

Spectrum Of Fungi in Covid-19 Associated Mucormycosis in A Tertiary Care Hospital, South India.

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Abstract: **Background:** Coronavirus disease (COVID-19) causes an immunosuppressed state and increases risk of secondary infections like mucormycosis. We studied the predisposing factors, diagnosis and isolated most common fungi causing mucormycosis among patients with COVID-19 infection. The aim of this study is to report the spectrum of fungi, causing Mucormycosis in RT-PCR positive COVID-19 patients, cultured on SDA and study the role of other factors responsible for the disease.

Methodology: A prospective, observational study on Mucormycosis in RT-PCR positive COVID-19 patients based on hospital records and fungal culture reports from 12th May 2021 to 21st July 2021. The study includes cultures conducted on Nasal debridement samples from patients admitted in the hospital with RT- PCR confirmed COVID-19 and typical symptoms of Mucormycosis.

Results: The mean age of the COVID-19 confirmed patients from whom Nasal debridement samples were collected was 52 years. Among the study group, 66% were Male and 89% among them had known history of Diabetes. The Mean time interval between the onset of COVID-19 disease and the diagnosis of Mucormycosis was 7 days (Range 1-37 days) in the study group. Out of 341 samples received and cultured on SDA, 85 samples (24.92%) were positive for Mucormycosis. Out of 85 samples 69 (81.17%) belong to the family mucoraceae of which 57 (82.60%) are of Rhizopus species, 8(11.59%) belonged to mucor species, 3 (4.34%) belonged Lichthemia and 1(1.14%) belonged to Rhizomucor species. The remaining 16 (18.83%) doesn't belong to the mucoraceae family. Among the non- mucoraceae, 7 (43.75%) are Aspergillus niger, 4(25%) were Aspergillus fumigatus, 3(19.75%) were Aspergillus flavus and 2(12.5%) belonged to Trichophyton species.

Conclusion: Patients of Mean age 56 years with known diabetes status hospitalized for Covid-19 are at higher risk of developing Mucormycosis with the most common causative organism isolated being Rhizopus species.

Keyword: Mucomycosis, COVID-19, Rhizopus, Aspergillus Fumigatus, Immunosupression.

Introduction:

Coronavirus disease 2019 (COVID-19), attributed to severe acute respiratory syndrome coronavirus 2 (SARS-CoV- 2), was declared a global pandemic by the World Health Organisation (WHO) in March 2020. The pandemic continues to be an ongoing public health concern with more than 162 million cases recorded, and more than 3 million deaths globally.¹

With the increase of cases worldwide, potential complications from COVID-19 are being increasingly appreciated, including the heightened vulnerability to secondary bacterial and fungal infections.^{2,3} The immune dysregulation associated with COVID-19 is further aggravated by medical conditions such as diabetes mellitus, and the widespread use of immunosuppressive agents and broad-spectrum antibiotics. The rate of hospital acquired secondary bacterial and fungal infection has been re-reported to be approximately 8%. It is observed that fungal infections were more likely to develop during the more advanced stages of COVID-19 infection, with higher mortality among patients with a fungal co-infections.³

Mucormycosis is known to affect aged, immunocompromised patients especially those with diabetes mellitus, prolonged corticosteroid use, solid organ transplant recipients, neutropenia and haematological malignancies. It is an opportunistic infection leading to invasion of blood vessels by fungal hyphae, causing infarction and necrosis of a variety of end-organ host tissues. Rhinoorbital infection with the mucorales species of fungus has a poor prognosis with a mortality rate reaching 50%, even with appropriate treatment. In India there was a sudden increase in the number of mucormycosis cases in patients of COVID-19. At the time of this study large number of cases of mucormycosis have been reported.

Material & Method:

The study includes cultures conducted on Nasal debridement samples received from 12th May 2021 to 21st July 2021 from patients admitted in the hospital with RT-PCR confirmed COVID-19 and typical symptoms of Mucormycosis. This study was approved by the research and ethics committee. Data entry and analysis were performed using SPSS for windows version SPSS 14.0 software. The diagnosis of COVID-19 was based on real-time polymerase chain reaction (RT-PCR) test from nasopharyngeal or oropharyngeal swabs. In clinically suspected patients, presence of fungal hyphae, by direct examination in 10% potassium hydroxide (KOH) from nasal debrided tissue was used for diagnosis. Mucormycosis was subsequently proven based on microbiological culture on SDA from debrided specimen. Apart from ascertaining COVID-19 status, blood investigations and

computed tomography (CT) and/or magnetic resonance imaging (MRI) of the orbit, brain and/or paranasal sinuses were performed for all cases to assess the extent of involvement from mucormycosis.

Statistical analysis: Data was collected and tabulated using Microsoft excel. Strata version 15 binomial regression model was used to derive incident rate ratios with 95% confidence interval for each outcome. The statistics of percentage was used

Result:

The mean age of the COVID-19 confirmed patients from whom Nasal debridement samples were collected was 52 years. Among the study group, 66% were Male and 89% among them had known history of Diabetes. The Mean time interval between the onset of COVID-19 disease and the diagnosis of Mucormycosis was 7 days (Range 1-37 days) in the study group.

Out of 341 samples received and cultured on SDA, 85 samples (24.92%) were positive for fungal elements. Out of 85 samples 69 (81.17%) belong to the family mucoraceae of which 57 (82.60%) are of Rhizopus species, 8(11.59%) belonged to mucor species, 3 (4.34%) belonged Lichthemia and 1(1.14%) belonged to Rhizomucor species.

The remaining 16 (18.83%) doesn't belong to the mucoraceae family. Among the non-mucoraceae, 7 (43.75%) are Aspergillus niger, 4(25%) were Aspergillus fumigatus, 3(19.75%) were Aspergillus flavus and 2(12.5%) belonged to Trichophyton species.

Discussion:

In recent years, there has been a substantial shift in the epidemiology of mucormycosis. The global prevalence of this very morbid and lethal disease is increasing, although it is greater in Asian countries.⁴ Extensive steroid use during COVID-19 therapy, poorly controlled diabetes mellitus (DM), haematological malignancy, solid organ transplant, immunosuppression, and other comorbidities were the primary risk factors, followed by hypertension and other co-morbidities.⁵ Mucormycosis, formerly known as zygomycosis, is a serious fungal illness caused by the mucoromycetes mould group. Because it might damage the sinuses, brain, or lungs, it is fairly prevalent in persons suffering with or recovering from COVID-19. Mucormycosis symptoms include swelling on one side of the face, fever, headache, nasal or sinus congestion, and black lesions on the nasal bridge or upper inside of the mouth. Many factors could have aided in creating an ideal environment for Mucorales fungus to thrive and propagate during Covid-19 illness, including immune dysregulation (suppressed cell-mediated immunity), steroid-induced hyperglycemia, acidotic environment (metabolic acidosis, diabetic ketoacidosis), hypoxia (pneumonia), hyper-ferritinemia, and complement-mediated thrombotic microangiopathy.^{2,3}

In study by Nehara H et al., documented COVID-19 is usually linked to secondary infections, both bacterial and fungal, which may be caused by immunological dysregulation. Aside from that, the extensive use of broad-spectrum antibiotics, steroids, or monoclonal antibodies in COVID-19 treatment may result in the development or worsening of pre-existing fungal illnesses. They documented in the case series with Rhizopus species as the common isolate among all the patients included in the study.⁶

Rhinocerebral mucormycosis is treated by surgical draining of the PNS and debridement of orbital or cerebral illness, as well as intravenous antifungal medications. Intravenous liposomal amphotericin-B (5-10 mg/kg/day) is used as first-line antifungal treatment, while second-line antifungals such as intravenous or oral posaconazole can be used as salvage therapy, with a course of at least 6 weeks being necessary. Strict glycemic control is also an important component of therapy. Depending on the underlying diseases, the mortality rate for rhinocerebral mucormycosis ranges from 40 to 80%.⁷ Prolonged hospitalisation, particularly in ICU patients receiving invasive or noninvasive ventilation and suffering from severe COVID-19, is more likely to predispose patients to the development of fungal coinfections.⁸ According to Khatri et al., the presence of fungal spores in this sort of equipment might lead to the development of hospital-acquired mucormycosis.⁹

Present study is one among the few literature which is available from India, specially from the southern India documenting the mucormycosis.

Conclusion:

Patients of Mean age 52 years with known diabetes status hospitalized for Covid-19 are at higher risk of developing Mucormycosis with the most common causative organism isolated being Rhizopus species. To combat the mucormycosis epidemic in the COVID-19 pandemic, a multidisciplinary strategy that includes timely diagnosis, treatment with intravenous and oral antifungals, surgical debridement, and medical care of underlying diseases is critical.

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Conflict of interest: Nil

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Tables and Figures

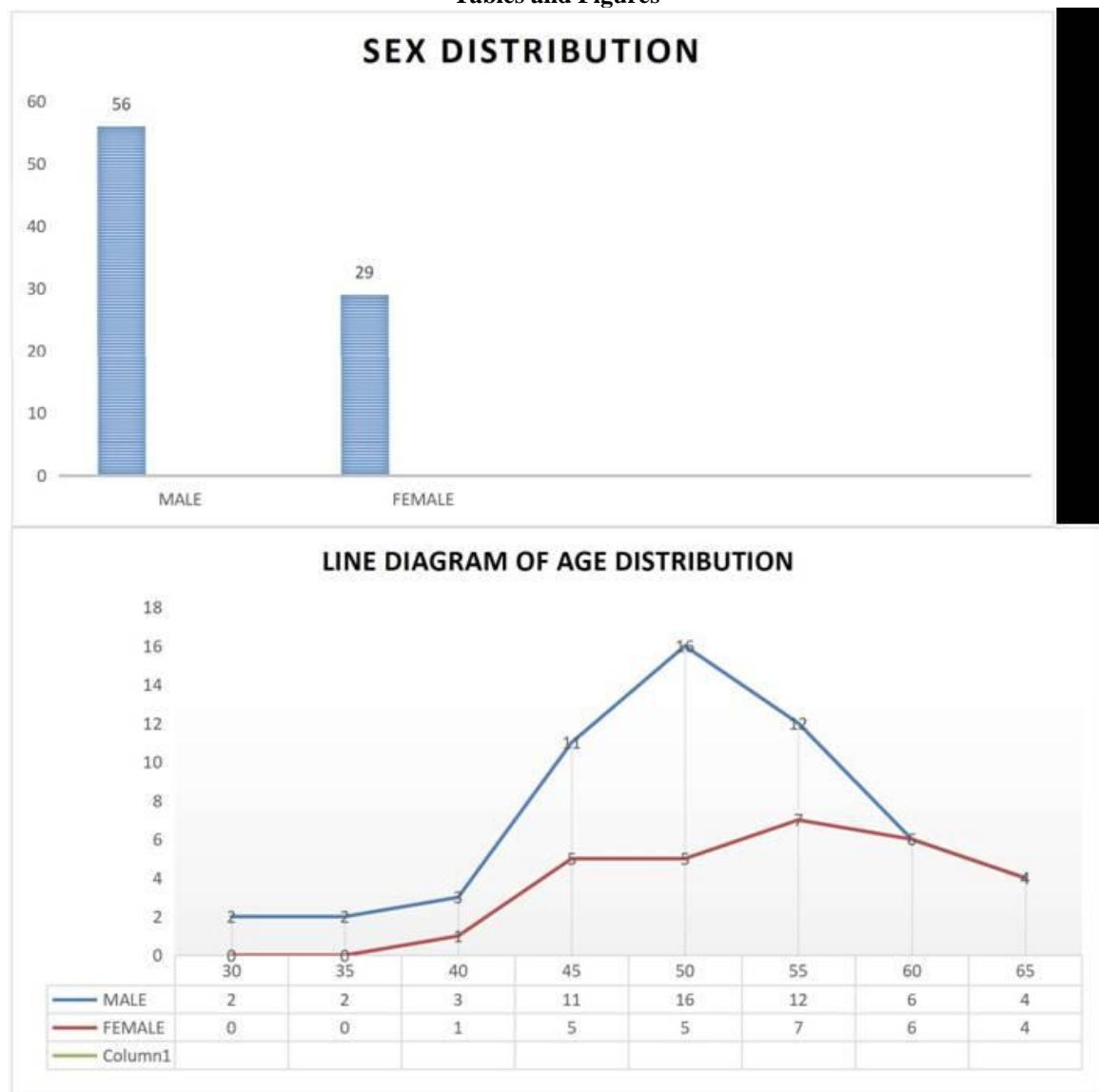


Figure 1: Showing gender and age distribution of patients

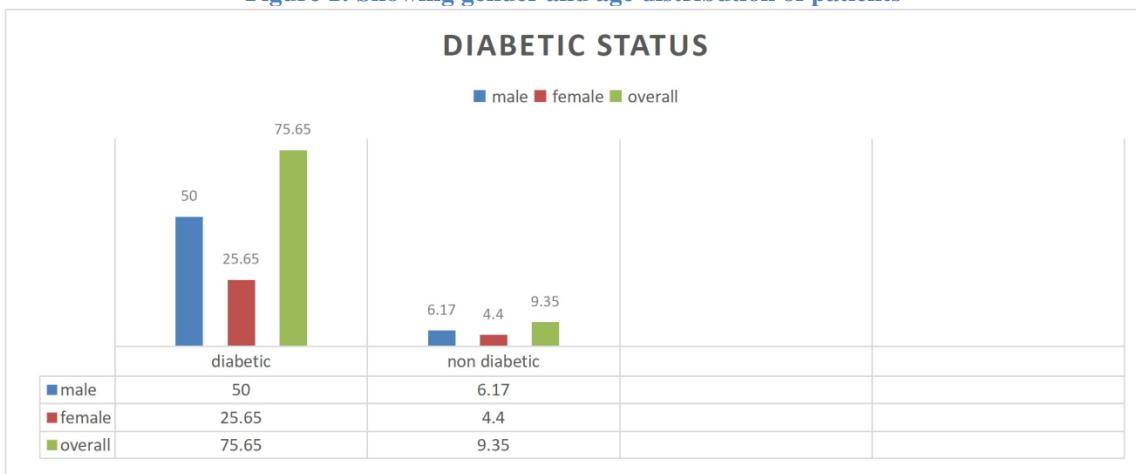


Figure 2: Showing the gender distribution

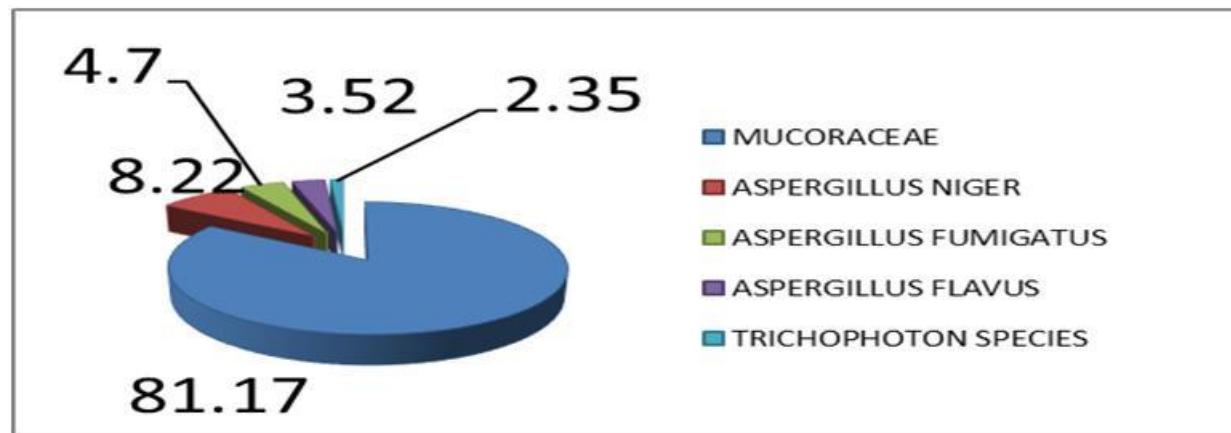


Figure 3: Pie diagram of fungi responsible for mucormycosis

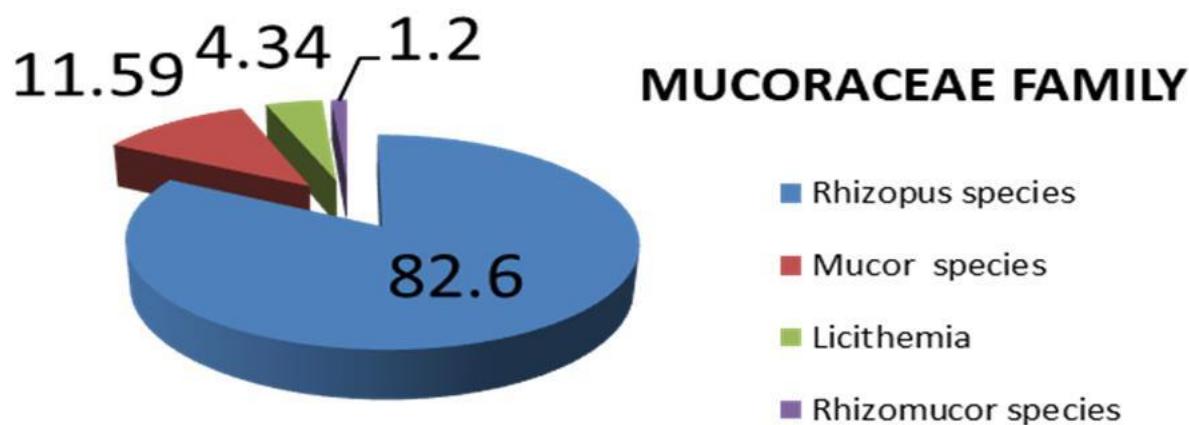


Figure 4: Pie diagram of genera from mucoraceae family responsible for mucormycosis