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**Topic 08: COVID-19 Pathogenesis**

**OP08.01 (135)**

**Characterization of the Nasopharyngeal Microbiota of COVID-19 Patients According to Disease Severity**

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**Purpose:** Increasing evidence indicates a possible relationship between the pathogenesis of COVID-19 and the nasopharyngeal microbiota. This study aimed to compare the nasopharyngeal microbiota of COVID-19 patients with different disease severity.

**Methods & Materials:** A comparative study was performed on patients classified into four groups according to their disease severity. A total of 26 patients were recruited for each of the following study groups. Group 1 (G1): patients with a confirmatory diagnosis of SARS-CoV-2 and hospitalized in the ICU. Group 2 (G2): patients with a confirmatory diagnosis of SARS-CoV-2 and hospitalized in regular hospitalization wards. Group 3 (G3): patients with a confirmatory diagnosis of SARS-CoV-2 who were not hospitalized and had mild or no symptoms. Group 4 (G4): healthy patients with a negative result for SARS-CoV-2. The diagnosis of SARS-CoV-2 was performed by reverse-transcriptase polymerase chain reaction (RT-PCR). The nasopharyngeal microbiota was characterized using polymerase chain reaction (PCR) targeting 13 representative bacteria genus.

**Results:** The detection of some bacteria genus was significantly more frequent in the hospitalized groups compared to healthy subjects. This is the case of Lactobacillus with 96.15% in G1, 96.15% in G2, 23.08% in G3 and 15.38% in G4. Similarly, Prevotella presented 96.15% in G1, 80.77 in G2, 0.00% in G3 and 19.23% in G4. Veillonella, Bacteroidetes and Firmicutes presented a similar prevalence. On the other hand, the detection of Eubacterium was more frequent among asymptomatic and healthy subjects, with 3.85% in G1, 19.23% in G2, 50.00% in G3 and 30.77% in G4. The relative abundance of the bacteria was evaluated and Lactobacillus and Veillonella were predominant in both of the hospitalized groups (G1 and G2). On the other hand, Actinobacteria and Eubacterium were predominant in the asymptomatic and healthy groups (G3 and G4).

**Conclusion:** In conclusion a unique nasopharyngeal microbiota profile was found in COVID-19 patients with different disease severity. Lactobacillus, Prevotella, Veillonella, Bacteroidetes and Firmicutes were the predominant bacteria genus in critical and hospitalized patients. While, Eubacterium and Actinobacteria were predominant in the groups of asymptomatic and healthy subjects. Further longitudinal studies are required to determine the prognostic role of the nasopharyngeal microbiota.

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**OP08.02 (221)**

**Risk Factors Associated with the Mucormycosis Epidemic During the COVID-19 Pandemic**

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**Purpose:** The second wave of the COVID-19 pandemic in India is associated with an unprecedented surge of patients with mucormycosis. This study assessed the risk factors driving the epidemic of COVID-19 associated mucormycosis (CAM) and addressing these risk factors could reduce morbidity and mortality among vulnerable populations.

**Methods & Materials:** This is a case-control analysis of risk factors in 164 adults from a prospective cohort database, the POISE Mucor Study, approved by the institutional review board and ethics committee with proven invasive mucormycosis of paranasal sinus admitted in a tertiary care hospital in South India from 01.07.2020 to 10.06.2021 included after informed consent. Cases were patients with COVID-19 confirmed by RT-PCR for SARS-CoV-2 on a nasopharyngeal sample within three months of mucormycosis. Patients with ROCM (Rhino-orbito-cerebral mucormycosis) negative RT-PCR for SARS-CoV-2 were the controls.

**Results:** The mean age of the 164 patients (132 cases and 32 controls) was 51 years, and 78% were men (table 1). Most patients with CAM had mild COVID-19 (76.7%); 16.3% and 7% had moderate and severe/critical disease, respectively. Almost all patients presented with acute ROCM within 3 months of COVID-19 occurrence. Diabetes mellitus (present in 97%) remained a strong predisposing factor in both groups.

Uncontrolled diabetes mellitus (HbA1c of >7.0%), 40% of which was newly detected, was associated with CAM (OR: 4.6; p = 0.026). Diabetic ketoacidosis and mean HbA1c values were not.

Steroid use was common, even in mild disease, and was strongly associated with CAM (OR:38.3; p <0.001). Oxygen use was uncommon among cases (14.4%). Serum ferritin was significantly higher among patients with CAM (p =0.041); whereas C-reactive protein was not. Acute presentation of ROCM was commoner in CAM. Involvement of brain and orbit were similar between groups. Multivariate analysis revealed that steroid use was independently associated with CAM (OR 28.4; p =0.001).

**Conclusion:** The current Indian mucormycosis epidemic (mostly acute ROCM) was precipitated by a unique confluence of risk factors – diabetes mellitus, widespread use of steroids, and the COVID-19 infection itself.
Restricting steroid use to patients with severe COVID-19 requiring oxygen therapy, screening for and optimally controlling hyperglycaemia can prevent CAM in a large majority.

Conclusion: The common risk factor for all cases of CIFRS was diabetes mellitus. Majority of patients also had history of steroid use and steam inhalation during their COVID-19 treatment. Their role in pathogenesis need to be ascertained by larger studies.

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Using Electron Microscopy to Detect SARS-CoV-2 in Human and Animal Tissues

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Purpose: Global efforts to combat the COVID-19 pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have placed renewed focus on the use of transmission electron microscopy (EM) for infectious disease diagnosis and detection. Recently, attempts to identify SARS-CoV-2 directly in human autopsy and animal necropsy tissues have inaccurately identified normal subcellular structures, including coated vesicles, multivesicular bodies, and rough endoplasmic reticulum, as coronavirus particles. Working with SARS-CoV-2 positive autopsy and necropsy tissues, the Infectious Diseases Pathology Branch at CDC sought to use EM to accurately detect coronavirus particles.

Methods & Materials: Two sample types were used, formalin-fixed wet tissue and formalin-fixed paraffin embedded (FFPE) tissue blocks. Wet tissue samples provide the best preservation of ultrastructure but require a time-intensive search for viral particles. FFPE tissues enable a targeted approach to finding viral particles but with deteriorated ultrastructure. Areas of formalin-fixed wet tissue showing evident disease pathology were selected for EM, while areas of interest from FFPE blocks were selected based on results from SARS-CoV-2 immunohistochemistry and in situ hybridization results. All samples were post-fixed with 1% osmium tetroxide, en-bloc stained with uranyl acetate, dehydrated, and embedded in Epon-Araldite resin.

Results: A multifaceted approach for SARS-CoV-2 detection in autopsy and necropsy tissues allowed for swift and accurate determination of the localization of coronavirus and correlation of histopathological and ultrastructural features of SARS-CoV-2 infection. Coronavirus particles were found associated with degenerating cells in the alveolar space, in pneumocytes, and near collagen of the heart in fetal tissue as well as in the syncytiotrophoblast of the placenta. In animal tissues, virus was found in the bronchiolar epithelium and type 1 pneumocytes.

Conclusion: Comprehensive studies of SARS-CoV-2 infection, and all emerging pathogens, are crucial to improving the understanding of pathogenesis and for the formulation of clinical treatments and transmission prevention measures. An important part of this process is providing robust EM evidence of SARS-CoV-2 localization within tissues to ensure that misinterpretations of subcellular structures as virus are reduced, enabling more accurate conclusions concerning COVID-19 pathology and disease.

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