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# CLINICAL PROFILE OF MUCORMYCOSIS INFECTION DURING COVID ERA IN A TERTIARY CARE HOSPITAL

General Medicine

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## ABSTRACT

**Background:** During the COVID pandemic, the burden of mucormycosis raised drastically. However, the exact prevailing picture of mucormycosis was not broadly studies in South Indian population. Hence this study was conducted to determine the clinical profile of mucormycosis cases in a tertiary care hospital. **Methodology:** This study was conducted as a cross sectional study in the Department of general medicine in Thanjavur Medical College and hospital, Thanjavur, a tertiary care Government teaching hospital during the period of October 2020 to August 2021. All patients with mucormycosis from both genders were included in the study. A total of 275 mucormycosis cases were included in the study. **Results:** In this study among 275 cases with mucormycosis, 58.5% of cases remains positive for COVID 19 and common type of mucormycosis were rhinocerebral type. The common risk factor noted was diabetes. All cases were treated with medical management however FESS was the common surgery performed. **Conclusion:** We infer that during COVID 19 pandemic times, mucormycosis should be strongly suspected in cases with COVID19 infections and among diabetes cases and vice versa.

## KEYWORDS

Mucormycosis, COVID 19, clinical profile, fungal infection

## INTRODUCTION

Due to COVID-19, which SARS-CoV-2 created, the entire world has been affected by a pandemic. There have been several changes in the disease's pathophysiology, diagnosis, therapy, and—most importantly—its consequences and sequelae since it was first discovered in Wuhan, China, in December 2019. From an early dry cough and high-grade fever to multisystem failure that could ultimately result in death, the COVID-19 symptom spectrum is constantly growing[1].

In India, COVID19 has killed 433,589 individuals and affected more than 30 million people[2]. A second spike in COVID19 cases was seen in India about a year after the SARS CoV2 pandemic was declared. The dominant strain was the Delta variation, which the Centers for Disease Control and Prevention (CDC) identified as a strain of concern due to its heightened transmissibility and the seriousness of the illness it produces[3,4]. During this second wave, an increased prevalence of mucormycosis was seen in COVID19 patients; this condition was known as COVID 19 associated mucormycosis (CAM)[5,6]. Because mucormycosis is a fungal infection that spreads quickly and can have fatal effects, both the medical community and the general population are concerned. In earlier COVID19 instances, secondary infections with bacteria and fungus were not frequently discovered. In comparison to co-infections in influenza sickness, studies found very low rates of bacterial coinfections and extremely low rates of fungal coinfections in COVID19 cases[7-9]. Co-infections with MERS and SARS CoV1 were similarly rare[7-10]. Aspergillus and Candida infections made up the majority of the fungus coinfections in COVID19 cases reported from other nations[11-14]. 43 cases of mucormycosis were detected in COVID19 cases, of which 71% were from India, according to a review paper on cases reports[15]. The current study's objective was to determine the clinical profile of mucormycosis cases in a tertiary care hospital.

## METHODS

This study was conducted as a cross sectional study in the Department of general medicine in Thanjavur Medical College and hospital, Thanjavur, a tertiary care Government teaching hospital during the period of October 2020 to August 2021. All patients with mucormycosis from both genders were included in the study. A total of 275 mucormycosis cases who attended the outpatient and inpatient department of general medicine during the study period were included in the study. All the cases were assessed for detailed history, clinical examination, COVID 19 RTPCR, culture and radiological investigations. Data were coded in Microsoft excel sheet and analysed using SPSS trial version 20. Categorical data were summarized as n with % and continuous data were summarized as mean with SD. Fisher's exact test was used to compare the proportions between the group. P value <0.05 was considered statistically significant.

## RESULTS

The mean age of patient noted was 53.7 years with SD of 11.5. In males (n=186), the mean age noted was 53.3 years with SD of 11.8 and in females (n=89), the mean age noted was 54.2 with SD of 10.9. Overall, the maximum age noted was 84 years and minimum age noted was 20 years.

**Table 1. Baseline characteristics of patients with mucormycosis observed in the study**

| Parameter | n | % |
|---|---|---|
| **Age in years** | | |
| 20 – 39 years | 33 | 12 |
| 40 – 59 years | 149 | 54.2 |
| 60 – 79 years | 90 | 32.7 |
| ≥80 years | 3 | 1.1 |
| **Gender** | | |
| Male | 186 | 67.6 |
| Female | 89 | 32.4 |
| **District** | | |
| Ariyalur | 22 | 8.0 |
| chennai | 1 | .4 |
| cuddalore | 6 | 2.2 |
| Karaikal | 2 | .7 |
| mayiladudurai | 5 | 1.8 |
| Nagapattinam | 10 | 3.6 |
| Perambalur | 2 | .7 |
| pudukottai | 6 | 2.2 |
| Thanjavur | 204 | 74.2 |
| Thiruvarur | 16 | 5.8 |
| Trichy | 1 | 0.4 |
| **Covid status** | | |
| Positive | 161 | 58.5 |
| Negative | 114 | 41.5 |
| **COVID severity (CTSS)** | | |
| Mild (0-7) | 43 | 15.6 |
| Moderate (8-17) | 162 | 58.9 |
| Severe (>17) | 70 | 25.5 |

**Table 2. Description of clinical characteristics of mucormycosis observed in the study**

| Clinical characteristics | n | % |
|---|---|---|
| **Type of mucormycosis** | | |
| Cutaneous | 0 | 0 |
| Disseminated | 0 | 0 |
| Gastrointestinal | 0 | 0 |
| Pulmonary | 2 | 0.7 |

| | | |
|---|---|---|
| Rhinocerebral | 273 | 99.3 |
| Uncommon presentations | 0 | 0 |
| **Outcome** | | |
| Cured | 197 | 71.6 |
| Death | 0 | 0 |
| Under treatment | 78 | 28.4 |
| **Presence of risk factors** | | |
| Covid positive status | 161 | 58.5 |
| Diabetes | 247 | 89.8 |
| Immuno-compromised state | 0 | 0 |
| Use of steroids | 62 | 22.5 |
| Prior oxygen therapy | 80 | 29.1 |
| **Comorbidities** | | |
| Diabetes | 247 | 89.8 |
| Hypertension | 53 | 19.3 |
| CAD | 3 | 0.7 |
| Carcinoma | 1 | 0.4 |
| Adrenaline insufficiency | 1 | 0.4 |
| Bronchial asthma | 1 | 0.4 |
| HBV & cirrhosis | 1 | 0.4 |

**Table 3. Description of specific investigations of mucormycosis observed in the study**

| Investigation | n | % |
|---|---|---|
| **CT imaging** | | |
| Pansinusitis | 82 | 29.8 |
| BL maxillary+ R-ethmoid+sphenoid | 77 | 28 |
| Right maxillary sinusitis | 72 | 26.2 |
| BL maxillary+Ethmoid+Sphenoid | 16 | 5.8 |
| BL maxillary+L-ethmoid+Sphenoid | 10 | 3.6 |
| BL maxillary+Ethmoid | 6 | 2.2 |
| L-maxillary sinusitis | 6 | 2.2 |
| L-maxillary+ethmoid+intracranial extension | 6 | 2.2 |
| Positive growth in culture | 117 | 42.5 |

**Table 4. Description of management of mucormycosis performed in the study**

| Management | n | % |
|---|---|---|
| **Surgical treatment** | | |
| FESS | 115 | 41.8 |
| FESS with hard palate curettage | 48 | 17.5 |
| FESS with retroorbital amphotericin-B injection | 6 | 2.2 |
| FESS and TRAM | 100 | 36.4 |
| FESS, TRAM and hard palate curettage | 6 | 2.2 |
| Medical: Amphotericin+B with posoconazole | 275 | 100 |

**Table 5. Comparison of age with respect to gender category in patients with mucormycosis**

| Age category | Female (N=89) | | Male (N=186) | | Chi square value | df | P value |
|---|---|---|---|---|---|---|---|
| | n | % | n | % | | | |
| 20 – 39 years | 7 | 7.9 | 26 | 14 | 4.4 | 3 | 0.22 (NS) |
| 40 – 59 years | 53 | 59.6 | 96 | 51.6 | | | |
| 60 – 79 years | 27 | 30.3 | 63 | 33.9 | | | |
| ≥80 years | 2 | 2.2 | 1 | 0.5 | | | |

Data are expressed as n with %. Fisher's exact test was used to compare the frequency between the groups. NS = Not significant.

**Table 6. Comparison of various factors observed in study with respect to positive fungal culture state**

| Parameter | Fungal growth in culture | | | | Chi square value | df | P value |
|---|---|---|---|---|---|---|---|
| | Yes (N=117) | | No (n=158) | | | | |
| | n | % | n | % | | | |
| Positive covid status | 70 | 59.8 | 91 | 57.6 | 0.138 | 1 | 0.805 (NS) |
| Presence of diabetes | 104 | 88.9 | 143 | 90.5 | 0.192 | 1 | 0.691 (NS) |
| Use of steroids | 29 | 24.8 | 33 | 20.9 | 0.586 | 1 | 0.468 (NS) |
| Prior oxygen therapy | 34 | 29.1 | 46 | 29.1 | <0.001 | 1 | >0.999 (NS) |
| CT imaging | | | | | | | |
| Pansinusitis | 49 | 41.9 | 33 | 20.9 | 38.8 | 7 | <0.0001 * |
| BL maxillary+ R-ethmoid+sphenoid | 35 | 29.9 | 42 | 26.6 | | | |
| Right maxillary sinusitis | 17 | 14.5 | 55 | 34.8 | | | |
| BL maxillary+Ethmoid+Sphenoid | 11 | 9.4 | 5 | 3.2 | | | |
| BL maxillary+L-ethmoid+Sphenoid | 5 | 4.3 | 5 | 3.2 | | | |
| BL maxillary+Ethmoid | 0 | 0 | 6 | 3.8 | | | |
| L-maxillary sinusitis | 0 | 0 | 6 | 3.8 | | | |
| L-maxillary+ ethmoid+ intracranial extension | 0 | 0 | 6 | 3.8 | | | |

Data are expressed as n with %. Fisher's exact test was used to compare the frequency between the groups. *indicates p<0.05 and considered statistically significant. NS = Not significant

## DISCUSSION

A rare, virulent, quickly spreading, angio-invasive fungus infection is known as mucormycosis or zygomycosis[16]. Most typically, Rhizopus arrhizus, a filamentous fungus from the family Mucoraceae of the order Mucorales, is responsible for this potentially fatal illness. Its spores can be found everywhere, including in the air, soil, and rotting produce. Mucormycosis can affect people with no obvious immunological impairment, in contrast to other filamentous fungi that are primarily opportunistic infections in immunosuppressed hosts such cancer patients and organ recipients[17]. However, mucormycosis has primarily been linked to diabetes mellitus, particularly in people who have diabetic ketoacidosis (DKA), haematological cancers, organ transplant, immunocompromise, trauma, and neutropenia[18,19]. Endothelial damage, thrombosis, and tissue necrosis are all caused by the fungal hyphae eroding tissues and blood vessels[20]. Due to the frequent case fatalities and deformity procedures required for therapy, survivors suffer disfigurement. The tissues appear black during necrosis. Mucormycosis is therefore referred to as a "black fungal disease," despite the fact that the fungus is not black.

Patel A et al[21] carried out a multicenter retrospective study across India to assess the outcomes of CAM cases. 65.2% of 287 mucormycosis patients had CAM, whereas hospitalised COVID-19 patients had a CAM frequency of 0.27%. According to their findings, mucormycosis increased by 2.1 times over the study period compared to September to December 2019. Between CAM and non-CAM patients, uncontrolled diabetes mellitus was the most prevalent underlying condition. The only underlying condition in 32.6% of CAM patients was COVID-19. CAM was independently linked to both incorrect glucocorticoid use and hypoxemia brought on by COVID-19. At 12 weeks, the case fatality rate for mucormycosis was 45.7%, but it varied little between CAM and non-CAM patients. Age, involvement of the rhino-orbital-cerebral system, and admission to an intensive care unit were all linked to higher fatality rates; however, therapy with subsequent antifungal medications boosted mucormycosis survival. In India, mucormycosis rates have increased as a result of the COVID-19 epidemic, in part due to incorrect glucocorticoid use.

During the second wave of COVID-19 in Pune, India, Samir Joshi et al[22] performed a retrospective chart analysis of 178 patients who had received COVID-19 treatment and had cerebral, rhinosino-orbital, or endoscopically or histopathologically confirmed rhinosino-orbital mucormycosis. The median time from COVID-19 detection to the start of symptoms was 28 days. 73% of individuals had moderate or severe COVID-19, and 74.2% had diabetes. 52.8% of the population received steroids. 75% of patients had eschar over or inside of the nose, but the clinical and laboratory baseline values were generally normal. 90% of cases had bone penetration, 30% had pterygopalatine fossa soft tissue enlargement, 7% had cavernous sinus thrombosis, and 60% had multifocal mucormycosis. 151 (85%) of the 178 studied patients had surgical debridement. Sixteen (62%) of the 26 people who passed away (15%) had multifocal mucormycosis.

Mucorales species induced four secondary fungal infections in COVID-19 patients, according to Buil JB et al[23]. One CAM outside the ICU and three CAMs related with COVID-19 occurring in the ICU. Three males, all older than 50 years were passed away. Clinical manifestations included lung, cerebral, rhino-orbital, and widespread infection. Their findings highlight the importance of being vigilant of

invasive mucormycosis, particularly in COVID-19 patients outside of the intensive care unit (ICU) and without diabetes mellitus.

Cases of rhinoorbital mucormycosis seen at our Regional Institute of Ophthalmology during COVID 19 were described by Ravani SA et al[24] in their paper. 31 patients were seen, with a mean age of 56.3 years, it was found. Uncontrolled diabetes (96.7%) and COVID-19 positive (61.2%) were the main risk factors, and 61.2% of patients also used steroids concurrently. Ophthalmoplegia and reduced vision were the most typical presentations (77.4%). Pansinusitis (77.3%) and orbital cellulitis (61.29%) were the most frequently observed imaging abnormalities. All patients received intravenous liposomal amphotericin B for an average of 18.93 days. 12.9% of cases required exenteration. On follow-up, 28 patients had made a full recovery and were still living. Three patients died, which is to be expected. A HbA1c score of less than 8 and cerebral involvement were revealed to be important predictors of survival in mucormycosis patients.

Sen M. et al[25] identified the patient's demographics, risk factors, such as comorbidities, and COVID-19 treatment drugs, as well as the patient's presenting symptoms and signs and the management's results. The states of Gujarat (22%) and Maharashtra (21%) recorded the greatest number of CAM out of the 2826 patients, according to their research. Patients were mostly men (71%), with a mean age of 51.9 years. While 87% of the patients received corticosteroid treatment, 57% of the patients required oxygen assistance because to COVID-19 infection. 78% of all patients had diabetes mellitus. The majority of cases had CAM symptoms appear between days 10 and 15 after the diagnosis of COVID-19; 56% did so within 14 days, while 44% had delayed onset symptoms that lasted more than 14 days. 72% of patients had orbital involvement, with stage 3c accounting for the majority (27%). Overall, 73% of patients received intravenous amphotericin B, 56% underwent functional endoscopic sinus surgery or paranasal sinus debridement, 15% underwent orbital exenteration, and 17% underwent both procedures. Amphotericin B injection intraorally was given in 22% of cases. Mortality was 14% at the last follow-up. The prognosis was worse for disease stages >3b. Patients with stage 4 illness with intracranial extension had a mortality rate that was lowered from 52% to 39% by paranasal sinus debridement and orbital exenteration. They came to the conclusion that the most significant risk factors for the emergence of COVID-19-associated CAM are corticosteroids and DM.

In their metaanalysis, Hussain S et al[26] calculated the combined prevalence of CAM and various related clinical outcomes. Six trials with a combined sample size of 52,916 COVID-19 patients and an average age of 62.12 years were included. After the COVID-19 diagnosis, mucormycosis often manifested 14.59 days later on average. Seven instances per 1000 patients, or the pooled prevalence of CAM, was 50 times greater than the highest background level of mucormycosis ever seen (0.14 cases per 1000 patients). With a combined prevalence incidence of 29.6%, CAM patients had a significant mortality rate. The strategy for combating the increase in CAM cases should be optimal glycemic management and the prudent use of steroids.

Meher R et al[27] recruited 131 CAM patients in their study, of which 111 had a history of SARS COVID 19 infection that was later verified by a positive RT-PCR report, while the remaining 20 patients had no such history. 67 patients with COVID 19 infection got therapy with steroids. Among the 131 patients, 124 made a full recovery, 1 got worse, and 6 passed away. Out of 101 known diabetics, 98 made a full recovery, while three died. Seven patients with a history of COVID infection lacked any indications of diabetes mellitus, steroid use, or any other comorbidities. They came to the conclusion that the CAM increase associated with COVID-19 in India was primarily associated with individuals who had uncontrolled diabetes, a compromised immune system as a result of SARS-COV-2 infection, and inappropriate corticosteroid use.

In a case-control study, Arora U et al[28] compared cases with CAM diagnoses to controls, recovered COVID 19 individuals without mucormycosis. According to their findings, the CAM group experienced mucormycosis symptoms that mostly affected the rhino-sinus and orbits and started on average 18.9 days following the commencement of COVID-19. All but one of the CAM cases had the traditional risk indicators of steroid usage and diabetes. Increased odds of CAM were found in multivariable regression to be related to diabetes, systemic steroid use, prolonged use of cloth and surgical masks, and frequent nasopharyngeal swab tests throughout the COVID-19 illness. It was discovered that zinc treatment was protective. Notably, the risk of CAM was unaffected by the need for oxygen supplementation or hospitalisation. They came to the conclusion that prudent steroid administration and strict glycemic control are essential for preventing mucormycosis. Utilizing clean masks, choosing N95 masks over others when they are available, and limiting swab testing after the diagnosis of COVID-19 may all help to lower the prevalence of CAM.

In their investigation, Fazeil MA et al[29] reported that 12 cases of CAM were found. All cases that were confirmed to have mucormycosis had a prior hospitalisation for COVID-19. Diabetes mellitus (83.33%) and hypertension (58.33%) were the two primary comorbidities. For the treatment of COVID-19, 75% of patients got corticosteroids. Rhino-sino-orbital (83%) and rhino-sino (17%) were the affected areas. The first-line treatment involved the use of amphotericin B/liposomal amphotericin B, either alone or in combination with surgical debridement or ocular exenteration. The mortality rate as a whole was 66.7%. They discovered that patients with COVID-19 had a high incidence of mucormycosis. The two main risk factors for mucormycosis were having diabetes mellitus and using corticosteroids.

In Germany, the illness burden was calculated and the clinical presentation of CAM was described by Seidel D et al[30] Twelve patients were reported to have severe or serious COVID-19, and eleven of them spent an average of eight days on mechanical ventilation prior to receiving a CAM diagnosis. Systemic corticosteroids were administered to eleven patients. All patients, with the exception of one, had additional underlying medical illnesses. Five patients had impaired immune systems as a result of cancer or organ transplantation, and three patients had diabetes. Pneumonia struck eleven patients. Despite therapy with liposomal amphotericin B and/or isavuconazole in 10 of 13 cases, the mortality rate was 53.8% with a median duration from mucormycosis diagnosis to death of 9 days. Compared to non-COVID-19 patients, CAM incidence was considerably greater among hospitalised COVID-19 patients overall and those admitted to the intensive care unit. They came to the conclusion that, in contrast to rhino-orbito- cerebral CAM, which is primarily seen in patients with mild COVID-19 in India, COVID-19-associated mucormycosis is rare in Germany and is typically reported in patients with comorbidities, immune system impairment, and severe COVID-19 treated in the ICU with high mortality. Compared to other patients, COVID-19 hospitalised patients have a higher risk of developing CAM.

## CONCLUSION

In this study among 275 cases with mucormycosis, 58.5% of cases remains positive for COVID 19 and common type of mucormycosis was rhinocerebral type. The common risk factor noted was diabetes. All cases were treated with medical management however FESS was the common surgery performed. We infer that mucormycosis should be strongly suspected in cases with COVID19 infections and among diabetes cases and vice versa.

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