

# Post-COVID Mucormycosis: A Retrospective Observational Study

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## Abstract

**Introduction:** Mucormycosis is a life-threatening fungal infection caused by fungi belonging to the family Mucorales, and the fungus mainly responsible for infection in humans is *Rhizopus oryzae*. Recently, several cases of coronavirus disease 2019 (COVID-19)-associated mucormycosis are being reported worldwide. **Subjects and Methods:** A retrospective observational study was conducted in the emergency department at a tertiary care hospital for 2 months. The primary objectives of this study were to assess the risk factors of post COVID-19 the signs and symptoms, to assess the relationship between steroidal usage and post-COVID-19 mucormycosis evaluating the treatment patterns. **Results and Discussion:** In the current study, 45 cases were examined. It was found that patients with comorbidities, especially diabetes mellitus, i.e., 80%, have more exposure to post-COVID-19 mucormycosis than any other comorbidity. It is also found that methylprednisolone is the major steroid used, accounting for 43% of the steroids used for the treatment of COVID. The treatment included the usage of lipophilic amphotericin B in 61% of the patients, which is associated with lipophilic posaconazole in 95% of the patients. **Conclusion:** Post-COVID-19 mucormycosis is a major threat to the individuals affected with COVID-19. The major risk factor is the presence of diabetes mellitus; therefore, proper measures must be undertaken in diabetic patients. Patient develops any symptoms related to the eyes, nose, face, lungs, and skin should seek a medical emergency to avoid chronic complications.

**Keywords:** Amphotericin B, COVID, diabetes mellitus, posaconazole, postcoronavirus disease 2019 mucormycosis

## INTRODUCTION

An ongoing worldwide pandemic of coronavirus disease (COVID-19) brought about by severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) was first distinguished in December 2019 in Wuhan China. The World Health Organization declared a public health emergency of global concern in regard to SARS-COV-2 on January 30, 2020, and later announced a pandemic on March 11, 2020.<sup>[1]</sup>

COVID-19 contamination brought about by novel SARS-COV-2 might be related to a wide range of disease patterns, ranging from asymptomatic to severe diseases requiring intensive care unit (ICU) admission. A wide range of bacterial and fungal coinfections might exist and may be connected with comorbidities such as diabetes mellitus, lung disease, chronic liver disease, and prolonged use of steroids or immunosuppressant medications, or may develop as hospital-acquired disease, for example, ventilator-related pneumonia. COVID-19 is caused by SARS-COV-2 and

turned out to be a highly contagious infection with a high mortality rate and economic morbidity worldwide with initial symptoms such as fever, cough, cold, fatigue, and in some cases multiorgan failure.<sup>[2]</sup>

Recently, several cases of COVID-19-associated mucormycosis (CAM) have been reported worldwide. Although a causal connection between COVID-19 mucormycosis remains unknown, multiple factors such as glucocorticoids, worsening blood glucose levels, ketoacidosis, and increased serum free iron, as iron is responsible for the growth and virulence of microbial pathogens<sup>[3]</sup> and viral-induced lymphopenia has been involved in the pathogenesis of CAM.

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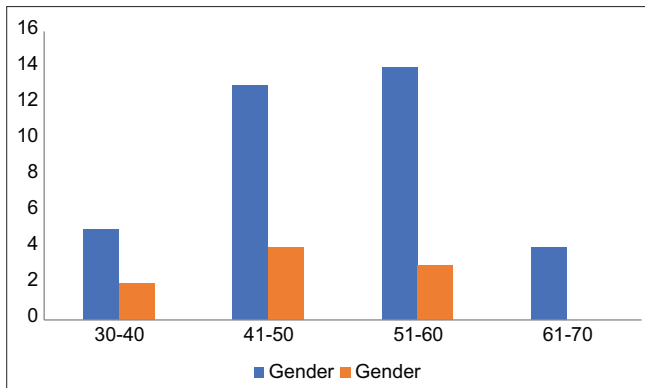


Figure 1: Age-wise gender distribution of the patients

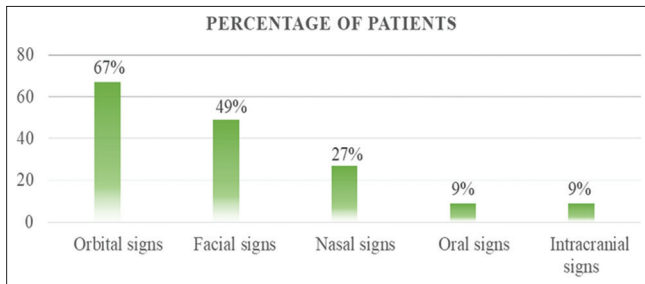


Figure 3: Percentage of patients with clinical signs of mucormycosis

Mucormycosis is a life-threatening fungal infection earlier known as zygomycosis, a disease caused by fungi belonging to the family Mucorales and the fungus mainly responsible for infection in humans is *Rhizopus oryzae*. tropical and subtropical climates (like India), the family *Apophysomyces* is commonly identified as an infective agents.<sup>[4]</sup> Inhalation of fungal spores does not cause harm in immunocompetent individuals, but is life-threatening in immunocompromised patients. Immunocompromised patients mainly with metabolic syndromes such as diabetes mellitus and hematological disease are at more risk of mucormycosis. India has the highest prevalence of diabetes mellitus (8.9% of adults, 77 million patients), which is a major risk factor.<sup>[5]</sup> Therefore, most CAM cases are reported in India and it has the highest cases of CAM globally, with an estimated prevalence of 140 cases per million people. In India, till May 2021, approximately 5500 people were affected by CAM. Therefore, CAM has been declared an epidemic disease in many states across the country. India has the highest cases of mucormycosis in the world.<sup>[6]</sup>

Based on the anatomical locations, the most commonly reported infection sites are rhino-orbital or rhinocerebral mucormycosis and pulmonary, cutaneous, disseminated, and gastrointestinal diseases. The multiple contributing factors responsible for mucormycosis among COVID-19 patients are diabetes mellitus, obesity, use of corticosteroids, and development of cytokine storms.<sup>[6]</sup>

The coronavirus pandemic has shaken the world over the previous year. Particularly, the second wave has been

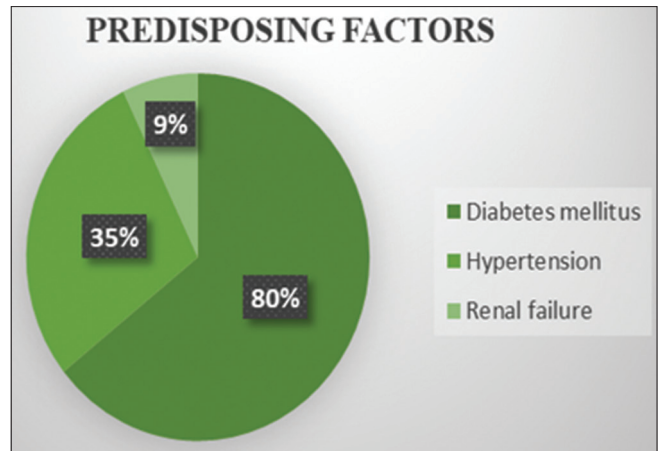


Figure 2: Incidence of underlying comorbidity in patients with mucormycosis

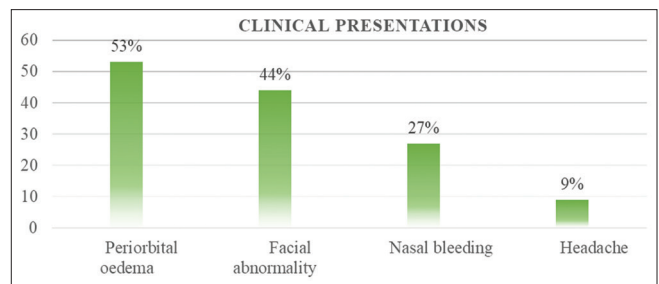


Figure 4: Symptoms at the time of presentation

Table 1: Age-wise gender distribution of the patients

Age group	Gender	
	Male, n (%)	Female, n (%)
30-40	5 (13.8)	2 (22.2)
41-50	13 (36.1)	4 (44.4)
51-60	14 (38.8)	3 (33.3)
61-70	4 (11.1)	0
Total	36 (80)	9 (20)

Table 2: Steroid usage versus nonsteroidal use

Corticosteroid use	Number of patients, n (%)
Steroid usage	39 (87)
Nonsteroidal usage	6 (13)

overwhelming in India. Millions of people were affected during April and early May 2021.<sup>[7]</sup>

Rapid diagnostic methods used to detect mucormycosis are biopsy, potassium hydroxide (KOH) mount, and Calcofluor stain. The biopsy is mainly used as it has more benefits and less risk. It is difficult to detect mucormycosis by routinely culture tests. In mucormycosis, treatment pattern mainly includes antifungal agents, surgical debridement, reversal of underlying predisposing factors, and adjuvant therapy. For invasive mucormycosis, amphotericin B has been the standard treatment, and patients with

**Table 3: Form of steroid usage during coronavirus disease 2019**

Form of steroid	Number of patients, n (%)
Inhalation	3 (07)
IV	16 (36)
Oral	6 (13)
IV and oral	12 (27)
IV: Intravenous	

**Table 4: Major steroid used in postcoronavirus disease 2019 mucormycosis**

Name of the steroids	Count (%)
Methyl prednisolone	19 (43)
Prednisone	2 (4.5)
Dexamethasone	2 (4.5)
Deflazacort	1 (2.2)
Budecort	2 (4.5)
Methylprednisolone, prednisone	3 (6.8)
Dexamethasone, prednisone	1 (2.2)
Dexamethasone, methyl prednisolone	4
Dexamethasone, prednisone, methyl prednisolone	1 (2.2)
Budecort, prednisone	2 (4.5)
Dexamethasone, hydrocortisone, methylprednisolone	1 (2.2)
Methylprednisolone, budecort, hydrocort	1 (2.2)

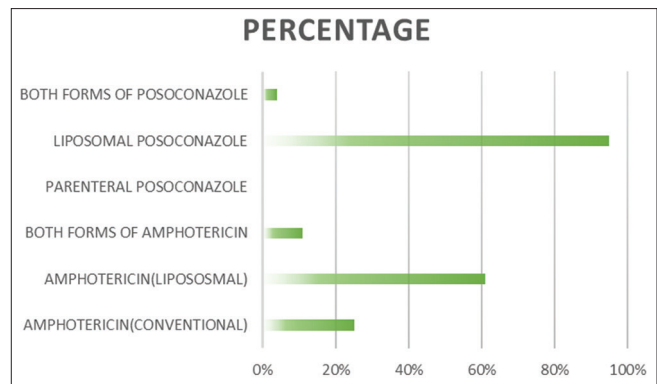
**Table 5: Treatment for postcoronavirus disease 2019 mucormycosis**

Drug	Count (%)
Amphotericin (conventional)	11 (25)
Amphotericin (liposomal)	27 (61)
Both forms of amphotericin	5 (11)
Parenteral posaconazole	0
Liposomal posaconazole	42 (95)
Both forms of posaconazole	2 (4)

COVID-19 who may develop acute or chronic liver failure should be switched to a nonnephrotic alternative. Therefore, posaconazole or isavuconazole have been recommended. The latter has an added benefit of shortening the QT interval, which might be influenced by hydroxychloroquine and azithromycin which numerous patients continue to receive. Surgical debridement before the better is vital in the management of mucormycosis. Mucormycosis should be managed by members of all departments in the hospital as therapy is toxic and very resource intensive.<sup>[8]</sup>

## SUBJECTS AND METHODS

A retrospective observational study was conducted in the emergency department at a tertiary care hospital for 2 months. Active cases of COVID-19 were confirmed by laboratory tests such as rapid antigen or nucleic acid amplification test and confirmed as SARS-COV-2 in the emergency department. Active cases of post- COVID mucormycosis were collected and Analyzed.



**Figure 5: Treatment for post-COVID-19 mucormycosis**

COVID-positive patients were included in the study, and non-COVID patients, pregnant women, and HIV patients were excluded from the study. The primary objectives of this study was to assess the risk factors of post-COVID-19 mucormycosis, to estimate the presenting signs and symptoms of the patients, to evaluate the relationship between steroidal usage and post-COVID-19 mucormycosis and to determine treatment pattern of post-COVID mucormycosis.

## RESULTS

A total of 45 cases were analyzed during the study, i.e., post-COVID mucormycosis [Tables 1-5 and Figures 1-5].

## DISCUSSION

In the current study, a total of 45 cases were examined and it was found that 80% of the patients were male, indicating that males are at higher risk than females. 38.8% of the male patients were of age group 51–60 years, followed by 36.1% of age group 41–50 years. Mucormycosis was predominantly seen in males, both in people who were recovering from COVID-19 or were still active.<sup>[8]</sup> Furthermore, patients with other comorbidities especially diabetes mellitus, i.e., 80% are more prone to post-COVID-19 mucormycosis compared to any other comorbidity, which is in congruence with the study conducted by Desai *et al.*, stating that diabetes mellitus Type II is the most common predisposing factor accounting for 80% of cases.<sup>[9]</sup> Similarly, Yohai *et al.*<sup>[10]</sup> and Ferry and Abedi<sup>[11]</sup> have found diabetes mellitus Type II to be the most common predisposing factor. Hence, monitoring should be done to reduce the risk of complications.

Furthermore, patients affected with mucormycosis have 67% of orbital signs. During the presentation, 53% of the patients had periorbital edema. In our study, out of 45 patients, the patients with the presence of steroidal usage during COVID-19, i.e., 87%, were affected with mucormycosis, which is similar to the study conducted by Mishra *et al.*, stating that the use of immunosuppressive medications such as steroids in patients with COVID-19 is more susceptible to mucormycosis.<sup>[12]</sup> It is also found that methylprednisolone is the major steroid used, which accounted for 43% of the steroids. Based on the form

of steroidal use during COVID, we found that patients who received IV therapy of steroids, i.e., 36%, are more prone to mucormycosis compared to oral and inhalation form. However, the treatment mainly focused on the reduction of the fungal load and reducing other complications. The treatment included the usage of lipophilic amphotericin B in 61% of the patients, which is associated with the use of lipophilic posaconazole in 95% of the patients, which is similar to the study conducted by Spellberg *et al.*, stating that the preferred first-line treatment for mucormycosis is lipid formulations of amphotericin and salvage therapy options include posaconazole and hyperbaric oxygen.<sup>[13]</sup> Some of the preventive measures to be taken for CAM are proper sanitization and handling of oxygen gas cylinders, proper decontamination of the hospital environment, use of disposable oxygen humidifiers, use of clean distilled water in oxygen humidifiers and oxygen concentrators, use of glucocorticoids for the management of COVID-19 at the lowest possible dose and the limited possible duration, avoidance of use of iron and zinc supplements for the management of COVID-19, avoidance of use of voriconazole as antifungal prophylaxis, and avoidance of use of broad-spectrum antibiotics, unless indicated.<sup>[14]</sup>

## CONCLUSION

Post-COVID-19 mucormycosis is a major threat for the individuals affected with COVID-19. The major risk factor in post-COVID mucormycosis is the presence of diabetes mellitus; therefore, proper measures must be undertaken in diabetic patients. It is more likely that the orbital signs are predominant which must be properly monitored in mucormycosis cases. Additional risk factors such as the use of steroids and oxygen inhalation should also be of concern. Patients on a high dose of steroids and prolonged ICU stay during COVID-19 should be monitored carefully to improve their quality of life of the patient. If a patient develops any symptoms related to the eyes, nose, face, lungs, and skin, immediate medical assistance should be received to avoid further complications.

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## Conflicts of interest

There are no conflicts of interest.

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