Review Article

The chronicles of green complex bacteria

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Abstract

Periodontal pathogens have always captivated the attention of periodontists and microbiologists as it account for causing periodontal disease in 90% of the population globally. Clinical and experimental studies have confirmed that destructive activity on the periodontium is due to certain strains of bacteria that occupy a relatively small portion of dental biofilm. Among them, the green and the red complex bacteria enjoy the popularity of being the most notorious strain in disease initiation and progression. The genera of green complex bacteria comprise three pathogens- *Aggregatibacter actinomyecetecomitans*, *Capnocytophaga*, and *Eikenella corrodens*. The group possesses several stratagems and key elements that aid them in escaping the immune surveillance and creating a harsh environment for the periodontium. The review focuses on defining the green complex bacteria and their role in periodontitis.

Keywords: *Aggregatibacter actinomyecetecomitans*, capnocytophaga, *Eikenella corrodens* virulence, endotoxins, leucotoxin

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Submitted: 29-Apr-2024, **Revised:** 13-Oct-2024, **Accepted:** 05-Nov-2024, **Published:** 31-Dec-2024

INTRODUCTION

It has been estimated that more than seven hundred species of bacteria comprise the oral microbiome among which roughly 40% remain uncultivable. An intricate balance exists between the commensal and pathogenic micro-organisms in a healthy oral environment. Any disruption in this balance due to systemic ailments, hormonal fluctuations, and smoking can lead to dysbiosis, i.e.; an alteration in the configuration of the bacterial population by an increase in the number of pathogenic strains.[1,2] To be classified under the "disease-causing bacteria", a micro-organism has to satisfy the four criteria proposed by Koch. Nevertheless, the postulates faced some criticism by microbiologists as this is not universally applicable to all pathogens. Socransky presented a modified version of the above postulate and highlighted the nature of periodontal pathogens. He further adopted a color-coded classification for periodontal pathogens.[3]

"Green complex bacteria" (the secondary colonizers in plaque formation) is the key etiological factor in causing aggressive and chronic periodontitis. This complex encompasses three different bacteria- *Aggregatibacter actinomyecetecomitans, Capnocytophaga*, and *E. corrodens*. Studies have confirmed the role of both red and green complex bacteria in the disease initiation and progression. New microbiological tools and devices like immunofluorescence, ELISA, DNA probes, DNA–DNA Hybridization, and PCR have been adopted to elaborate the deleterious effects of these bacterial interactions with the periodontium.[4,5] Despite huge efforts and extensive research in this area,

Access this article online

Quick Response Code:

Website: https://journals.lww.com/JPAT/

DOI: 10.4103/jomfp.jomfp_121_24

How to cite this article: Ojha M, Amrita, Gupta D, Verma V. The Chronicles of green complex bacteria. J Oral Maxillofac Pathol 2024;28:633-40.

our knowledge regarding the core mechanism behind their pathogenicity and molecular genetics remains unclear.[6] The current review reflects on the potential and crucial elements of the green complex bacteria in eliciting a rapid destructive response on the periodontium

AGGREGATIBACTER ACTINOMYCETECOMITANS (AA)

Aggregatibacter actinomycetecomitans is a gram-negative, exogenous bacteria capable of causing true infections in the oral cavity. Its role in causing aggressive periodontitis in young and middle-aged adults has been well-acknowledged in microbiological studies. The disease is characterized by the rapid destruction of tooth-supporting structures without the presence of many etiological factors.[7,8] Its hostile behavior towards the host tissues makes them to receive special attention in the microbiological arena of periodontology.[9] The bacteria has been accused of causing other diseases like endocarditis, meniningitis, osteomyelitis, brain abscesses, facial cellulitis, thyroid abscess, and pneumonia. A lot of information about this bacteria needs to be comprehended thoroughly to unravel its secret weapons against the periodontium.[10,11]

A short history

Aa was first familiarized by Klinger as *A. comitans*- a coccobacilli that was extracted from the actinomycotic lesions of humans.[8] It was renamed by Topley and Wilson as Actinobacillus actinomycetemcomitans (actis: a ray; myces: fungus and comitans: associated).[9] Further Potts *et al.* retitled the bacteria "Haemophilus actinomycetemcomitans."[10] Nørskov-Lauritsen N and Kilian M remarked on the possibility of these bacteria sharing phylogenetic resemblance with *Haemophilus aphrophilus* and *Haemophilus segnis*. Hence the term "agrgregatebacter" was prefixed as genus which means "collective".[11,12]

Characteristics

AA is fastidious, non-motile, non-hemolytic, non-sporulating, gram-negative rods with a diameter of 0.4-0.5 μm *1-1.5 μm. They are mesophilic, microaerophilic, and capnophilic microbes requiring 5-10% of carbon dioxide for their growth. AA can be cultured on chocolate agar medium that exhibits small-sized colonies of 0.5 mm after a day, ut may surpass 1-2 mm after 48 hours.[13,14] The primary cultures are rough-textured and strongly adhere to the agar plates. However, several variants of such colonies concerning its texture have been detected as transparent rough, transparent smooth or opaque smooth colonies. The organisms are capable of producing acids from glucose, maltose or fructose, can reduce nitrate, and can yield alkaline phosphate. They are oxoxidase-negative weakly-positive, indole-negative, and catalase-positive in nature.[15]

Prevalence

It has been proposed that cultivable Aa happens to be present in 10% of periodontally healthy children, 30% in periodontally healthy adults, 50% in chronic periodontitis patients and 90% in juvenile periodontitis patients.[16]

Serotypes

Six different serotypes (based on the O-polysaccharide of LPS) of AA have been observed so far: a, b, c, d, e of which the first three are prevalent in the oral cavity. The serotype b displays enhanced leucotoxic activity and has been associated with juvenile periodontitis. This serotype displays repeated trisaccharide units of L-rhamnase, D-fucase, and N-acetyl-D galactosamine. The serotype c occurs in healthy individuals. Indirect immunofluorescence and immunodiffusion techniques are utilized to distinguish the type of serotype.[17,18]

Selective medium

Aa is typically incubated in a serum-containing medium that has added antibiotics to suppress the growth of gram-positive bacteria. The latter develops star-shaped or cross-cigar-shaped colonies which disappear upon sub-culturing, building up new smooth isolates. The initial culture media used by Socransky was Malachite green with bacitracin which was incubated for 5 days. Slots employed Tripticase soy broth medium with added vancomycin that demonstrated excellent growth of these organisms. Tsuzukibashi O selected a novel medium- AASM which was supplemented with vancomyin, bacitracin, dextrose, sodium bicarbonate, trypticase soy broth, yeast extract, and agar. Unlike many other members of the genus, Aa cannot be cultured on McConkey's agar.

The growth rate of the micro-organisms is augmented at an optimal Ph of 7-8 and in a medium containing 0.5-1% sodium chloride. Also, the colonies establish favorable growth when yeast extracts, cysteine, thiamine, steroids, and iron is added to the media. Currently, RPMI–1640 and Dulbecco's modified Eagle are being preferred to culture the bacteria.

Ultrastructure

- **Fimbriae:**

Fimbriae are small, filamentous cell surface appendages that project in a peritrichous manner. The attachment apparatus facilitates attachment to the host tissue and abiotic surfaces. The colonies can be fimbriated (that displays star-shaped

colonies) or non-fimbriated. The diameter of each filament measures more than 2 μm in length and 5 nm in diameter. Fimbriated strains exhibit star-shaped colonies whereas the vice versa is true for the non-fimbriated strains. The most abundant protein associated with these fimbriae is Flp which has a molecular mass of 6.5kda. This protein is regulated by tad operon genes. The inactivation of this gene will fail to express the fibrils.[19,20]

- **Vesicles/blebs:**

Aa bears numerous vesicles or blebs which may contain leucotoxin, endotoxin, or bacteriocin (actinobacillin). The vesicles possess adhesive properties and may function as delivery vehicles for toxic materials. Highly leucotoxic stains exhibit more vesicles in contrast to minimally or non-leucotoxic strains.

- **Extracellular amorphous materials:**

Amorphous material is a glycoprotein occurring on the cell surface of Aa that mediates adhesion and bone resorption. This aids the bacteria in implanting themselves into the underlying matrix. Studies have confirmed that bacteria without such matter exhibit reduced adhesion and virulence. The material can be easily washed off by phosphate-buffered saline.

Virulence mechanism

As defined by Slots (1999), a microbe can cause a disease[21]

A. Adhesion:

This is a key virulence factor that promotes the adhesion of the microbe to the host tissue. The bacteria own distinct proteinaceous machinery on the cell surface called adhesins that bind with specific substrates/receptors (cells, tooth, matrix, collagen, fibronectin).

Another distinguishing feature of Aa is the possession of Hap protein which migrates from the periplasm to the exterior of the cell and enables them to attach to the host surface.

Strains bearing fimbriae adhere 3-4 folds better. With the help of adhesins, bacteria themselves can form chains that cannot be disrupted by sonification.[22]

B. Invasion

Another important property required for virulence is the ability to invade eukaryotic cells. Aa can penetrate gingival epithelial cells, pocket spaces, and basal lamina.

C. Toxins:

Leucotoxin

The discovery of this heat-labile toxin by Taichman dates back to 1979. Baehni and his colleagues were credited with characterizing them biochemically. This endotoxin is a derivative of fatty acids that has a direct lethal action on the leucocytes and other granulocytes. The toxin is a primary virulence factor that is secreted mostly by the serotype b of Aa. The same is also secreted by other bacteria like *M. (Pasteurella) haemolytica, and Fusobacterium necrophorum*[23,24]

It is a 116kda protein consisting of 1055 amino acids and is a member of the RTX (Repeated in toxin) family which exists in the periplasmic space or in the vesicles of the pathogens. The gene (ltxA, ltxB, ltxC, and ltxD) responsible for imparting this toxin to Aa has been studied extensively by researchers. The secretion of this toxin depends on several factors like the Ph, oxygen, quorum sensing, growth pattern of the bacteria, the age of the culture as well as the age of the media. Epithelial cells, endothelial cells, and fibroblasts are particularly resistant to this toxin.[25] However, the toxin does not spare neutrophils, macrophages, and monocytes. The cells become susceptible to the toxin due to:

- Formation of pores on the target cell membrane
- Membrane depolarization
- Loss of intracellular potassium and rapid efflux of calcium
- Osmotic swelling

Leucotoxins allow the bacteria to escape the innate immunity without being noticed by the immune surveillance system of the body. It also aids in the bacterial attachment to LFA-1 receptors (containing CD 18/CD 11a) on the leucocytes which thereby leads to their death by membrane perforation or apoptosis. In the process, the lysosomal ingredients comprising reactive species are spilled into the surrounding tissue triggering inflammation.[26]

It was soon realized that Aa exhibits further two different leucocyte phenotypes: the minimally leucotoxic and the highly leucotoxic (JP2 strains/652 types). The expression of the mentioned phenotype is controlled by two different promoters. DNA analysis of the JP2 strain has revealed a missing ~500 bp at the 3' end. It has been hypothesized that due to the missing portion, the bacteria exhibit an enhanced transcription. Schaeffer *et al.* (2008) proposed that the protein OrfA regulates the transcription process in highly leucotoxic strains. The toxin is now being investigated for its anti-carcinogenic properties and its potential as a therapeutic agent in leukemia, lymphoma, and myeloma.[27] Sampathkuma *et al.*[28] constructed a hyper-leukotoxin-producing A. actinomycetemcomitans strain and identified a terminator located in the promoter region

extending from 298–397 that alters *ltx*A expression. Dileepan *et al*.[29] via his study confirmed that human CD18 acts as receptors for *A. actinomyce temcomitans* strain.

Cytolethal distending factor

First described by Johnson, these are heat-labile heterodimeric holotoxins expressed by three genes –cdtA, cdtB and cdtC. The protein is secreted by other bacteria like Campylobacter, *E. coli*, and Shigella. The damaging effects of the noxious substance are:

- The results of many studies convinced that this protein contributes to gingival epithelial breakdown by separating the keratinized layer. Histopathologically, the affected cells reveal a swollen appearance, loss of structural integrity, loss of desmosomal connections, thickening of rete pegs, and alteration in the expression of intracellular scaffolding proteins (E-cadherin).
- Lymphocye toxicity: The toxin is known to arrest the cell cycle at the G1/S or G2/M checkpoint. The DNAse enzyme is stimulated which induces damage to DNA response inside the cell and is responsible for apoptosis.
- Studies have also demonstrated its role in provoking inflammation. The toxin activates NLRB inflammasome by PAMPs (Pathogen-associated molecular patterns) and DAMPs (danger-associated molecular patterns) and inhibits the production of nitric oxide in macrophages which encourages the release of inflammatory mediators. Also, it induces the expression of NF-kb ligands on the osteoclasts impelling bone resorption.[30]

Fc binding protein

Also termed omp34, this noxious product is found over the cell surface and is known to inhibit complement activation.

Lipopolysaccharide (LPS)

This complex forms an important component of the cell wall of gram-negative bacteria. It has three major constituents- O antigen, Core oligosaccharide, and Lipid A. Core oligosaccharides protect the organism from defense cells. Lipid A has a toxic effect on monocytes and macrophages and also induces the release of IL-6, IL-1, IL-8, TNF-α, and PAF and prompts the activation of the coagulation cascade. The same also enhances the activities of pro-apoptotic mediators like caspases, cytochrome c, and BAK. Studies have suggested its role in periodontal medicine as well. Hematogenous dissemination of this toxin or bacteria from the oral cavity to the placenta in pregnant women can lead to low birth weight in infants.[31]

Heat shock protein (HSP)

These are molecular chaperons associated with the surface structure which at low concentrations induces cell proliferation and osteolytic activity at high concentrations.[32,33]

Cag E

Another defensive property of Aa, the toxin is concerned with causing cellular alteration in terms of motility, proliferation, apoptosis, and structural changes.

Morphogenesis protein C (Mor C)

The protein boosts the secretion of leucotoxins and assists in auto-aggregation of bacterial cells.[34]

JP2 Strains of Aa

In the mid-1990s, a highly leucotoxic strain of *Aa* was identified as causing aggressive periodontitis among the North and West African population. It is believed that this strain originated more than 2000 years ago. The leukotoxin secreted by this bacteria has a shortage of 530 base pairs and the expression for the same is exhibited in the promoter region of the leukotoxin gene operon. Hence, these microbes present with heightened toxicity.[35]

Over the years, advancements in microbiological analysis and molecular biology have simplified the detection of pathogens. PCR and loop-mediated isothermal amplification methods have been used to identify the JP2 strains in the African population. Studies conducted in Morocco, Uganda, Sudan, and Ghana demonstrated a definitive association between JP2 strains and rapid attachment loss of the periodontal apparatus.[36,37]

CAPNOCYTOPHAGA

Like *Aa*, these are micro-aerophilic, fusiform, fastidious, gram-negative bacilli which is a part of regular oral microbiota. The term "capnos" means smoke whereas "cytophaga" means cell engulfment. As the name suggests, the organisms grow best in 5-10% of carbon dioxide. The dimensions of this organism range from 4 to 40 μm in length and 0.3–0.5 μm in width. Three main species have been isolated from the pockets of periodontitis patients- *Capnocytophaga ochracea, Capnocytophaga sputigena, and Capnocytophaga gingivalis*. On a recent note, a few other species *Capnocytophaga canimorsus*, *Capnocytophaga cynodegmi*, and *Capnocytophaga haemolytica* have been isolated from dental plaque. However, their role in causing periodontitis is still a vague subject. The genus of this bacteria has been implicated in several systemic diseases like empyema, endocarditis, sinusitis, cellulitis, osteomyelitis, etc.[38]

Culture media

The organisms can be cultured on Columbia agar containing 5% sheep blood, brain heart infusion broth, thioglycolate broth (Oxoid), Schaedler agar (Oxoid), and chocolate agar at 37 degrees Celsius. Tripticase soy agar accompanied with horse serum, collagen or hemoglobin has also been proven to be a suitable growth medium. Yellow-orange colonies are formed on the medium of culturing. Identification of the microbes can be done via RAPID-ANA II System and MALDI-TOF MS. The organisms are catalase, oxidase, ONPG (O-nitrophenyl-β-D-galactoside) and arginine dihydrolase positive Members of the genus Capnocytophaga can use various carbohydrates like glucose, dextran, glycogen, inulin or starch as fermentable substrates and energy source.[39]

Virulence factors

The organism releases several toxins like aminopeptidase, phospholipase A2, lipid A, lipopolysaccharide and immunoglobulin A protease.[40,41]

EIKENELLA

Eikenella is gram-negative, slow-growing, non-motile facultative anaerobes that have been isolated from the oral cavity, intestinal and genital tracts. Eikens in the year 1958, described the features of this species and initially named them "bacteroides corrodens". The term *E.corrodens* was proposed by Jackson and Goodman. The bacteria was classified under the HACEK group of the Neisseria family. Mostly the disease caused by them is trifle and mild but can take severe forms in immunocompetent individuals. Newman and Sims investigated samples that were derived from pockets in patients with periodontitis or periodontal abscess. Later this bacteria was isolated from patients suffering from nasopharyngeal malignancy, pleural effusion, sinusitis, arthritis, endocarditis, pancreatic abscess, and urinary tract infection.[42]

The organisms demand high nutrition and can be cultivated on TSBV medium producing visible orange and grey colonies with diameters less than 3 mm. As the name suggests, they present themselves in corroding colonies which are circular, rough, and irregular. If cultured on blood agar, they stand distinct and prefer to pit the medium.

Favorable growth is observed at 37 degrees Celsius and a pH of 6–9 with 0–1% (w/v) NaCl. Acid is secreted by these microbes from D-galactose, d-glucose, d-fructose, d-mannose, amygdalin, aesculin ferric citrate, maltose, lactose, Sucrose, inulin, raffinose, starch, glycogen, xylitol and gentiobiose.[43]

The cell wall of this bacteria has a layer of an inner membrane, a peptidoglycan layer, and an outer membrane which may be sheltered by loosely structured slime. It is believed that this organism retains fimbriae with a diameter of 5 nm. Bacteria like *Kingella kingae, Moraxella bovis, and Kingella denitrificans* show similar phenotypic features when compared with this bacteria.

The organisms display a typical antimicrobial susceptibility configuration- susceptible to penicillin and resistance to penicillinase resistance penicillin, macrolides, aminoglycosides, and azoles.[44]

Virulence Factors

1. Lipopolysaccharides
2. Exopolysaccharide layer
   The bacteria are protected from the immune cells by capsules which are tightly bound exopolysaccharides over the surface of the cell membrane.
3. Outer membrane proteins
4. Adhesins
   The proteins help in the attachment of the pathogen to the substrate receptor.

UNDERLYING PATHOGENESIS

Compared to Adult periodontitis, the physiopathology of Aggressive periodontitis is less discussed in the literature as the prevalence of such disease is limited. Traits like significant bone destruction on first molars with incisor involvement, arc-shaped bone loss bilaterally which might exhibit mirror patterns of each other, and abnormalities in the microbiological presentations make them distinct from usual periodontitis cases.

These findings are uncommon situations; however, patients with permanent teeth also have suffered from the same. Histological investigations in generalized AgP patients with multiple root anatomical diversities revealed significant changes in the gingival epithelial layer and connective tissue. Furthermore, it has been noted that the lamina propria had inflammatory cell infiltration and collagen fiber disarrangement. These occurrences are indicative of a fully formed recurrent lesion.

The following characteristics are shared by both the generalized and localized forms of aggressive periodontitis as per the recorded cases in the literature.

- Patients have periodontitis but are otherwise clinically healthy.
- Rapid loss of periodontal structure and deterioration of alveolar bone health.

- Tendencies to aggregate in the family.
- The degree of periodontal tissue loss does not correspond with the amount of dental plaque deposits.
- Increased amounts of *Aggregatibacter actinomycetemcomitans*, formerly known as Actinobacillus actinomycetemcomitans. In a few microbiological samples, there was a heightened amount of P.gingivalis bacteria.

In addition, the localized periodontitis patients demonstrated features like:

- Occurs around puberty.
- Localised first molar or incisor presentation clinically and containing no more than two teeth other than first molars and incisors, and at least two permanent teeth (at least one of which is a first molar) with interproximal attachment loss.
- Robust serum antibody reaction

Following were the features found in aggressive generalized periodontitis.

- Affects people under thirty in most cases, though sufferers may be older.
- Generalised lack of interproximal attachment in three or more permanent teeth, excluding incisors and first molars.
- The loss of the alveolar bone and attachment loss is episodic.

According to the present accepted facts, it was discovered early on in the investigation of early-onset forms of periodontitis that those who were afflicted either had hereditary host response deficiencies or a metabolic imbalance. The innate immune response, which includes neutrophils, macrophages, fibroblasts, epithelium, and dendritic cells, is the first line of defense against periodontal disease. These cells are typically constantly responding to bacterial plaque in a state of initial subclinical "physiological" inflammation. Antigen-presenting cells trigger an adaptive immune response when this reaction is unable to limit the buildup of microorganisms. This response progresses from a lesion that is primarily T-cell dominated to one that is controlled by B cells, which is characteristic of periodontitis. As the evidence of neutrophils in gingival lesions and on the root surfaces of AgP cases grew, it became apparent that a variety of possible dysfunctions, such as increased adhesion, decreased chemotaxis, increased production of superoxide and nitric oxide, and decreased phagocytosis, could be attributed to the neutrophils of AgP patients and the disease's predisposition. The 1999 Workshop proposed that "Hyper-responsive macrophage phenotype, including elevated levels of prostaglandin E2 (PGE2) and interleukin (IL)-1β" is one of the secondary characteristics of AgP. AgP cases have recently been linked to an exaggerated local and systemic inflammatory response that is particular to the reaction to the bacterial endotoxin in LAgP and to the macrophage inflammatory protein (MIP)-1α.

Remarkably, in an experimental gingivitis model, even treated AgP cases showed an increased inflammatory response, pointing to a potential constitutive hyper-inflammatory state. These hints led to the conclusion that the substantial and rapid tissue damage to the periodontium observed in these cases may be caused by the host response if it is continuously stimulated by specific microbial triggers. Putative host response genotypes, which would result in constitutive neutrophil abnormalities or dysfunctions in other inflammatory/immune response pathways, have been the subject of genetic studies examining heritable AgP characteristics [Tables 1 and 2].

CURRENT CONCEPTS AND CONTROVERSIES

The 2017 classification of periodontal diseases eliminates the need to consider aggressive periodontitis as a separate entity since clinical and microbiological features fail to define it as a distinct disease but rather staging and grading the disease in terms of clinical

Table 1: Depicting the various virulence factors of the green complex bacteria responsible for causing rapid attachment loss in aggressive periodontitis

Virulence factor	Significance
Leucotoxin	Attacks neutrophils, macrophages and monocytes by forming • Formation of pores on the target cell membrane • Membrane depolarization • Loss of intracellular potassium and rapid efflux of calcium • Osmotic swelling
Adhesins	Promotes the adhesion of the microbe to the host tissue.
Cytolethal distending factor	• Lymphocye toxicity • Activates NLRB inflammasome by PAMPs (Pathogen associated molecular patterns) and DAMPs (Danger associated molecular patterns) and inhibits the production of nitric oxide in macrophages
Fc binding protein	Inhibit complement activation
Lipopolysaccharide (LPS):	Toxic effect on monocytes and macrophages and also induces the release of IL-6, IL-1, IL-8, TNF-α, and PAF and prompts the activation of the coagulation cascade. The same also enhances the activities of pro-apoptotic mediators like caspases, cytochrome c, and BAK
Heat shock protein (HSP)	Induces osteolytic activity
Cag E	Cellular alteration in terms of motility, proliferation, apoptosis, and structural changes.

Table 2: Above listed are the several host factor alterations that have been demonstrated in Aggressive periodontitis

Host factor	Response
Neutrophils	Reveals abnormalities including increased adhesion, reduced chemotaxis, increased superoxide and nitric oxide production and reduced phagocytosis, inability to form NETs, as they are responsible for evacuating pathogen-associated dental plaque molecular patterns.
Activated cytotoxic T cells, CD8+/ CD28+ cells	Enhanced levels
Pro-inflammatory cytokines (IL-1, IL-6, TNF-α, Nicotinamide phosphoribosyltransferase (NAMPT))	Enhanced secretion
Gingival crevicular fluid calprotectin, PGE2 nuclear factor-kB (NF-kB)	Elevated in GCF, fluids and tissues

attachment loss, bone loss, and risk factor assessment. However, the importance of these bacteria and their toxins have been implicated in various periodontal pathologies.[45]

The concept of green complex bacteria causing aggressive periodontitis has been challenged by several authors. More recent research has stressed the role of genetic polymorphism, leucocyte abnormalities, hyper-responsiveness of macrophages chromosomal defects, and systemic influences as be root cause of such diseases. Also, it has been proposed that the red complex bacteria can be responsible for aggressive periodontitis.[46] Also, the association of *Capnocytophaga* and *E. Corrodens* with periodontitis has been controversial. Newman *et al*.[47] have implicated *Capnoytophaga* as a periodontal pathogen, whereas a study by Dzink *et al*.[48] questioned this association and stated that these are beneficial species in the oral environment. Likewise, though *E. corrodens* have been isolated from periodontal pockets, the role of *E.corrodens* in causing periodontitis is still doubtful as this is not the chief periodontopathogen.

CONCLUSION

Recent studies have employed metatranscriptomics and metagenomics to figure out the pathogenesis of periodontal diseases and have suggested the significance of the polymicrobial community resulting from dysbiosis in initiating the disease. The green complex has been considered an opportunistic pathobiont and assaults the periodontal tissues when host resistance is altered. Although, the latest periodontal classification has abolished the concept of aggressive periodontitis, the strategies and tactics used by the bacteria in tissue invasion have always been appreciated. Hence, this review was an effort to unfold the basic nature, pathogenicity, and controversies associated with the green complex bacteria.

Data availability statement

The data used in the study are available on request by contacting the corresponding author

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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