RESEARCH ARTICLE

RELATION BETWEEN COVID-19 AND PERIODONTITIS DISEASE

Dr. Pratibha Chaudhary*, Dr. Pravesh Mehra**, Dr. Ali Asger Nakib***

ABSTRACT

Periodontitis disease is a chronic multifactorial inflammatory disease characterized by progressive destruction of the periodontium. Though the bacterial biofilm accumulation and maturation initiates gingival inflammation, progression of periodontal disease occurs consequent to the host response and dysbiotic changes in the microbiome. Various concomitant factors have been associated with PD such as diabetes, obesity, aging, hypertension, and so on; although, underlying mechanisms or causal associations have not been established completely. Interestingly, these same factors have been widely associated with progression or severe coronavirus disease 2019 (COVID-19), an illness caused by coronavirus SARS-CoV-2. Coronavirus infection has become a matter of serious concern for the world these days. Due to the continuous production of aerosol in periodontal clinics and because of the fact that the virus remains alive for 12 h, periodontists are highly susceptible for the same. This article is an attempt to throw light on coronavirus infection and how it has put a hault to periodontits clinical practice.

KEY WORDS

Coronavirus, SARS-COV-2, Periodontitis, gingival inflammation

ABOUT THE AUTHORS

* MDS
**HOD, LHMC New Delhi
***Assistant Professor, Bankura Sammilani Medical College And Hospital, West Bengal

CORRESPONDING AUTHOR

Dr. Pratibha Chaudhary
MDS
e- Mail Id : pratibha.chaudhary17@gmail.com

INTRODUCTION

COVID-19 is a disease caused by novel coronavirus named SARSCoV-2 that causes damage to the respiratory system which includes lungs, nasopharynx mucosa, salivary cells and oral epithelial cells[1]. Coronavirus infection was declared as a pandemic by the World Health Organization on March 11, 2020[2] and on April 13, 2020, this virus was recognized in over 158 countries worldwide claiming 105,952 lives and infecting 1,696,588 confirmed people worldwide.[3] The virus is thought to have a zoonotic origin closely related to bat coronaviruses[10] and SARS-CoV.[11] HENCE, It is believed that the virus possibly originated in bats of the Rhinolophus genus. It is a positive-sense, single-stranded RNA (+ssRNA) virus produces at least three virulence factors that promote shedding of new virions from host cells and inhibit immune response.[15] While investigations are still underway worldwide to better understand transmission dynamics and the spectrum of clinical illness, new guidelines are proposed daily with measures on how to better manage infected patients and put a hault to spread.

As the COVID-19 pandemic persists, two important questions were recently raised in the periodontal research community:

1) Does SARS-CoV-2 harbors in active periodontal disease?[3];

2) Can periodontitis disease increase the risk of COVID-19?[4]. these two querys are worth to ponder on, as they might help to re-model the future guidelines for periodontal therapy on periodontitis patients positive for COVID-19.

Periodontitis and relation with various Viruses

Periodontal disease is a chronic multifactorial inflammatory disease characterized by progressive destruction of the periodontium, alveolar bone destruction around the tooth and ultimately mobility and tooth loss. Though the bacterial biofilm accumulation and maturation initiates gingival inflammation, progression of periodontal disease

occurs consequent to the host response and dysbiotic changes in the microbiome. Dysbiosis may be modulated by inflammatory and tissue breakdown products, which selectively enrich certain bacterial species and by anti-inflammatory products released at the site of inflammation[5].

Since 1990s, viruses have been described as pathogens related to periodontal disease, with Epstein-Barr virus type 1 (EBV-1) being detected in 43% of periodontal sites and in only 18% of healthy sites[6]. Later, Herpes simplex virus and Human Cytomegalovirus have been described as positive in periodontal pockets of 26-78% and 42-58%, respectively, of patients with periodontitis, showing different virus families be found in unique rates across the population[7].

To substantiate, shot-gun DNA sequencing subgingival plaque was studied and samples collected from healthy and periodontitis patients showed that even though bacteria was present in 95% of the subgingival plaque samples, viruses were also present in these complex communities associated with bacterial biofilm complexes[8].

Does Periodontal Pockets harbor SARS-CoV-2?

Badran et al.[3], gave a hypothesis assuming that periodontal pockets help in virus replication as it provides conducive environment that could, therefore, be an additional focus of infection in COVID-positive patients.

The initial coronavirus infection of periodontal tissues may commence through direct infection from the oral cavity or basement membrane cells by hematogenous spread or infected immune cells[9]. The unceasing inflammatory response present in affected sites of periodontal disease could bring mononuclear cells infected by SARS-CoV-2[10]. Thus, it is reasonable to think that the crevicular fluid on the periodontal pocket could reservoir virus arriving from infected mononuclear cells and further mix with patient's saliva.

The SARS-CoV-2 single stranded RNA binds with the Angiotensin-converting enzyme-2 (ACE-2) receptors which are present in lungs , nasopharyngeal mucosa, salivary gland and oral epithelial cells to gain access to human cells[11]. This leads to elevated viral load in the saliva, active periodontal pockets and crevicular fluid basically entire oral cavity. But in dental operatory this can be controlled by antimicrobial prerinses with povidone-iodine mouthwash which is highly effective in viral killing[12].

Hence, with this hypothesis it seems reasonable that periodontal pockets need to be tested as potential reservoirs for SARS-CoV-2, as they present interactions with the oral cavity and bloodstream via capillary complexes, although nothing concrete has been proved, experimentally to support the same. This could be further extrapolated to the peri-implant environment, as increased inflammation is also found around implants and increased EBV prevalence has also been described in peri-implant sites when compared to healthy sites[13].

Is there increased risk of covid-19 in periodontistis patients?

Balaji et al.[4], explained a theory based on the fact that the periodontitis patients exhibit high levels of osteopontin in the gingival crevicular fluid from sites with periodontal destruction[14], and its byproducts play a major role in enabling the SARS-CoV-2 to infect the host cells.

Osteopontin (OPN), also known as bone sialoprotein I (BSP-1 or BNSP) is a noncollagenous, calcium-binding, glycosylated phosphoprotein, commonly found in the mineralized phase of bone matrix, which is mainly synthesized by pre-osteoblasts, osteoblasts and osteocytes and its levels are elevated in periodontal disease[15]. Increased levels of osteopontin induces NF- κB activation, which then increases furin expression[16]. During inflammatory process, interleukin - IL-6 is secreted by gingival fibroblasts cells which results in increased expression of Cathepsin L, a cysteine protease[17]. Both, furin and cathepsin L play a major role in enabling the SARS-CoV-2 to infect the host cells by cleaving S glycoprotein of the SARS-CoV-2 into S1 and S2 subunits by furin, allowing S1 subunit attaches itself to the ACE2 receptors present in the host cells. Finally, endosomal fusion is mediated by cathepsin B/L, allowing cell fusion and infection[18].

Unravelling which cellular factors are used by SARS-CoV-2 for cell entry might provide insights into viral transmission and reveal therapeutic targets. Recently, Hoffmann et al.[18] demonstrated a protease inhibitor (TMPRSS2, approved for clinical use) was able to block the virus entry on the host cells. Hence, this proves there is a similarity between SARS-CoV-2 and SARS-CoV infection and identify a potential target for antiviral intervention.

CONCLUSION

Since there is currently no vaccine or specific antiviral treatment, ongoing rigorous research is giving us a ray of hope and paving the way for development of a vaccine in near future. Meanwhile, in order to control spread of COVID-19 infection it is important to maintain social distancing and taking extraordinary preventive and safety measures, and also simultaneously recognizing the possible virus reservoirs in covid- positive patients, and potential targets for antiviral intervention on SARSCoV-2 infection

The two recent advances in publications in the periodontal field highlight that periodontal therapy could be considered a parameter of care in the global clinical management of COVID-positive patients,

aiming the reduction of viral reservoir in the periodontal pockets. Active periodontal treatment could decrease the expression of furin and cathepsin L, reducing the ability of SARS-CoV-2 to infect the host cells.

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