



# Mucormycosis in COVID- 19 Patients Poses a Challenge to Public Health

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## Abstract

Mucormycosis is an emerging and re-emerging mycosis that is reported from many countries of the world including India. The disease is caused by filamentous fungi that belonged to the genus *Absidia*, *Cunninghamella*, *Mucor*, *Rhizomucor*, and *Rhizopus*. These fungi are widely prevalent in our environment, and have the potential to invade any organ of the body including the sinuses, lung, brain, heart, kidney, joint and others. The source of infection is exogenous, and the respiratory tract is considered as the prime portal of entry of the fungi. Mucormycosis can occur in sporadic as well as in epidemic form. The maximum cases of mucormycosis are caused by *Rhizopus oryzae*. Globally, disease due to *Rhizopus oryzae* affects over 10,000 persons each year. The recent pandemic of COVID-19 has posed a great challenge to the public health authorities. Mucormycosis in COVID-19 patients are reported from India, and also other nations. Rhino-orbital-cerebral form of mucormycosis is frequently encountered in clinical setting throughout the world. Diabetes mellitus and steroid therapy are the most important risk factors that predispose the patients to mucormycosis. The laboratory help is imperative to confirm an unequivocal diagnosis of disease. Liposomal amphotericin-B and posaconazole are the antifungal drugs that are recommended for the treatment of mucormycosis the patients.

**Keywords:** COVID-19; Diabetes Mellitus; Liposomal Amphotericin; Mucormycosis; Posaconazole; Steroids

## Introduction

COVID-19, a life threatening viral disease, is caused by a new severe acute respiratory syndrome (SARS-CoV-2) that was first time reported from China in 2019; and it resulted in significant morbidity and mortality in the susceptible people [1]. The disease has rapidly resulted in a pandemic affecting over 200 countries of the world including India [2]. Globally, more than 2.5 million people are infected with COVID-19 with a mortality rate ranging from 5 to 10%. In India, there are 2,96,33,105 cases and 3,79,573 deaths from this devastating disease till June 16,2021 [M.Pal Personal Communication]. Covid-19 inflicted insurmountable damage both to the human lives as well as global economy. It affects both sexes,

and all age groups. However, elderly people with underlying medical conditions, such as diabetes mellitus, chronic heart disease, chronic obstructive pulmonary disease, cancer, chronic kidney disease and hypertension are at a higher risk of getting COVID-19 infection [3]. The maximum cases are observed in adults as compared to children [M.Pal Personal Communication].

Mucormycosis is an emerging opportunistic life threatening mycosis that is reported from developed as well as developing nations of the world [4]. The disease is caused by the fungi that belonged to the genus *Mucor*, *Rhizopus*, *Cunninghamella*, *Rhizomucor*, and *Absidia*, order *Mucorales* and class *Zygomycetes* [5-7]. These fungi are ubiquitously

present in nature. They are found in the soil, air, polluted water, decaying vegetables and fruits, stored grain, bread, rice, wheat, barley, groundnuts, dung, compost, etc. [6]. The fungi usually colonize the nose, sinuses, and eyes, and from there, it can reach to the brain. The causative agents of mucormycosis have preference for elastic lamina of large and small arteries causing hemorrhage, infarction and thrombosis [7]. The disease can occur in sporadic and also epidemic form causing significant morbidity and mortality in the susceptible individuals especially having weak immune system [7,4]. Very recently, zygomycosis has posed another challenge in fighting COVID-19 menace [8].

A number of factors, such as leukemia, diabetes mellitus, solid organ transplant, stem cell recipient, intravenous drug abuser, severe burns, acidosis, malnutrition, debility, emaciation, HIV/AIDS, prolonged use of hydrocortisones and broad spectrum antibacterial antibiotics etc. may predispose the host to zygomycosis [6,4,9-12]. Rhinocerebral zygomycosis is most often encountered in patients with diabetes mellitus, and is recognized as a very severe form of the disease that carries mortality rate of 30 to 70% [4,11]. It is pertinent to mention that around 40% of the cases of mucormycosis are related to diabetes mellitus [4]. Nosocomial outbreaks have been recorded in leukemic patients [6].

Due to the dramatic surge of COVID-19 in India, the number of cases of mucormycosis has risen sharply posing a great challenge to public health [8]. According to the NDTV News [13], 51,775 cases of mucormycosis were recorded in India till November 29, 2021. Cases of mucormycosis have been diagnosed among COVID -19 patients from several states of India, such as Gujarat, Maharashtra, Madhya Pradesh, Karnataka, Rajasthan, Tamilnadu, Bihar, Odisha, Rajasthan, Telangana, Uttar Pradesh, Haryana, Chandigarh, and Delhi [14]. It is pertinent to mention that maximum cases of mucormycosis are encountered in patients who were either suffering from chronic diabetics or undergone irrational therapy with corticosteroids [6,12]. The mucormycosis in patients with COVID-19 is reported from many nations including Austria, Brazil, France, India, Iran, Italy, Mexico, Turkey, UK, and USA [12]. Very recently, Singh and others [12] reviewed 101 cases of mucormycosis in patients with COVID-19 of which 82 cases belonged to India. The present communication delineates public health challenges posed by mucormycosis in COVID-19 patients.

### Clinical Spectrum

Several clinical forms, such as cutaneous, subcutaneous, rhinocerebral, gastrointestinal, pulmonary, and systemic mucormycosis are recorded [6,4]. Other unusual forms include pyelonephritis, endocarditis, and osteomyelitis

[4,6,11]. The clinical manifestation of mucormycosis in patients show fever, headache, shortness of breath, chest pain, coughing, hemoptysis, eyelid edema, pain and redness around eyes and nose, blurred or double vision, protruding eyes, sudden loss of vision, nasal discharge, stuffy nose, poor smell, facial paresthesia, skin lesion, toothache, and altered mental status [4,6,7,9-11,15].

### Diagnosis

The X-ray, computer tomography, and magnetic resonance imaging are helpful to spot the lesions in the body of the patient. The isolation of the fungus from the clinical specimens in pure and luxuriant growth on mycological media (Sabouraud dextrose agar, Pal M, et al. sunflower seed agar [16], and APRM (Anubha, Pratibha, Raj, Mahendra) agar [17], and its direct microscopic detection as broad, aseptate hyphae in the wet mount, KOH (potassium hydroxide) preparation, PHOL Pal M, et al. [18], Pal M, et al. Narayan stain [19], and Gram's stain are still widely used as the golden standard of diagnosis. In addition, histopathological, and molecular techniques are also employed to confirm the disease [6,4,20]. There is need to undertake further research to elucidate the role of immunological methods for the diagnosis of disease.

### Treatment

A combination of surgical debridement of necrotizing tissue if possible and antifungal therapy along with management of underlying disease is important to save the life of the patient. Immediate surgical removal of debridement of infected and necrotic tissues and administration of liposomal amphotericin-B helps to reduce the severity of disease [4]. Very recently, posaconazole, a broad spectrum antifungal drug, has shown encouraging results in the patients suffering from mucormycosis [4].

### Prevention and Control

Currently, there is no vaccine available for mucormycosis. Therefore, certain measures, such as judicious use of steroids, rational use of antibiotics, correcting the predisposing factors, especially managing the diabetes mellitus, proper use of face mask by immune compromised persons when visiting heavily polluted environment, use of clean potable water in humidifiers, avoiding contact with dirty surfaces, proper hand hygiene, avoiding to live in poorly ventilated, wet, moist and humid houses, early recognition of disease, and rapid institution of appropriate antifungal antibiotics [6,4] will certainly help to mitigate the incidence of mucormycosis [7,4]. It is hoped that these preventive measures will certainly be useful to effectively manage mucormycosis in COVID-19 patients.

## Conclusion

Mucormycosis is an opportunistic life threatening fungal disease of global public health concern. Uncontrolled diabetes and extensive use of corticosteroids ascribed to most cases of disease. It is advised that to have a team of multidisciplinary experts that include microbiologist, ENT specialist, ophthalmologist, maxillofacial surgeon, radiologist, neurologist, and pathologist for the better management of this life threatening opportunistic fungal disease that has caused serious health problem in COVID-19 patients. As liposomal amphotericin-B and posaconazole are very expensive antifungal drugs, further research should be conducted to develop low cost, safe, and effective drugs that can be widely used for the better management of mucormycosis, particularly by the poor resource nations of the world.

## Dedication

This paper is dedicated in the memory of all the Physicians, Surgeons, Microbiologists, Pathologists, and other medical staff who lost their lives while treating the people affected with COVID-19.

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