



Mucormycosis at the Time of COVID-19 Pandemic: A Review

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Abstract

Mucormycosis, an opportunistic fungal illness, has become a global health problem in the aftermath of the COVID-19 pandemic. This is mostly owing to a dramatic spike in COVID-19 infection in recent months in India, which was exacerbated by this fungal co-infection. Mucormycosis has an exceptionally high probability of death and lasting damage to the affected area. Although early action can save lives and mitigate the fungus's impact, it is frequently hard for the already overwhelmed health system in India due to the pandemic. Other variables, such as diabetes, have had a significant impact on the disease's outcome. [Bangladesh Journal of Infectious Diseases, April 2022;9(suppl_1):S55-S57]

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Introduction

Mucormycosis is an opportunistic fungal infection caused by *Rhizopus*, *Mucor*, *Rhizomucor*, *Cunninghamella*, and *Absidia* fungi¹. The pathogen may be present in the environment, on the skin, or in the orifices of the body. Mucormycosis is classified into numerous forms, including Rhinocerebral, Pulmonary, Gastrointestinal, Cutaneous, and Disseminated². In individuals with weakened cellular and humoral defences, the spores invade the paranasal sinuses and nasopharynx, spreading to the

orbit and brain cavity. During the continuing COVID-19 epidemic, an increase in instances of rhino-orbital mucormycosis has created a potentially fatal combination—early detection and intervention are the only ways to save the infected patient's vision and life.

Presentation and Management in Clinical Practice

The most aggressive kind is rhino cerebral orbital mucormycosis (RCOM). As implied by its name, the

infection begins in the nose, progresses up the nasal canal, spreads to the orbital region, and eventually reaches the brain. At that point, the patient's death is probably certain. Mucormycosis is typically manifested clinically by oedema on one side of the face, headache, blockage of the nasal sinuses, and blood-tinged nasal discharge. Ptosis, proptosis, and ophthalmoplegia are all common in the orbital area. Fever is frequently accompanied by rapidly intensifying black sores on the bridge of the nose or the inside of the lips. It is characterized pathologically by giant cell invasion, thrombosis, and eosinophilic necrosis of the surrounding tissue.

A comprehensive history, physical examination, and imaging are all necessary to rule out mucormycosis. Bone destruction is a common finding on a cranial CT scan in diabetic patients. A cranial magnetic resonance imaging (MRI) is indicated for greater sensitivity, as it will reveal any involvement of the brain, sinuses, or orbit. On imaging, the stage will be determined by the extent of sinus and brain involvement.

A biopsy should be performed and sent for direct microscopy, standard culture media at 30 and 37 degrees Celsius, or PCR analysis. Susceptibility testing might then be requested³. Early diagnosis and a well-planned interdisciplinary approach can help save the patient's sight and life. Clinical and microbiological diagnosis should be followed by prompt treatment of the underlying immunosuppressive condition, which in COVID-19 is either corticosteroid usage, coinfection with diabetes mellitus, or hyperglycemia caused by corticosteroid use. Initiating appropriate antimicrobial treatment and surgical debridement of necrotic tissue may prevent exenteration, permanent facial disfigurement, and death.

Brunet et al⁴ recommended that mucormycosis be treated with liposomal amphotericin B in combination with surgical debridement as first-line therapy. In another study conducted in India, authors reported, in all cases of rhino orbital cerebral mucormycosis sinus debridement is necessary⁵.

Factors increase the Risk

As an opportunistic infection, any condition that weakens the immune system increases the likelihood of developing a fungal infection such as mucormycosis. Apart from COVID-19, additional significant risk factors include the following: Uncontrolled diabetes mellitus is the most frequently encountered co-morbidity in RCOM. According to a

meta-analysis, 80 per cent of mucormycosis cases also had diabetes. Globally it is associated with 46.0% of mortality due to its association with the fungus⁶. Diabetic ketoacidosis escalates the risks. A recent meta-analysis by Sing et al, in India repeatedly emphasized the significance of uncontrolled DM and hyperglycemia as the major contributors of mucormycosis in COVID-19 patients⁷.

Even in the absence of diabetes mellitus, a patient who had new-onset hyperglycemia (mainly steroid-induced) during COVID-19 treatment had a greater risk of developing mucormycosis. In the United States of America and Europe, haematological malignancies and organ transplantation are significant risk factors⁸. During this pandemic, steroid use is arguably the most significant risk factor. As a potentially life-saving medication, doctors must prescribe steroids to COVID-19 patients in accordance with management guidelines. Lionakis et al⁹ have demonstrated in their study that a combined dose of 600 mg prednisolone and 2 to 7 grams methylprednisolone is a risk factor for mucormycosis in immunocompromised people⁹.

Other immunocompromised states, such as iron overload, deferoxamine treatment, burn injuries, AIDS, malnourishment, and IV drug abuse, are risk factors for mucormycosis as well.

COVID-19 and Mucormycosis

There are several reasons why COVID-19 patients are more susceptible to fungal co-infection. *Aspergillus* and *Candida* are two primary pathogens infecting people with COVID-19¹⁰. However, the recent emergence of mucormycosis as a COVID-19 co-infection, particularly in India, has catapulted it to a global issue. This is largely due to the aggressiveness of the rhino-orbital-cerebral (ROCM) form of the disease. While it is a rare disease worldwide (0.005 to 1.7/million people), India has the greatest prevalence (0.14/1000 people) in 2019-2020¹¹. According to several studies, India's large diabetic population may be the fundamental reason for the high prevalence of this opportunistic infection¹².

Steroids are well-known for suppressing the immune system. Corticosteroids became a life-saving medicine throughout this pandemic. Additionally, the association between corticosteroid use and opportunistic infection is widely recognized. Numerous studies have found opportunistic infections such as aspergillosis, candidiasis, and

mucormycosis following short-term or long-term steroid use⁹.

In recent months, as India battles the worst-case scenario of a pandemic, the surge in mucormycosis cases become a reason to be concerned, as the disease has a fatality rate of up to 90.0% when intracranial involvement occurs¹³. Additionally, the fungus's rapid spread within hours leaves clinicians with little time for identification, without which the sickness will almost always kill the patient¹⁴. Singh et al¹⁵ recently published a meta-analysis in which they discovered some critical evidence regarding the relationship between COVID-19 and mucormycosis by studying 101 cases from ten countries, including 82 patients from India.

Mechanism of Mucormycosis in COVID-19

The relationship between COVID-19 and mucormycosis can be explained by linking immunosuppression from COVID-19, DM, and corticosteroid use in COVID-19 patients. Sing et al⁷ suggested a multifaceted aetiology for mucormycosis in COVID-19-infected patients in their recent meta-analysis. Diabetes mellitus and hyperglycemia are both independent risk factors. Uncontrolled hyperglycemia is a typical side effect of corticosteroid therapy in COVID-19 patients.

Steroids also affect WBC function and macrophage activity. Additionally, an acidic environment in DKA promotes mucor growth. COVID-19 itself damages the endothelium and depletes T-cells, resulting in opportunistic infections. Free iron in the body is an ideal environment for mucor. Due to hyperglycemia, ferritin glycosylation results in an increase in free iron, which aids mucor proliferation. Increased cytokine levels in COVID patients, such as IL-6, also result in an increase in free iron. Apart from this, the acidic environment created by DKA further raises the iron level in some patients. Thus, the combination of hyperglycemia, an acidic environment, free iron, WBC deficiency, and mucormycosis creates the ideal condition for devastation¹⁶.

Conclusion

The triple combination of COVID-19, DM, and mucormycosis is lethal. Healthcare practitioners

should take every precaution to maintain optimal blood glucose levels, administer corticosteroids judiciously, and act quickly to treat disease at its earliest stage to save lives.

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