therefore they have been underestimated of the clinical importance of infections caused by *Viridians streptococci*. They are considered as contaminants when isolated from blood cultures in routine sampling. One of this group gained special attention, the *Streptococcus mutants* for its pathogenicity of causing dental caries, various other diseases such as infective endocarditis, Bacteremia, toxic shock – like syndrome (ie., also called VSSS (*viridians streptococcal* syndrome that causes characteristic hypotension and acute respiratory disease syndrome (ARDS). *Streptococci* readily colonize mucosal tissues in genitourinary, gastrointestinal, respiratory, nasopharynx and skin. Most pathogens are opportunistic and part of them is colonizers that are attributed to spectrum of proteins expressed in their surfaces. These adherins interact with extracellular matrix components, host cells, other microbes, serum and saliva. This is the essential step to colonization and later invasion of host tissues. This review is given to brief the picture of *Viridians* group of *Streptococci* organisms. Interestingly multi-resistant *Viridians Streptococcal* colonization reported neonatal sepsis, which shows increased on mechanical ventilation with increased frequency of producing nosocomial infections and ventilation associated phenomena.

KEY WORDS: *Viridians Streptococci*, acute respiratory disease syndrome, *Viridians Streptococci* group Colonization, Oral infections,



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Received on : 22-09-2016

Revised and Accepted on : 06-02-2017

DOI: <http://dx.doi.org/10.22376/ijpbs.2017.8.2.b20-26>

INTRODUCTION

The normal oral flora of the adult comprises several hundred species, but few become established in the mouth of the neonate¹. The credit for having first observed and reported bacteria belongs to Antony Van Leeuwenhoek, in 1683. He set down accurate descriptions of bacteria and communicated them to the Royal Society of London. It was only some two centuries later that their importance in medicine and biology as a whole came to be recognized².

STREPTOCOCCUS VIRIDANS WHAT IS STREPTOCOCCUS VIRIDANS?

Streptococci are gram positive cocci arranged in chains or pairs². The introduction of DNA-based approaches during the 1960s heralded an era when genotypic studies combined with chemotaxonomic data allowed major developments to be made in the classification of bacteria in general, and of Gram positive cocci in particular. DNA-DNA base pairing experiments enabled genetic relationships within and between small groups of species or within single species to be measured while DNA-ribosomal (r)RNA homology studies and comparative oligonucleotide cataloguing of 16S rRNA provided information concerning the genetic relationships of a wide range of species of *Streptococci*. Today, the VGS are classified into 6 major groups: us both intra- and intergenerically. The mid 1980s marked a transition in *streptococcal* classification during which several major studies were reported that, together, can now be seen to reflect the shift away from traditional approaches, including numerical taxonomy, towards chemo taxonomic techniques and, ultimately, nucleic acid hybridization and comparative gene sequence analyses. The 'viridans' division was made up of species largely from the mouths and intestines of man and animals and included *Strep. salivarius*, *Strep. equinus*, *Strep. bovis*, 'varieties of *Strep. bovis*' and *Strep. thermophilus*. *Streptococci* from dairy sources comprised the 'lactic' division and included *Strep. lactis* and *Strep. cremoris*. The fourth division of Sherman termed 'enterococci' was made up of streptococci of faecal origin and included *Strep. faecalis*, *Strep. liquefaciens*, *Strep. zymogenes* and *Strep. Durans*³.

VIRIDANS STREPTOCOCCI

The *viridans* group *streptococci* (VGS) are a heterogeneous group of organisms that can be both commensal flora and pathogens in humans. They are the "grab bag" that remains when the beta-hemolytic *streptococci*, *enterococci*, and *pneumococci* are excluded from the *streptococci*. Perhaps the only consistency observed in discussions regarding the taxonomy of the VGS is a lack of consistency. Taxonomy is very controversial, and for many years, a standardized naming scheme or typing system for this group of organisms was lacking include the phrase "poorly classified." There are now at least 30 recognized

species of VGS. Today, the VGS are classified into 6 major groups: the *S. mutans* group, *S. salivarius* group, *S. anginosus* group, *S. mitis* group, *S. sanguinis* group, and *S. bovis* group³.

PHENOTYPIC AND BIOCHEMICAL IDENTIFICATION

Identification of VGS to the species level can be difficult, and phenotypic identification is not always accurate. The name "*viridans*" is somewhat of a misnomer, as many species do not produce any hemolysis on blood agar. From a classification perspective, it is not useful to try to differentiate alpha-hemolysis from a lack of hemolysis on blood agar plates (sometimes referred to as "gamma-hemolysis"); this feature can vary widely with the growth medium used to cultivate the organism, as well as the incubation temperature. The VGS are a group of catalase-negative, Gram-positive cocci with a chaining morphology on microscopic examination. They are leucine aminopeptidase positive, pyrrolidonyl-aryl-amidase negative, and do not grow in 6.5% NaCl, and almost all species are negative for growth on bile esculin agar. They differ from *pneumococci* in that they are optochin resistant and are not bile soluble³. The identification of *viridans streptococci* is a difficult undertaking due to lack of uniformity in cultural and biochemical characteristics and the existence of different nomenclature and classification scheme¹.

CLASSIFICATION AND ANTIGENIC TYPES

Streptococci are classified on the basis of colony morphology, hemolysis, biochemical reactions, and (most definitively) serologic specificity. They are divided into three groups by the type of hemolysis on blood agar: β - hemolytic (clear, complete lysis of red cells), α hemolytic (incomplete, green hemolysis), and γ hemolytic (no hemolysis). Serologic grouping is based on antigenic differences in cell wall carbohydrates (groups A to V), in cell wall pili-associated protein, and in the polysaccharide capsule in group B *Streptococci*.² The non-hemolytic *streptococci* are those whose colonies do not produce clear zones on blood agar by the complete destruction of erythrocytes; that is, they are not beta-hemolytic. Because many produce greenish discoloration on blood agar (alpha hemolysis), the group is also called the *viridans streptococci*, although many are completely indifferent to blood. They usually do not react with Lancefield grouping sera. They are human commensals and are a major component of the oral flora. Even within this loose definition, exceptions abound: some types of *Streptococcus anginosus* are beta-hemolytic, and many react with Lancefield A, C, F, or G antiserum; *S. bovis* has some characteristics of the enterococci, including a Lancefield D reaction. The human nonhemolytic *streptococci* can also be defined in a practical way by the exclusion of other *streptococci*; the viridans group is what remains when human pathogens and commensals that are *S. pyogenes*, *enterococci* (a

separate genus now) *pneumococci*, Lancefield group B, and "large colony" group C and G are eliminated⁴

STREPTOCOCCAL ADHERENCE AND COLONIZATION

Streptococcal adherence and colonization are complex multilevel processes that define the success or failure of the organism in human ecosystems. As such, *streptococci* devote considerable resources to ensuring the availability of an appropriate repertoire of effector molecules with sufficient redundancy to be robust in situations where one particular activity is unavailable or impeded by host or other bacterial factors. Moreover, these are not passive events; rather, streptococci are continuously monitoring the local environment and fine-tuning the expression of adhesins, communication systems, and metabolic pathways to optimize fitness under the prevailing conditions. The universal presence of *streptococci* in humans (and in many other animal hosts) reflects the success of these strategies. Paradoxically, the strengths of the *streptococcal* colonization mechanisms may also turn out to be weaknesses that can be exploited to develop new ways to control colonization and infection. Vaccination against pathogenic species is very much a pre-ferred strategy because it reduces the usage of antibiotics. These may be harmful, as in the case of application to pregnant mothers to act against potential VGS infection of neonates, or simply add to the ongoing problem of antibiotic resistance development. However, the vaccine route is fraught with difficulties, a major one being that the best protective (opsonic) antibodies are directed against cell surface components that are highly antigenically variable⁵.

ORAL MICROBIOTA AND SALIVARY IMMUNOGLOBULINS

Saliva also contains several specific and nonspecific defense factors. SIgA is the principal specific defense factor of saliva, and its role is discussed more extensively below. The nonspecific defense factors include mucins, nonimmune salivary glycoproteins, lactoferrin, lysozyme, peroxidase, histatins, and cystatins. Mucins are high-molecular-weight glycoproteins produced by submandibular, sublingual, and numerous minor salivary glands. They are the principal organic constituent of mucus, the slimy viscoelastic material that envelopes all mucosal surfaces of the body. The IgG, IgM, and IgA antibodies directed against a variety of oral microorganisms have been detected in plasma and crevicular fluid even in healthy individuals. These antibodies may influence the oral microbiota by interfering with adherence or by inhibiting bacterial metabolism. Furthermore, the IgG antibodies may enhance phagocytosis and killing of oral microorganisms through activation of complement or opsonization. It has been demonstrated that systemic immunization of animals with periodontopathogens may reduce the colonization of these bacteria in the gingival crevice and reduce periodontal destruction. However,

since periodontal diseases are of multifactorial origin, systemic immunization with periodontopathogens may also enhance the destruction of alveolar bone⁶.

PCR-BASED METHODS FOR GENOTYPING VIRIDANS GROUP STREPTOCOCCI

The viridans group, or oral, *streptococci* are a heterogeneous group of bacteria primarily isolated from the oral cavity and the gastro- and urogenital tracts. These bacteria and, in particular, members of the *anginosus* group (*Streptococcus anginosus*, *Streptococcus intermedius*, and *Streptococcus constellatus*) and the *mitis* group (*Streptococcus mitis*, *Streptococcus oralis*, *Streptococcus anguinus* [*Streptococcus anguis*], *Streptococcus parasanguinis* [*Streptococcus parasanguis*], *Streptococcus gordonii*, *Streptococcus cristatus* [*Streptococcus crista*], *Streptococcus infantis*, and *Streptococcus peroris*) may be associated with extraoral diseases including deep-seated abscesses in the liver and brain, infective endocarditis, and septicemia, while members of the *mutans* group (*Streptococcus mutans* and *Streptococcus sobrinus*) are associated with dental caries. The typing of strains of individual species of viridans group *streptococci* is not often reported, and consequently, the range of techniques used to type members of these species has been limited. Ribotyping has been used to demonstrate the oral origin of viridans group *streptococci* isolated from patients with infective endocarditis, while restriction fragment length polymorphism analysis, ribotyping, and arbitrary primed PCR (AP-PCR) have been used to study the ecology and person-to-person transmission of *S. mutans*. The genotypic variation of *S. mitis* biovar has also been studied by ribotyping. However, the non-PCR methods are time-consuming and technically demanding, and especially with regard to restriction fragment length polymorphism analyses in particular the resulting DNA fragment patterns can be very difficult to interpret given the large number of bands present in the patterns that are produced⁷.

TAXONOMIC AND NOMENCLATURE CHANGES

The changes in the nomenclature and taxonomy of the *Streptococcus* genus are numerous and varied. Eleven species and four subspecies of *streptococci* are beta-hemolytic and can be identified by Lancefield grouping and a few phenotypic tests. Nearly all these species and subspecies are isolated from human infections. However, among the non-beta-hemolytic species, 26 different species of viridans *streptococci*, 5 different species of what was termed *S. bovis*, 5 different species of nutritionally deficient *streptococci*, 9 different species of other *streptococci*, and 3 new genera of gram-positive cocci in chains have been described. The majority of changes in the non-beta-hemolytic 3 have been the addition of species. These additions for the most part

have complicated the recognition of each specific species⁸

ORAL FLORA AND SUBACUTE ENDOCARDITIS

Streptococcus mutans, known to be an aetiological agent of dental caries, also causes infective endocarditis (IE), although a comparison of isolates from the oral cavity and infected heart valve of the same patient has not been reported. The recent development of molecular techniques has enabled prompt identification of targeted bacterial species in specimens, with significantly improved specificity and sensitivity. PCR methods using primers constructed with a species-specific nucleotide alignment are widely used for the detection of specific species. In addition, a broad-range eubacterial PCR assay with amplification of bacterial DNA and subsequent direct sequencing is considered to be a reliable diagnostic tool⁹. Since Horder's classic description of infective endocarditis nearly three quarters of a century ago antibiotics and valve replacement have transformed the then hopeless prognosis. Studies have shown a changing pattern of the disease, but despite the enormous advances in microbiology, particularly the speciation of the *streptococci*, the source of the infection is often not known and the proportion of cases related to dental procedures or sepsis is probably smaller than previously believed¹⁰.

INTERACTIONS AMONG COMMENSAL STREPTOCOCCI

A freshly cleaned tooth surface is colonized by pioneer oral *streptococci*. However, even this early event is not immune to interspecies competition. *S. sanguinis* and *S. gordonii* are among the first species to colonize the tooth surface and can be isolated from the same intraoral sites. Both organisms express specific cell surface adhesion molecules with similar binding capacities. Nobbs and colleagues demonstrated an interspecies antagonism for host-derived binding sites between *S. sanguinis* and *S. gordonii*¹¹.

STREPTOCOCCAL TOXINS

While several toxins are found across *streptococcal* species boundaries, each of these species expresses a specific repertoire of toxic molecules that target specific aspects of host immunity and physiology. Indeed, many clones within individual species express distinct toxin profiles. These toxins play crucial roles within the host-pathogen interaction, allowing the pathogen to colonize, proliferate and disseminate. Several of these toxins have demonstrated utility as candidate vaccine antigens, in inactive forms, and in several instances, the specificity of toxin action has been experimentally utilized in the development of novel therapeutics, such as anti-cancer agents. Deepening of our knowledge of the mode of action of these toxin molecules will aid in

our efforts to prevent disease caused in humans and animals by the various *streptococcal* pathogens¹².

VIRIDANS STREPTOCOCCI IN NEUTROPENIC PATIENTS

Patients with hematologic malignancies are at high risk for the development of nosocomial bloodstream infections due to viridans group *streptococci*, with *S. mitis* and *S. oralis* being recovered most frequently. Epidemiologic typing of these isolates substantiates the concept that bloodstream infection due to viridans group *streptococci* usually derives from an endogenous source rather than from patient-to-patient transmission. True reinfection with the same strain during repeated episodes of neutropenia may occur¹³.

VIRIDANS STREPTOCOCCI AND RESPIRATORY INFECTIONS

VS can cause respiratory tract infection through the following routes: (1) aspiration of oral secretions; (2) direct implantation due to trauma or surgery; (3) by extension from contiguous foci of infection; and (4) via the bloodstream from distant sites. VS are generally considered harmless commensals but their introduction to sterile sites outside of normal habitats can cause severe infections, such as endocarditis. Although VS were previously thought to rarely cause community-acquired pneumonia (CAP), they have emerged as a causative agent of lung abscess and empyema in several case series¹⁴.

VIRIDANS STREPTOCOCCI AND BLOOD IN CANCER PATIENTS

The bloodstream infection usually occurs in cancer patients with mucositis and neutropenia due to antineoplastic chemotherapy-related toxicity. In these patients, studies have found that viridans *streptococci* are among the most common organisms isolated from the cultures of bacteremia samples. As cancer care has improved and intensified over recent decades and the patients survive longer, these and other infectious complications become more pronounced. The most common *viridans streptococci* that cause neutropenic bacteremia have been *S. oralis*, *S. mitis*, and *S. salivarius*. Identification of these species, however, was reached through traditional biochemical reactions that may be variable and overlapping among different as well as closely related species¹⁵.

VIRIDANS STREPTOCOCCAL BACTEREMIA

Bacteremia is identified in 10-27% of febrile neutropenic patients with hematologic malignancies, and 18-29% of the bacteremia is caused by *viridans streptococci*. Although Gram negative bacteria were the most common isolates to cause bacteremia in febrile neutropenic patients in the past, *viridans streptococci*

are currently one of the most common isolates in both adults and children. *Viridans streptococcal* bacteremia (VSB) has been reported to cause severe complications such as shock and acute respiratory distress syndrome (ARDS) in 18-39% of infected neutropenic patients and death in up to 20%. A higher occurrence rate of these severe complications was reported in children compared to adults¹⁶. VSB was defined as growth of *viridans streptococci* from at least one peripheral or central blood sample. Neutropenia was defined as having an ANC lower than 500/ μ L or an ANC lower than 1,000/ μ L that was predicted to be lower than 500/ μ L within two to three days, and fever was defined as a body temperature higher than 38.0°C with a tympanic thermometer or 37.5°C with an axillary thermometer. Severe complications included shock, any kind of mechanical ventilator care, ARDS, and death. Shock was defined as hypotension (mean arterial pressure less than 60 mmHg in adults, and systolic blood pressure less than the 5th percentile to age in children) requiring an intravenous fluid bolus or inotropic agents to maintain normal blood pressure, and ARDS was defined as PaO₂/FiO₂ < 200 in arterial blood gas analysis of a patient with hypoxia of SpO₂ < 90% and bilateral pulmonary infiltrates on the chest X-ray. The severe complications were considered to be attributable to VSB if there was no clinical improvement after the diagnosis of VSB with severe complications, no other infectious isolates were detected, no deterioration in underlying malignancy was observed, and no other clinical diagnoses were made. Death attributable to VSB was defined as death accompanied by severe complications attributable to VSB within 14 days after the diagnosis of VSB, and overall death included death from all causes within a month after the diagnosis of VSB¹⁶.

IDENTIFICATION OF *STREPTOCOCCUS VIRIDIANS* CLINICAL ISOLATES

Viridans Group *Streptococci* (VGS) species-level identification is fundamental for patients management. Matrix-assisted laser desorption ionization—time of flight mass spectrometry (MALDI-TOF MS) has been used for VGS identification but discrimination within the *Mitis* group resulted difficult. In this study, VGS identifications with two MALDI-TOF instruments, the Biotyper (Bruker) and the VITEK MS (bioMérieux) have been compared to those derived from *tuf*, *sodA* and *rpoB* genes sequencing. VGS isolates were clustered and a dendrogram constructed using the Biotyper 3.0 software (Bruker). *RpoB* gene sequencing resulted the most sensitive and specific molecular method for *S.pneumonia* identification and was used as reference method. The sensitivity and the specificity of the VITEK MS in *S.pneumonia* identification were 100%, while the Biotyper resulted less specific (92.4%). In non pneumococcal VGS strains, the group-level correlation between *rpoB* and the Biotyper was 100%, while the species-level correlation was 61% after database upgrading (than 37% before upgrading). The group-level correlation between *rpoB* and the VITEK MS was 100%, while the species-level correlation was 36% and

increases at 69% if isolates identified as *S.mitis/S.oralis* are included. The less accurate performance of the VITEK MS in VGS identification within the *Mitis* group was due to the inability to discriminate between *S.mitis* and *S.oralis*. Conversely, the Biotyper, after the release of the upgraded database, was able to discriminate between the two species. In the dendrogram, VGS strains from the same group were grouped into the same cluster and had a good correspondence with the gene-based clustering reported by other authors, thus confirming the validity of the upgraded version of the database. Data from this study demonstrated that MALDI-TOF technique can represent a rapid and cost saving method for VGS identification even within the *Mitis* group but improvements of spectra database are still recommended¹⁷.

IDENTIFICATION OF *S.PNEUMONIAE* FROM VGS

The genus *Streptococcus* currently consists of more than 50 species, most of which belong to one of six phylogenetic clusters that are revealed by comparative analysis of 16S rRNA gene sequences. In addition to the pyogenic group, which includes the traditional pathogenic species (i.e., hemolytic streptococci), these clusters are the *anginosus* group, the *mitis* group, the *salivarius* group, the *bovis* group, and the *mutans* group. Many of the species of these five clusters are major constituents of the commensal microbiota of the human oral cavity and upper respiratory tract and are occasionally implicated in various pathologies. The *anginosus* group, formerly called "*Streptococcus milleri*" in some parts of the world, includes three recognized species (*Streptococcus anginosus*, *Streptococcus intermedius*, and *Streptococcus constellatus*) that are primarily associated with suppurative infections of tissues of the mouth and various body sites, including the meninges. The *mitis* group currently includes 12 species, *Streptococcus pneumoniae*, *Streptococcus pseudopneumoniae*, *Streptococcus mitis*, *Streptococcus oralis*, *Streptococcus infantis*, *Streptococcus sanguinis* (formerly *S. sanguis*), *Streptococcus gordonii*, *Streptococcus parasanguinis* (formerly *S. parasanguis*), *Streptococcus cristatus* (formerly *S. crista*), *Streptococcus peroris*, *Streptococcus australis*, and *Streptococcus sinensis*. Although they are commensals of the upper respiratory tract, *S. pneumoniae* is a major cause of both local and systemic infections and several of the other *mitis* group *streptococci* have long been recognized as important etiologic agents of subacute bacterial endocarditis; septicemia, particularly in neutropenic cancer patients; occasional cases of meningitis; and eye infections. The two species of the *salivarius* group associated with humans (*Streptococcus salivarius* and *Streptococcus vestibularis*) are usually considered to be of low virulence, although occasional life-threatening infections such as bacteremia and meningitis have been reported. Some species of the *bovis* group, which is undergoing taxonomic reconstruction, cause endocarditis, particularly associated with colonic neoplasia. The *mutans* group *streptococci* (primarily *Streptococcus mutans* and

Streptococcus sobrinus) are considered the prime causative agents of human dental caries and also cause subacute endocarditis¹⁸.

SPINAL EPIDURAL ABSCESS AND VIRIDIANS STREPTOCOCCI

Spinal epidural abscess is a surgical emergency that requires immediate decompression. The common causes of epidural abscess are surgical interventions in the spinal canal and spread from nearby bone or soft tissues. Conservative management of epidural abscess is reserved for patients with poor surgical risk or patients without any neurological deficit. The association between spinal epidural abscess and infective endocarditis (IE) has rarely been described. Spinal epidural abscess rarely accompanies IE. When encountered *Streptococci viridians* is the most common causative organism, and accounts for 50% of IE cases. It is important to be aware of the possibility of a spinal epidural abscess accompanying *Streptococci viridians* endocarditis¹⁹.

PELVICOSTEOMYELETIS AND VIRIDIANS STREPTOCOCCI

Pelvic osteomyelitis is a rare entity with a highly variable clinical presentation. Patients usually present with hip or groin pain, difficulty walking, and sometimes fever. In children, it can mimic septic arthritis of the hip, an acute abdomen, and an inguinal hernia, making it a diagnostic challenge for many physicians. Predisposing risk factors include immunodeficiency, intravenous drug abuse, pelvic or urologic surgery, and young age. A more unfamiliar predisposing factor is strenuous physical activity in athletes, suggesting the presence of osseous microtrauma occurring in the setting of excessive stress to the pelvis during exercise. The most common organism responsible for osteomyelitis is *Staphylococcus aureus*, with the metaphysis of long bones being the most common site of infection. However, there are unusual organisms that should be suspected in certain patient situations; for example, *Salmonella paratyphi* osteomyelitis is more prevalent in patients with sickle cell disease, while *Bartonella henselae* is associated with cat scratches, and osteomyelitis caused by coagulase-negative *staphylococci* is more frequently found in patients with prosthetic joint implants. In an effort to highlight another possible osteomyelitis etiology association, we describe a novel case of isolated *Streptococcus viridians* osteomyelitis of the acetabulum in an otherwise healthy adolescent male following extensive dental treatment. The *viridans streptococci* are a group of alpha-hemolytic Gram-positive cocci, which are a part of the normal oral flora and are important agents involved in dental caries and subacute bacterial endocarditis. *Streptococcus viridians* is an unusual causative organism of osteomyelitis, but other documented cases of hematogenous osteomyelitis following dental procedures may alert physicians to begin more seriously considering this association.²⁰

OSTEOMYELETIS AND FOLLOWING ENDOCARDITIS DENTAL TREATMENT

Osteomyelitis is a serious and debilitating condition of which 6% of cases are associated with infective endocarditis, a disease which can have life threatening consequences. Both conditions are thought to develop following spread of a bacteraemic focus via the haematogenous route. This report highlights the case of a patient who presented with back pain and fever following a visit to a dentist to receive minor dental treatment. Blood cultures taken subsequently grew *streptococcus viridans* and an echo showed mitral valve vegetations. The case thus shows the importance of investigating back pain and looking for associated conditions such as infective endocarditis which can lead to serious consequences if not treated early. Gram-positive organisms such as *Staphylococcus aureus* and *Staphylococcus epidermidis* have been shown to be the predominant pathogen in pyogenic vertebral osteomyelitis. *Streptococcus viridians* is an unusual organism to be associated with both osteomyelitis and endocarditis with only few studies having reported such a finding. For example out of 91 patients with osteomyelitis and endocarditis, only 6 out of 25 cases of gram positive organisms grew *Streptococcus viridans*, however, *Staphylococcus aureus* being the most common organism isolated.²¹

VIRIDANS GROUP STREPTOCOCCI IN PEDIATRIC CANCER PATIENTS

The VGS are common causes of bacteremia in pediatric cancer patients, specifically those that are febrile and neutropenic. In the late 1980s, an increase in VGS bacteremia in this patient population was thought to be due to an increase in central venous catheter use. Since that time, anywhere from 11 to 30% of blood cultures from febrile, neutropenic cancer or stem cell transplant patients have been positive for VGS in various series. VGS bacteremia often results in complications, the most serious of which is *viridans streptococcal* shock syndrome (VSSS), with published mortality rates in children ranging between 40 and 100%.²²

CONCLUSION

Streptococcal viridans group organisms are most commonly resides in oral cavity, gut and genital regions. These organisms are susceptible to cause various life-threatening infections in newborns, young children and adult population. In case of neonates, stillbirths occurs due to viridans group of organisms. Adult respiratory distress syndrome, Sub-acute infective endocarditis and pneumonia are said to attack adults including neutropenic patients. Henceforth, diagnosis is most important. Firstly, most of the minor infections can be diagnosed by salivary samples from oral cavity and swabs from affected site, to rule out streptococcal species. Blood test can be performed to rule out bacteremia and spinal fluid to rule out meningitis, in

case of invasive infections. Since recent researches portrays the susceptibility of disease causing depends on the subtypes of the bacteria, proper analysis of the bacteria should be made clear. Moreover it was found that most of these organisms as commensals, the virulence of bacteria remains dreadful because most of the *viridians* group of organisms possess drug resistance. As the *streptococcal* speciation is not routinely performed globally, mortality rate increases

day to day. To overcome these harmness, further prospective research in speciation should be emphasized in improving better health to the mankind.

CONFLICT OF INTEREST

Conflict of interest declared none

REFERENCE

- Pearce C, Bowden GH. Identification of Pioneer *Viridans Streptococci* in the oral cavity of human neonates. *J Med Microbiol*. 1995; 42 : 67-72.
- Ananthanarayan, Paniker. *Streptococcus*. Textbook of microbiology; 8th ed. University press (India) ;2009. P. 204-217.
- Hardie JM and whiley RA . Classification and overview of the genera *Streptococcus* and *Enterococcus*. *J Appl Microbiol*. 1997; 83: 1S-11S.
- Coykendall AL. Classification and Identification of the *Viridans Streptococci* . *Clin Microbiol Rev*. 1989; 2(3):315-28.
- Nobbs AH, Lamont RJ, Jenkinson HF . *Streptococcus* Adherence and Colonization . *Microbiol Mol Biol Rev*. 2009 Sep; 73(3): 407–50.
- Marcotte H, Lavoie MC, Oral microbial ecology and the role of Salivary immunoglobulin A. *Microbiol Mol Biol Rev*. 1998. Mar; 62(1):71-109.
- Alam S, Brailsford SR, Whiley RA, Beighton D. PCR-Based methods for genotyping *viridans* group *streptococci*. *J Clin Microbiol*. 1999 sept; 37(9): 2772–76.
- Facklam R. What Happened to the *Streptococci*: Overview of Taxonomic and Nomenclature Changes. *Clin Microbiol Rev*. Oct. 2002; 15(4): 613–30.
- Nomura R, Nakano K, Nemoto H, Fujita K, Inagaki S, Takahashi T, Taniguchi K, Takeda M, Yoshioka H. Isolation and characterization of *Streptococcus mutans* in heart valve and dental plaque specimens from a patient with infective endocarditis. *J Med Microbiol* (2006); 55: 1135–40.
- Bayliss R, Clarke C, Oakley CM, Somerville W, Whitfield AGW, Young SEJ. The microbiology and pathogenesis of infective Endocarditis. *Br Heart J* 1983; 50: 513-19.
- Kreth J, Merritt J, Qi F,. Bacterial and Host Interactions of Oral *Streptococci*. DNA and cell biology. 2009; 28(8) : 397–403.
- Barnett TC, Cole JN, Rivera-Hernandez T, Henningham A, Paton JC, Nizet V, Walker MJ. *Streptococcal* toxins: role in pathogenesis and disease. *Cellular Microbiology*. 2015 Dec; 17(2):1721-41.
- Wisplinghoff H, Reinert RR, Cornely O, Seifert H. Molecular relationships and antimicrobial susceptibilities of *viridans* group *streptococci* isolated from blood of neutropenic cancer patients. *J clin microbiol*, 1999 June; 37(6): 1876–80.
- Choi SH, Cha S, Choi K, Lim J, Seo H. Clinical Characteristics of Community-Acquired *Viridans Streptococcal* Pneumonia. *Tuberc Respir Dis* 2015; 78:196-202.
- Han XY, Kamana M, Rolston K. *Viridans Streptococci* Isolated by Culture from Blood of Cancer Patients: Clinical and Microbiologic Analysis of 50 Cases. *J clin microbial*. 2006 Jan; 44(1): 160–65.
- Han S, Bae EY, Lee JW, Lee D, Chung N, Jeong D, Cho B. Clinical characteristics and antimicrobial susceptibilities of *viridans streptococcal* bacteremia during febrile neutropenia in patients with hematologic malignancies: a comparison between adults and children. *BMC Infect Dis* 2013; 13:273.
- Angeletti S, Dicuonzo G, Avola A, Crea F. *Viridans* Group *Streptococci* Clinical Isolates: MALDI-TOF Mass Spectrometry versus Gene Sequence-Based Identification. *PLoS one*. 2015 Mar; 10(3): e 0120502.
- Hoshino t, Fujiwara T, Kilian M. Use of Phylogenetic and Phenotypic Analyses To Identify Nonhemolytic *Streptococci* Isolated from Bacteremic Patients. *Eur J clin Microbiol*. 2005 Dec; 43(12) :6073–85.
- Oh J, Shim J, Lee K, Doh J. Cervical Epidural Abscess: Rare Complication of Bacterial Endocarditis with *Streptococcus Viridans*: A Case Report. *Korean J Spine*. 2015 Mar; 12(1):22-25.
- Hayden R, DO TS. *Streptococcus viridians* pelvic osteomyelitis after dental procedures in an adolescent male: a case report illustrating the importance of dental history. *Pediatr Therapeut* 2014, 4:4, ISSN:2161-0665.
- Choudhury M, Patel BR, Patel M, Bashir T. cases. *Streptococcus viridans* osteomyelitis and endocarditis following dental treatment: a case report. *Cases J*. 2009 Sep ;2:6857..
- Doern c, Burnham CD. It's Not Easy Being Green: the *Viridans* Group *Streptococci*, with a Focus on Pediatric Clinical Manifestations. *J Clinical Microbiol*. 2010 Nov; 48(11) 3829–35.

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We sincerely thank the above reviewers for peer reviewing the manuscript