

A Review on Updated Species List of Viridans Streptococci causing Infective Endocarditis

S.S. Jaya Lakshmi*  and K.V. Leela 

Department of Microbiology, SRM Medical College Hospital and Research Centre, Faculty of Medicine and Health Sciences, SRM Institute of Science and Technology, SRM Nagar, Kattankulathur - 603 203, Chengalpattu, Tamil Nadu, India.

Abstract

Viridans streptococci are important causative organism of infective endocarditis, which is a disease having long-lasting effects among the patients who live with the disease as well as those who are cured. Infective endocarditis due to viridans streptococci generally usually affects persons with structural heart disease and is also associated with intravascular prosthetic devices. After the onset of bacteremia with the pathogenic viridans streptococci, vegetation is formed in one or more heart valves. The diagnosis of infective endocarditis due to viridans streptococci is difficult to establish in patients with underlying risk factors and it involves the correlation of microbiological (in-vitro growth of viridans streptococci), clinical, and echocardiography results (modified Duke criteria). The common microorganisms are *Staphylococcus spp.*, *Enterococcus spp* followed by viridans streptococci. The details of viridans streptococci causing infective endocarditis were reviewed in detail. Viridans streptococci possess a challenge in identification up to its species level and which helps in the identification of the source of infection as well as treating the infection.

Keywords: Infective Endocarditis, *S. mitis* Group, Bacteremia, Viridans Streptococci, Platelet–fibrin Thrombus, *S. anginosus* Group, MALDI TOF–MS, and *S. salivarius* group

*Correspondence: drjayalakshmi24@gmail.com

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INTRODUCTION

The antigenically and biochemically diverse group of organisms causing oral and gastrointestinal infections are grouped into viridians streptococci, which also includes agents causing bacterial endocarditis.¹ Viridans streptococci are alpha-hemolytic streptococci. It is one of the causative agents of infective endocarditis. The risk factors causing infective endocarditis are age >60 years, dental caries or poor dental hygiene, acquired valvular diseases, prosthetic heart valves, congenital heart defects, intravenous drug users and previous history of bacterial endocarditis.² Infective endocarditis affects the endothelium of the heart and is due to bacteria when introduced into the bloodstream. Various infectious etiology contribute to causing infective endocarditis.³ It is due to minor injury during tooth brushing, poor dental hygiene, chronic skin infections, and implanted devices, viridans streptococci which lodge on the heart valves leading to infection of the endocardium.⁴

Infective Endocarditis

Infective endocarditis can be broadly classified into two types based on the duration of illness, which is due to the injury to the heart endothelium. They are acute, subacute, and chronic infective endocarditis. In acute infective endocarditis, the onset of the disease is within a few days, and it can be life-threatening. The patient generally presents with high-grade fever, persistent cough, palpitations, and swelling of the feet. In subacute or chronic infective endocarditis disease develops slowly and presents after weeks to several months. The patient presents with mild fever, fatigue, sweating, anemia, and weight loss.⁵

Causative Organisms of Infective Endocarditis

1. Native valve endocarditis: (i) Hospital-acquired: *Staphylococcus aureus*, Coagulase Negative *Staphylococcus*, *Enterococcus spp.*, viridans streptococci, *Candida spp.* (ii) Community-acquired: viridans streptococci, Coagulase Negative *Staphylococcus*, *Enterococcus spp.*, and *S. aureus*.⁶
2. Prosthetic valve endocarditis: Coagulase Negative *Staphylococcus*, viridans

streptococci, *Enterococcus spp.*, *S. aureus*, *Pseudomonas spp.*⁷

Updated Species of Viridans Streptococci

The various species of viridans streptococci contribute to causing infective endocarditis are listed in Table. This is the current updated (2022) grouping of viridans streptococci 8 and they are grouped into 5 groups namely,

- (i) *S. mitis* group
- (ii) *S. anginosus* group
- (iii) *S. mutans* group
- (iv) *S. salivarius* group
- (v) *S. bovis* groups

Pathogenesis of Viridans Streptococci

The above-mentioned risk factors contribute to the invasion of viridians streptococci into the bloodstream. This leads to direct injury of the inner lining of the heart muscle (endocardium) of heart. The initial phase is the preparation of the cardiac valve for bacterial adherence, followed by adhesion of circulating bacteria to the prepared valvular surface and finally survival of the adherent bacteria on the surface, with the propagation of the infected vegetation.¹¹ The alteration in the endothelial cells leads to either disruption of the surface and deposition of platelets and fibrin or other phenomena that render the surface susceptible to colonization by circulating bacteria. Bacterial colonization of vegetation leads to the formation of platelet–fibrin thrombus, due to transient bacteremia.¹² The formation of fibrin clots encasing the vegetation guides to valve destruction with loss of function. In the case of underlying structural heart disease and patients with the absence of host defenses, viridans streptococci proliferate forming small vegetations and it is shed into the bloodstream.¹³

Laboratory Diagnosis of Viridans Streptococci

It involves the isolation of viridans streptococci from the blood culture collected under aseptic conditions. Two sets of the blood sample are drawn more than 12 hours apart or three/four separate blood samples, with the first and last drawn at least 1 hour apart according to modified Duke criteria to arrive at a diagnosis of infective endocarditis.¹⁴

Table. Various species of viridans streptococci^{9,10}

<i>S. mitis</i> group*	<i>S. anginosus</i> group	<i>S. mutans</i> group	<i>S. salivarius</i> group	<i>S. bovis</i> group
<i>S. mitis</i>	<i>S. anginosus</i> subsp. <i>anginosus</i>	<i>S. mutans</i>	<i>S. salivarius</i> subsp. <i>salivarius</i>	<i>S. equinus</i> (<i>S. bovis</i>)
<i>S. infantis</i>	<i>S. anginosus</i> subsp. <i>whileyi</i>	<i>S. criceti</i>	<i>S. salivarius</i> subsp. <i>thermophilus</i>	<i>S. galloyticus</i> subsp. <i>galloyticus</i>
<i>S. sanguinis</i>	<i>S. constellatus</i> subsp. <i>constellatus</i>	<i>S. downei</i>	<i>S. vestibularis</i>	<i>S. galloyticus</i> subsp. <i>pasteurianus</i>
<i>S. parasanguinis</i>	<i>S. constellatus</i> subsp. <i>pharyngis</i>	<i>S. ratti</i>		<i>S. galloyticus</i> subsp. <i>macedonicus</i>
<i>S. pneumoniae</i>	<i>S. constellatus</i> subsp. <i>viborgensis</i>	<i>S. sobrinus</i>		<i>S. infantarius</i> subsp. <i>infantarius</i>
<i>S. pseudo pneumoniae</i>	<i>S. intermedius</i>			<i>S. infantarius</i> subsp. <i>coli</i>
<i>S. australis</i>				<i>S. alactolyticus</i>
<i>S. cristatus</i>				
<i>S. gordonii</i>				
<i>S. lactarius</i>				
<i>S. massiliensis</i>				
<i>S. oralis</i> subsp. <i>oralis</i>				
<i>S. oralis</i> subsp. <i>figurinus</i>				
<i>S. oralis</i> subsp. <i>dentisani</i>				
<i>S. peroris</i>				
<i>S. rubneri</i>				
<i>S. sinensis</i>				

*Excluding veterinary species.

Viridans streptococci show general characteristics similar to other streptococcal species. They are facultative anaerobes and catalase-negative. Gram staining shows Gram-positive spherical cocci in long chains. In blood agar, it produces alpha-hemolytic colonies. These bacteria can be differentiated from *S. pneumoniae* by optochin resistance, bile insolubility, inulin non-fermenter,¹⁵ absence of capsule, and arrangement, i.e., cocci in chains (whereas *S. pneumoniae* are diplococci).¹⁶ On a liquid medium, it shows granular turbidity. Viridans streptococci have no Lancefield antigen on the cell wall. Hence they are not classified serologically.¹⁶

After the conventional techniques of identification of the alpha-hemolytic colonies, they are subjected to species-level identification using MALDI-TOF MS: The bioMérieux VITEK® MS (MALDI-TOF MS) system,¹⁷ Matrix-Assisted Laser Desorption Ionization–Time of Flight based on mass spectrometry. Updated version 3.2 software of Vitex-2 MS identifies most of the pathogenic viridans streptococci species.¹⁸ The commonly associated species with infective endocarditis are *S. anginosus* subsp. *anginosus*, *S. gallolyticus*, *S. infantarius* subsp. *coli* and *S. sanguinis*. Identification up to species level of viridans streptococci is so challenging.¹⁹

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CONFLICT OF INTEREST

The authors declare that there is no conflicts of interest.

AUTHORS' CONTRIBUTION

Both authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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DATA AVAILABILITY

The data generated during and/or analysed during this review are available from the corresponding author on reasonable request.

ETHICS STATEMENT

Not applicable.

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