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Exploring the Role of Mucosal Immunity in COVID19 patients with Periodontitis - An Approach via Salivary Cytokines and Chemokines.

Bagavad Gita Jayaraman, Priya kannian, Gunaseelan Rajan, Raghavi V, Ranganathan Kannan, Kumarasamy N, Lavanya C, Vedavalli Subramanian, Stephen Challacombe, Newell Johnson, David Moyes, Mark Ide

Introduction

The role of mucosal immunity is more relevant in understanding the host response to the SARS CoV-2 virus as it gains entry into the body via the respiratory mucosa. Immune compromised individuals with co-morbidities such as diabetes mellitus, chronic obstructive pulmonary disease and cancer have been observed to have increased circulating systemic pro-inflammatory markers in response to the SARS-CoV2 virus increasing the risk of a cytokine storm. and disease severity. Mucosal immunity as reflected in the oral cavity plays a critical role in susceptibility/severity of COVID-19. It is known that in viral diseases T-cells and cytokines are altered in both systemic and mucosal immunity but have not been much explored in the mucosal response of the upper aero-digestive tract.

Periodontitis is associated with systemic diseases including respiratory illnesses like pneumonia and COPD. The anatomical continuity of the aerodigestive tract facilitates the translocation of potential respiratory pathogens from the oral cavity. Both diseases are characterized by an exaggerated immune response. A hyperinflammatory host response to a dysbiotic oral microbiome in periodontitis can result in a breakdown of the connective tissue around the teeth. Significantly higher levels of chemokines and cytokines have been detected in the saliva and gingival crevicular fluid of periodontitis patients.

In this study, we primarily aimed to understand if pre-existing periodontal disease increases susceptibility to SARS-CoV2 infection and affects mucosal immunity to COVID-19. We also aimed to estimate the levels of salivary cytokines and chemokine in COVID 19 patients and periodontitis and explore any possible association between salivary cytokines and chemokines in the UK South Asian /White British and the South Indian populations.

Methods

This cross-sectional analytical study included 232 subjects from VHS – IDMC (Infectious diseases medical centre) Chennai, India, who are participating in the *Role of oral microbiome & mucosal immunity in COVID-19 disease: diagnostic and prognostic utility in South Asian populations (MIMSA)* under UK-India partnership (UKRI-DBT COVID 19 Initiative). Subjects initially included the healthy, asymptomatic, mild, moderate and severe COVID-19 subjects. We also recruited patients with no apparent exposure to covid, post-covid and recovered groups.

Periodontal status was recorded by periodontal screening and recording index (PSR) in 180 subjects. A self-reported questionnaire for COVID-19 symptoms and previous history of periodontitis was given.

Patient-related characteristics: Covariates lincluding age, sex, smoking habits and other COVID 19-related comorbidities/risk factors such as diabetes, hypertension, pulmonary disease, chronic

kidney disease, cancer, coronary artery disease, obesity and any other co-morbidities were also recorded.
Stimulated whole mouth fluid (SWMF) and serum samples were collected from the subjects. Salivary Cytokines and chemokine MIG, MCP-1, TNF-a, Il-8, Il-6 and Il-1B of 55 Indian subjects and 39 white British and South Asians subjects living in the UK were estimated.

Results
The average age for males was 38.3±16.9 and for females 34.3±68.4 years (mean±SD). 68% of examined subjects were found to have gingivitis and 23% early periodontitis. 61% of the subjects belonged to the recovered COVID group and 23% to the mild covid group. Salivary IL-6 was significantly high in the mild COVID group ($p<0.05$). Post- COVID patients were found to have higher mean probing depth ($p<0.01$) than non-infected controls.

Conclusion
In the South Indian population, salivary IL-6 was significantly higher in mild COVID subjects than asymptomatic or control patients. Post- COVID patients were found to have higher mean probing depths. However there was no significant association between COVID-19 and periodontitis in these subjects. Early periodontitis patients had significantly high UCFP levels. IL-6 and TNF alpha showed high statistical significance in the advanced periodontitis group. There were no significant differences in salivary cytokine levels between the UK and South Indian subjects. Based on these findings we can conclude that mucosal immunity particularly IL-6 can play a pivotal role in COVID 19 subjects with periodontitis in the South Indian population.

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