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ORAL MICROBIOME DYSBIOSIS IN MECHANICALLY VENTILATED COVID-19 PATIENTS: NOVEL PATHOGENIC AND PSYCHOBiotic SIGNATURES

Background/Aim. Severe COVID-19 requiring mechanical ventilation profoundly disrupts the oral microbiome, yet species-level characterization remains limited. This study aimed to identify clinically relevant oral microbiota signatures in COVID-19 patients compared with healthy controls. **Methods.** Oral DNA from 50 patients with severe COVID-19 (ICU/MV) and 20 controls was profiled using the Ion AmpliSeq Pan-Bacterial Panel (Ion GeneStudio S5 Plus; Torrent Suite). Comparisons used Mann-Whitney U and Fisher's exact tests. Multiple testing was controlled by Bonferroni and Benjamini-Hochberg FDR. Beta-diversity was assessed using PERMANOVA and ANOSIM, with Betadisper verifying homogeneity of dispersion. Clinical confounders were not independently assessed and represent a study limitation. **Results.** A total of 192 (COVID-19) and 177 (control) taxa were identified; 141 shared, 51 COVID-19-exclusive, 36 control-exclusive. PERMANOVA revealed significant compositional separation (Bray-Curtis: $F = 4.5$, $p = 0.001$; Jaccard: $F = 3.4$, $p = 0.001$; ANOSIM $R = 0.13$, $p = 0.030$). Betadisper showed higher within-group dispersion in COVID-19 (Jaccard $p = 0.029$), indicating greater microbiome heterogeneity. Pseudomonadota were enriched in COVID-19 (30.7% vs. 15.2%), and Bacillota were reduced (42.1% vs. 61.0%). The strongest signal was a 10-fold reduction of *Streptococcus thermophilus* (0.7% vs. 7.0%; prevalence 20% vs. 90%; $p_{\text{adj}} = 1.79 \times 10^{-7}$). *Staphylococcus aureus* and *Pseudomonas* sp. were detected exclusively in COVID-19. A HACEK cluster was COVID-19-exclusive, warranting further investigation of potential endocarditis risk. Mycoplasmatota formed a COVID-19-exclusive phylum. *Neisseria meningitidis* was elevated in COVID-19 (2.45% vs. 0.76%; $p = 0.003$). **Conclusions.** The oral microbiota of patients with severe COVID-19 shows robust compositional divergence, with enrichment of Pseudomonadota and depletion of Bacillota. The 10-fold reduction in *Streptococcus thermophilus*, a species with reported psychobiotic properties, suggests potential functional relevance warranting further investigation. The COVID-19-exclusive ESKAPEE pathogens, HACEK-cluster, and Mycoplasmatota highlight a distinct microbiological profile with potential clinical relevance in ventilated patients.

Keywords: COVID-19, oral microbiome, 16S rRNA, ESKAPEE.

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