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Porphyromonas Gingivalis A Domain of Periodontal Disease: An Overview

Sushmita Yarlagadda[1*] Sindhura H[2]

[1]Intern, Department of Periodontology and Oral Implantology, Navodaya Dental College and Hospital, Raichur, India.
[2]Senior Lecturer, Department of Periodontology and Oral Implantology, Navodaya Dental College and Hospital, Raichur, India.

ABSTRACT

Background: Periodontal disease is probably the most widespread inflammatory disease caused by a specific periodontal pathogens included in the plaque biofilms. These organisms initiate a complex series of events resulting in an inflammatory response mediated by the host immune mechanism. When the balance of the pathogen-host equilibrium becomes tilted in favour of the invasive organisms, the immune response becomes exaggerated. Hence when this virulent species exist in an environment in greater proportions leads for an opportunity of periodontal destruction. Various species have been reported but, numerous studies have focused on the virulence of *P.gingivalis (Pg) because* of its strong association with periodontal diseases. It produces a repertoire of virulence factors that enhance its survival in the oral cavity and enable it to circumvent the host's protective strategies. The purpose of this review is to provide an overview of one of the main pathogen *Pg* a poly bacterium that consortium in periodontal disease.

Keywords: *Porphyromonas gingivalis*, Virulence factors, Host response, Periodontitis.

INTRODUCTION

A periodontal disease is characterized by chronic inflammatory lesions with destruction of the supporting periodontal tissues, which is associated with specific microbial complexes in subgingival biofilms. These micro-organisms attach to the tooth, epithelial surfaces or periodontal pocket. *Porphyromonas gingivalis* is an asaccharolytic and anaerobic bacterium that possesses a complex proteolytic system which is essential for its growth and evasion of host defence mechanisms. Several researches show *P.gingivalis* is the major etiological agent which contributes in destruction of periodontium. Socransky et al has stated that *Pg* is one of the major pathogens that leads to the chronic inflammatory periodontal disease. It can be present in both healthy as well as periodontitis subject. [1, 2]

Porphyromonas gingivalis is asaccharolytic obligatory, gram-negative, non-sporing, anaerobic and non-motile coccobacilli pleomorphic cells, ranging from medium length rods (1.5µm) to cocci. Darveau et al. classified this small, gram-negative, Black-pigmented anaerobe as a bonafide periodontal pathogen. [3, 4]

BIOCHEMICAL PROPERTIES: Porphyromonas gingivalis colonizes sites where oxygen tension is low but nitrogenous substrates are present. Thus isolation from saliva or mucous membrane of tongue & tonsils of the strains represents a temporary transition of this species. Subgingival ecosystem provides ideal environment. It possesses electron transport system in which protoheme & menoquinones are major carriers. It can be cultured in the absence of exogenous menodione as it can synthesize it from simple precursors in the medium. [5]

Site specificity

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*Correspondence Dr. Sushmita Yarlagadda.
Department of Periodontology and Oral Implantology, Navodaya Dental College and Hospital, Raichur, India.
Email: sushsushndc@gmail.com

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Van Winkelhoff et al confirmed the absence of *Porphyromonas gingivalis* in supragingival plaque of patients with loss of periodontal bone despite the high levels found in their subgingival plaque. This species can account for up to 50% of the anaerobic component of the cultivable flora and has a high correlation with disease progression, severity and bone loss. [6]

Virulence Factors

Porphyromonas gingivalis produces an unusually large array of potential virulence factors which may play a role in pathogenesis of periodontitis. [7] These can be broadly divided into factors that cause tissue destruction & those that cause host evasion. (Table 1)

Table 1: Factors that cause tissue destruction & those that cause host evasion

TISSUE DESTRUCTION	
Collagenase Trypsin-like protease Gelatinase	Keratinase Heparinase Nuclease Epitheliotoxin
Arninopeptidase Phospholipase A Alkaline phosphatise	Fibroblast growth inhibitors Endotoxicity
Acid phosphatise	LPS induced bone resorption Volatile sulphur compounds
Chondroitin sulfatase	Short-chain acid end Products
Hyaluronidase	Indol, Ammonia,H2S
Host evasion	
Lysis and intracellular Killing	Degradation of plasma protease inhibitors
Resistance to C' killing C'3/ C'5 degradation	Degradation of iron transport proteins
Immunoglobulin proteases	Inhibition of PMN's
Fibrinolysin	Chemotaxis inhibitors
Superoxide dismutase NADH oxidase Free-radical formation	Decrease phagocytosis

Capsule: The presence of a capsule in *P.gingivalis* is an important anti-phagocytic virulence. Increased encapsulation is correlated with increased resistance to phagocytosis, serum resistance, and decreased induction of PMN chemiluminescence. Thick capsule physically mask the lipopolysaccharide, and therefore the complement cascade cannot not be activated. Hence invading bacteria are therefore protected from opsonisation and phagocytosis. [8, 9]

Fimbriae: P.gingivalis fimbriae are responsible for binding the bacterium to host tissues i.e. Saliva-coated hydroxyapatite, the salivary proteins statherin and the salivary proline-rich protein, epithelial cells, fibroblast that adheres and colonize in the oral cavity. The fimbriae do not bind to red blood cells, indicating that the fimbriae possess host cell specificity. [10]

Fimbriae are important virulence factors involved in tissue destruction. They have chemotactic properties & demonstrate cytokine induction, which induces the production of IL-1α, IL-1β, IL-6, and IL-8 & TNF-α. [11]

Outer membrane proteins

20 major proteins ranging in size from approx. 20 to 90 kDa, many of which are heat modifiable.

24 kDa: fibroblast activating factor, this protein have significant role on fibroblast.

75 kDa: stimulates polyclonal B cell activation & elicits IL 1 production. It is major outer membrane protein that exits as a high molecular weight.

83, 26 kDa: hemin regulatory protein, it produces haemolysin which lysis the blood cells.

They also help in co aggregation with other bacteria's through specific adhesin-receptor

molecules this helps the bacterium to compete effectively for hemin in the periodontal pocket. [12]

Lipopolysaccharide:

The outer membrane of gram-negative bacteria is attached to host by selected lipoproteins. It shows an immunobiological importance. The endotoxin activity is confined to the lipid A, this lipid A is a stronger inducer of IL – receptor antagonist, IL-6 & 8, IFN gamma, GM-CSF.

P gingivalis lipopolysaccharide does not stimulate the expression of E-selectin by human endothelial cells and thereby hinders extravasation of leukocytes. Hence the activity of leukocytes is altered. It also inhibits E-selectin expressed by endothelial cells. All these data are in agreement with the involvement of P gingivalis in suppressing the host immune response. [13]

Proteinases [14]

One of the potentially significant virulent characteristic of P.gingivalis is large number of hydrolytic, proteolytic & lipolytic enzymes produced by all of the known strains. Many of these are exposed:

- At the surface, where they are able to come in contact with the host cell and tissue.
- Within the periplasmic space capable of being transported to the cell surface.
- In outer membrane vesicles which are sloughed from outer membrane during growth.

The classification of the proteinases has relied upon their catalytic functions. To date, four proteinases are recognized serine, aspartate, Thiol and metalloproteinase. Of these, the collagenases, amino peptidases, and the trypsin-like proteinases are critical to pathogenesis.

These latter proteinases have received most interest and since they cleave polypeptides after arginine + lysine residues, they are classified as either arginine - (Arg) or lysine - (lys-) specific proteinase.

The Arg and Lys proteinases are cysteine proteinases and have been given the common name **Gingipains** (Gingipains R1 R2). There is increasing excellent evidence that Gingipains are important proteins in the clinical events of periodontitis. The *P.gingivalis* collagenase has been classified as a proteinase with a hydrolytic predilection for collagen. The studies of Bourdeau et al. (1992) suggests that these collagenases are cysteine proteinases. At least 40 different proteins is produced by *P.gingivalis*. The secreted cysteine proteinase has also been shown to lyse RBCs. This purified haemolytic protein called *gingivain (Gingipains).* [15]

"GINGIPAINS" possess strong trypsin like activity that brings about hydrolysis of synthetic substrates like BANA. These constitute a group of cysteine endopeptidases that are responsible for 85% of general proteolytic activity & 100% of so called trypsin like activity. They cleave polypeptides after arginine & lysine residues, called as Arg Gingipains & Lys Gingipains. Arg-gingipain is encoded by two genes, while Lys Gingipains is encoded by only one gene (Kgp). The gene encoding Gingipains R with hemagglutinin/adhesion domain should be referred to as rgpA & the gene that encodes Gingipains R without this carboxy terminal domain should be referred to as rgpB. Sequence analysis has revealed that both the Arg-gingipain and the Lys Gingipains are unique proteinases, and do not share any similarity with any of the other known cysteine proteinase. [16, 17]

Function of *P.gingivalis* proteinases

The Gingipains have been shown to be potent vascular permeability in human plasma that cleaves bradykinin directly from the high-molecular-weight-kininogen. This ability significantly increases the gingival vascular permeability in periodontitis sites resulting in increased gingival fluid flow. Hence there will be an increased GCF flow in periodontitis site.

Since the Gingipains are chemotactic for PMNLS there is an increased concentration of neutrophils cells at sites of potential tissue destruction. This leads to the generation of higher level of proteinases. This provides a favourable environment for sub gingival plaque bacteria to thrive due to the presence of higher concentration of amino acids and peptides, which aggravates in further tissue destruction. [18]

With the accumulation of these neutrophils in the confines of the developing periodontal pocket, there is the potential for host cells to activate+ secrete numerous host destructive enzymes such as elastases, cathepsins, gelatinases, and collagenases. All of these participate in the destruction of periodontal tissues. [19]

Gingipains are also considered important in degrading the antibacterial peptides, such as neutrophil-derived α-defensins, complement factors like C3 and C4, T cell receptors they also reduce the expression of innate immune receptors CD14, which result in macrophage hypo responsiveness to bacterial infection. [20]

CONCLUSIONS

Porphyromonas Gingivalis is one of the much spoken about but lesser studied bacteria which has slowly but surely found its way into the etiology of the chronic form of periodontitis. With all its ability to evade and destroy the host, it remains as one of the most intelligent bacteria that we have had to deal with it. Much research is needed to remove this bacteria from the periodontal environment and evolve newer therapeutic strategies in dealing with this seemingly innocuous microbe.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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