



Short Communication

The human oral microbiome – is it altered in covid times?

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ABSTRACT

After the gut microbiota the second largest microbial community harbouring the human system is the oral cavity. The Human Oral Microbiome (HOM) comprise of over 700 species of bacteria, viral, fungi, protozoa, archaea which can affect the initiation and development of numerous localized and systemic diseases. Respiratory problems, mechanical ventilation and poor oral hygiene are the considered risk factors that offer a pathway for entry of microorganisms from oral cavity to the lower respiratory tract which leads to respiratory problems. A worldwide public health emergency presently of high concern, SARS-CoV-2, the cause of COVID-19 is intently related to co-infections in the lungs. Effective oral health care measures are essential to prevent infections, specifically in severe COVID-19 patients.

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1. Introduction

Joshua Lederberg, a Nobel Prize laureate, refer the ecological network of symbiotic, commensal and pathogenic microorganisms as the “microbiome” that reside in our body as microbial residents. In human the microorganisms located in the oral cavity are referred as Oral microbiome, oral microbiota or oral microflora. Dutchman Antony van Leeuwenhoek, a pioneer and the father of microbiology was the first to recognize Oral microbiome which constitutes both bacteria and protists and stated as “little living animalcules moving” in his own dental plaque in 1674. The range of microbes found in our bodies is nearly equal or maybe greater compared to that of human cells.¹

Oral viruses in human saliva are dominated by bacteriophages, notably few eukaryotic viruses recognized including herpes viruses, papilloma viruses, entero viruses and circo viruses in the oral cavity. Comparing stool

examination mouth has been determined to have more genetic elements, i.e., Viruses, transposons, plasmids and notable bacterial counts. Bacteriophages act as reservoirs for genes in the oral cavity involved in resistance to degradation of immunoglobulins, antibiotic resistance, adhesion to cell lining the oropharynx and complement.²

In December 2019 a contagious disease hastily confirmed with extreme worldwide spread emerged in Hubei, the Chinese province in the Wuhan City, Coronavirus 2019 Disease (COVID-19).³ Most patients appear to have wide range of signs from mild form of the disorder, while progression of 20% to severe disease, such as respiratory failure, pneumonia, or even death. The virus spreads faster but lower fatality rate than its precursors the SARS-CoV and Middle East respiratory syndrome coronavirus (MERS-CoV). The worldwide effect of this new epidemic is yet uncertain.⁴

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2. Oral Microbiome: Naturally Derived Adjuvants

From the existence of Human birth, a wide variety of microorganisms co-develop as a host, adapt to the mucosal tissues which has been evolved over thousands of years. The human oral microbiome consists of a core microbiome and a variable microbiome including yeasts, protozoa, archaea, bacteria and bacteriophages/viruses.⁵ The variable microbiome is unique to individuals depending on physiological and lifestyle changes, whereas core microbiome is common to all individuals. Stress, tobacco consumption, diet, Modern lifestyle alter our microbiome and its properties, where the ecosystem is no longer in balance. Organisms via way of means of a cooperative or synergistic manner and the interspecies interactions is remarkable for this microbiota commensals.⁶ Another noteworthy characteristic is that the phylogenetic microbial structure and the microbiome composition vary with ageing.

2.1. Acquisition of a normal oral microbiome

The dorsum surface of the tongue is one habitat niche of oral microbes, where the dominant microflora is *Veillonella* and *Prevotella*, with an increased risk of death due to pneumonia in older, frail patients. Oral and the respiratory tract microbiota express enzymes similar as transmembrane serine protease 2 (TMPRSS2), which enhance entry of viral organism into host cells and further causing infection.⁷ Bacteriophages inhabit through Dental plaque aggravating pneumonia, including *P. gingivalis*, which synergistically enhance pathogenicity. The poor oral hygiene habits lead to the accumulation of many periodontal microorganisms in the oral cavity causing oral dysbiosis which increase the incidence of pneumonia, which in turn accelerates lung function decline. *P. aeruginosa* and *H. influenzae*, were high risk factors for pneumonia progression, the respiratory pathogens colonizing the tongue and calculus. The oral hygiene measures, such as removal of tongue biofilm and calculus, help to reduce the condition.⁸

2.2. Oral microbiome and sars-CoV-2 as a co-infection

The profile of oral microbiome appeared to be profoundly altered in COVID-19 patients. In severely acute respiratory syndrome (SARS-CoV-2) patients, virus target tissues together with the brain, gut, lungs and kidneys, proinflammatory macrophages and lymphocyte infiltrates. It is diagnosed that alterations in bacterial communities of modifying heparan sulphate, required for SARS-CoV-2 binding to angiotensin converting enzyme 2 (ACE2) and TMPRSS2 virus receptors, the host-derived receptor for SARS-CoV-2 cause the virus to enter the body mainly through the oropharynx.³ An increased life threatening complications of COVID-19 are related to four major comorbidities, reason why the poor oral health and COVID-19 complications is suggested.

Mechanisms which has been proposed to explain the pathogenesis of a respiratory infection and the potential role of oral bacteria in;⁹

1. Oral pathogens been aspirated into the lungs.
2. Associated enzymes in the Periodontal disease modify the mucosal surfaces that allow adhesion and colonisation of respiratory pathogens.
3. The salivary pellicles on bacteria may be destroyed by Periodontal disease-associated enzymes which hinder clearance from mucosal surfaces.
4. Periodontal-associated cytokines may alter the Respiratory epithelium to promote infection by the respiratory pathogens.

2.3. Oral microbiome: Temporal changes in Covid-19 patients¹⁰

Opportunistic oral microorganism, including *Veillonella parvula*, *Capnocytophaga gingivalis*, *Leptotrichia buccalis*, and *Prevotella melaninogenia* were increasingly present in bronchoalveolar fluid of patients with COVID-19, suggesting that in COVID-19 patients oral cavity may serve as a carrier of bacteria in coinfection with SARS-CoV-2. whereas decrease in *Rothia*, *Streptococcus sanguinis*, *Haemophilus*, *Streptococcus infantis*, *Parvimonas*, *Streptococcus parasanguinis* clade 411, *Fusobacterium*, *Prevotella denticola*, *Streptococcus peroris*, *Prevotella oris*, *Saccharibacteria* strain HMT356 and *Gemella* spp. and increase in *P. pallens*, *Actinomyces* sp. HMT180, and *Treponema* spp and, and an additional *Streptococcus* spp.

At the species level, COVID-19 patients had decreased amounts of *Haemophilus parainfluenzae* and *parahaemolyticus*, *Gemella morbillorum*, *Parvimonas micra* and *sanguinis*, *Neisseria mucosa*, *Neisseria subflava*, *Veillonella parvula*, *Lactobacillus fermentum*, *Enterococcus faecalis*, *Acinetobacter baumannii*, *Atopobium parvulum* were increased.

Notably, many species of periodontopathogenic bacteria (*Eikenella corrodens*, *Aggregatibacter aphrophilus*, *Prevotella melaninogenica*, *oris*, *jejuni*, *denticola*, and; *Capnocytophaga gingivalis* and *sputigena*;) were significantly increased in COVID-19 compared to control subjects. The species *Aspergillus fumigatus*, *Malassezia restricta*, *Saccharomyces cerevisiae*, *Candida albicans* were identified at a fair level.

Staphylococcus (*Staphylococcus* phage ROSA), *Streptococcus* (*Streptococcus* phage EJ-1 and phage PH10), *Herpes simplex virus* type 1 (HSV-1) and four bacteriophages targeted, respectively, toward *Lactobacillus* (*Lactobacillus* phage), were increased in COVID-19 patients compared to controls. Interestingly, in COVID-19 patients the microbial community, oral virome appeared

more abundant representing 0.07% of in controls, where the relative abundance increased to 1.12%.

3. Conclusion

By balancing the Oral Microbiome of humans and by proper Oral hygiene measures humans could be protected to respiratory infections who are vulnerable in development of severe symptoms in COVID-19. For better understanding of how immunity is shaped by our microbiome, investigation on microbial products and their metabolites, responsible for coordinating specific immune protection will likely be a fruitful endeavour for identifying adjuvants.

4. Source of Funding

None.

5. Conflict of Interest


None.

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