

# Oral lesion and microbiome diversity in COVID-19 hospitalized patients.

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## Abstract

**Introduction:** The oral cavity is an important site for the entry and multiplication of respiratory viruses, and the immune system and oral microbiome act as antiviral barriers. Data regarding oral microbiome and COVID-19 is scarce. Therefore, a prospective cohort was conducted at the Hospital das Clínicas of FMUSP to evaluate the frequency of oral lesions associated with COVID-19 and the diversity of the oral microbiome on disease severity. **Methods:** Oral samples from SARS-CoV-2 positive patients were collected. After DNA extraction from the whole saliva samples, sequencing of the 16S rRNA gene using the Ion Torrent PGM platform was performed. Alpha and beta diversity analyses were conducted using the R program. Clinical data from electronic medical records were collected and multiple logistic regression model was constructed to assess the association between oral microbiome diversity and COVID-19 severity (oxygen therapy, mechanical ventilation). **Results:** The study included a total of 115 samples from 125 patients, 14 had oral lesions, the majority were female (54.8%), with a mean age of 55.4 years old. Around 59.1% of patients were in intensive care units(ICUs), 87.2% were using antibiotics, and 18.3% died. The most frequently antibiotics used were third-generation cephalosporins(35.7%), piperacillin/tazobactam(27%), and glycopeptides(21.7%). In general, the most abundant phyla were *Firmicutes*, *Proteobacteria*, and *Bacteroidetes*, representing 86.3% of the oral microbiome. Oral microbiome diversity analysis revealed statistical differences in COVID-19 severity (Shannon  $p=0.05$ ), presence of oral lesions Shannon  $p=0.05$ ), antibiotic use(Shannon  $p=0.04$ ), and oxygen therapy Observed  $p=0.04$ ). Differential abundance analysis identified specific taxa related to each variable, such as *Prevotella* in severe patients and *Staphylococcus* in individuals with oral lesions. Multivariable logistic regression pointed out that the SARS-CoV-2 PCR positive on the oral cavity and the age (above 60 years) were risk factors for disease severity. **Conclusion:** Despite the small number of participants with oral cavity lesions, we found significant differences in the microbial communities, particularly in the genus *Staphylococcus* associated with oral lesions. Although the abundance of *Prevotella* was associated with severity of COVID-19 on the microbiome analysis, the multivariate model showed that only age and RT-PCR positive for SARS-CoV-2 on the oral cavity were independent risk factors for severity.

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