



## Mucormycosis (Black Fungus) in Covid 19 Patient

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### Abstract:

**Background:** Mucormycosis, is also known as 'Black Fungus' which was previously a rare fungal infection and now suddenly come to light post in the COVID-19- pandemic, mainly during the second wave in India. Mucormycosis, is a serious and rare fungal infection, has recently been reported in COVID-19 patients worldwide. This study aims to map all the emerging evidence on the COVID-19-associated mucormycosis (CAM) with a special focus on clinical presentation, treatment modalities, and patient outcomes. An extensive literature search was performed in MEDLINE (Ovid), Embase (Ovid), Cochrane COVID-19 Study Register, and WHO COVID-19 database till 9 June 2021. Data were summarized using descriptive statistics and presented in tabular form. This evidence mapping was based on a total of 167 CAM patients with a mean age of  $51 \pm 14.62$  years, and 56.28% of them were male. Diabetes mellitus (73.65% (n = 123)), hypertension (22.75% (n = 38)), and renal failure (10.77% (n = 18)) were the most common co-morbidities among CAM patients. The most common symptoms observed in CAM patients were facial pain, ptosis, proptosis, visual acuity, and vision loss. Survival was higher in patients who underwent both medical and surgical management (64.96%). Overall mortality among CAM patients was found to be 38.32%. In conclusion, this study found a high incidence of CAM with a high mortality rate. Optimal glycemic control and early identification of mucormycosis should be the priority to reduce the morbidity and mortality related to CAM.

### AIM & OBJECTIVES

Isolation, identification and speciation of "MUCORMYCOSIS IN COVID -19 PATEINT COMMONLY KNOWN AS BLACK FUNGUS" from different clinical specimens.

Determine the prevalence of Black fungus infections.

Diagnosis of Mucormycosis.

**Key words:** Mucormycosis, hypoxia, acidosis, hyperglycemia CAM, COVID-19.

### 1. INTRODUCTION :

Mucormycosis is a systemic fungal infection caused by members of the class Zygomycetes, order Mucorales. It is seen in patients debilitated by immune or metabolic disorders. Patients contracting this infection uniformly suffer from predisposing conditions: acidosis, uncontrolled diabetes mellitus, leukemia, lymphoma, AIDS, severe malnourishment, severe burns, cytotoxic therapy, and immune suppression from corticosteroid use. It has also been observed in patients with chronic renal failure, liver problems, and dialysis patients on deferoxamine therapy. Mycology is study of fungi. It belongs from the phylum thallophyte. mucormycosis has emerged as an important fungal infection with high associated mortality rates. Zygomycoses are uncommon, frequently fatal diseases caused by fungi of the class Zygomycetes (consisting of the orders Mucorales and Entomophthorales) with distinct patterns of clinical infection. The majority of human cases are caused by Mucorales fungi; therefore, the terms mucormycosis and zygomycosis are used



interchangeably (the term phycomycosis is also used) [1, 2]. The Mucorales species most often recovered from clinical specimens are those of the genera *Rhizopus* (the most common genus associated with mucormycosis), *Lichtheimia* (formerly known as *Absidia* and *Mycocladius*), and *Mucor* [11, 7, 6] Species of other Zygomycetes genera.

**2. REVIEW OF LITERATURE :**

**Mucormycosis is commonly known as Black Fungus**

Patients contracting this infection uniformly suffer from predisposing conditions: acidosis, uncontrolled diabetes mellitus, leukemia, lymphoma, AIDS, severe malnourishment, severe burns, cytotoxic therapy, and immune suppression from corticosteroid use.

It has also been observed in patients with chronic renal failure, liver problems, and dialysis patients on deferoxamine therapy. There are no known predispositions based on age, race, or sex. Most cases are acute surgical emergencies, though a few chronic, indolent forms have been reported with signs and symptoms developing over a 4-week period. The primary sites of invasion are the paranasal sinuses, lungs, skin, and the GI tract. [7]

Clinical symptoms, signs, and pathological findings are similar in mucormycosis, regardless of etiology. These fungi show a predilection for arterial invasion, causing extensive emboli and necrosis of surrounding tissues. Vein and lymphatic invasion can occur later in the course of the infection. [1,2]

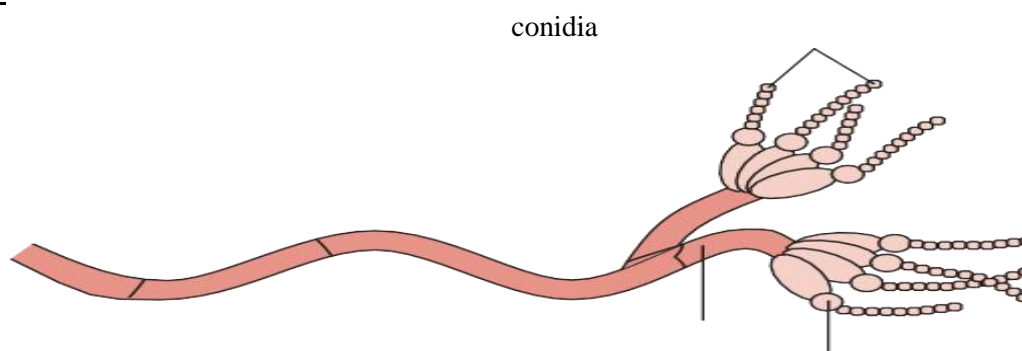
The acidotic, hyperglycemic environment existing in patients with ketoacidotic diabetes mellitus particularly favors the growth of *Rhizopus*. It is thought that diabetic and immunocompromised patients lack normal phagocytic activity on their nasal and oral mucosal surfaces. This allows proliferation of fungus, which does not occur in people with intact phagocytic activity, and the fungus spreads via the blood vessels

**Scientific classification of “mucormycosis commonly known as black fungus”:**

Kingdom:	Fungi
Division:	Mucoromycota
Order:	Mucorales
Family:	Mucoraceae
Genus:	<i>Mucor</i> Fresen.

*Mucor* is a microbial genus of approximately 40 species of moulds in the family Mucoraceae. Species are commonly found in soil, digestive systems, plant surfaces, some cheeses, rotten vegetable matter and iron oxide residue in the biosorption process.

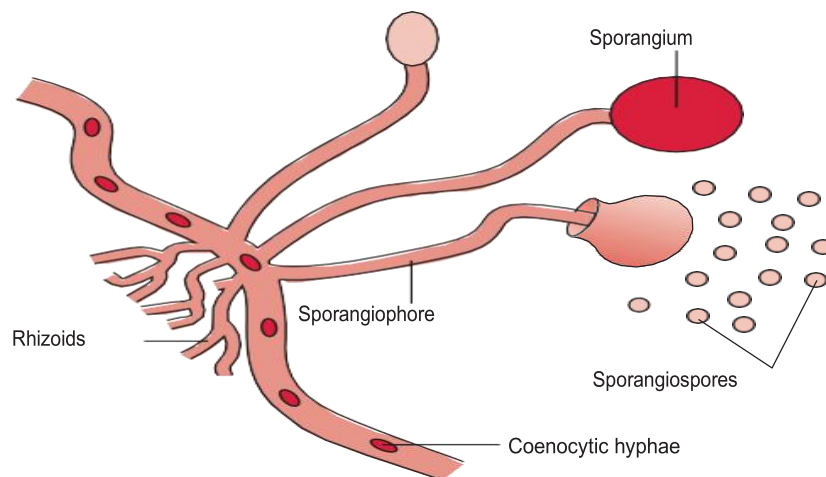
**Mucor species**



## Conidiophore Metulae

Zygomycosis, also known as mucormycosis or phycomycosis, is an infection caused by saprophytic molds, such as *Mucora* and *Rhizopus*

### Rhizopus species



*Rhizopus* species are the most common causative agents of zygomycosis in humans. Of many *Rhizopus* species, *Rhizopus arrhizus* is the most common agent of zygomycosis.

### **Predisposing conditions and forms of the disease are reviewed:**

**Rhino cerebral:** This is the most common form, usually seen in patients with keto acidotic diabetes mellitus. This form presents with sinusitis, facial and eye pain, proptosis, progressing to signs of orbital structure involvement. [5] Necrotic tissue can be seen on the nasal turbinates, septum, and palate. This may look like a black eschar. Intracranial involvement develops as the fungus progresses through either the ophthalmic artery, the superior fissure, or the cribriform plate.[7]

**Pulmonary:** This is most frequently seen in patients with neutropenia, such as those with leukemia or lymphoma. This form presents with fever, dyspnea, and possible hemoptysis.

**GI tract:** This form is seen in severely malnourished patients, particularly in kwashiorkor, and has been seen in patients with amoebic colitis and typhoid. The stomach, ileum, and colon are usually involved, mimicking intra-abdominal abscess.

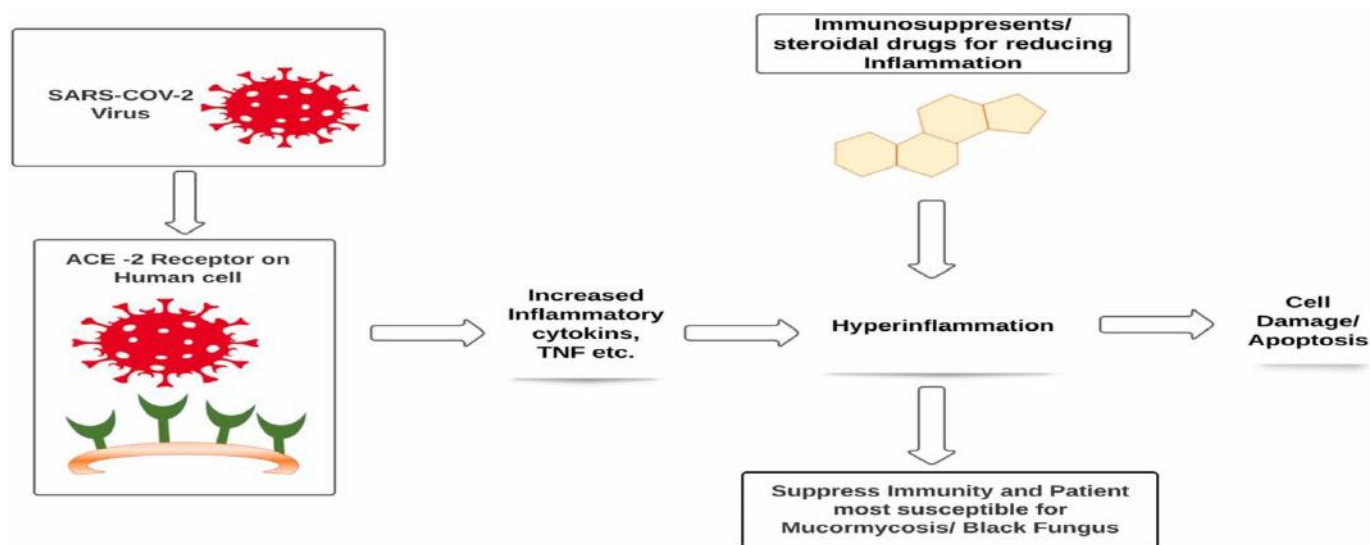
**Cutaneous:** This form can follow minor trauma, insect bites, wounds, burns, and use of non-sterile dressings.[5]

Necrotic lesions occur on the epidermis that are painful and hardened, usually with a blackened central area. These lesions can progress into the dermis and even muscle.

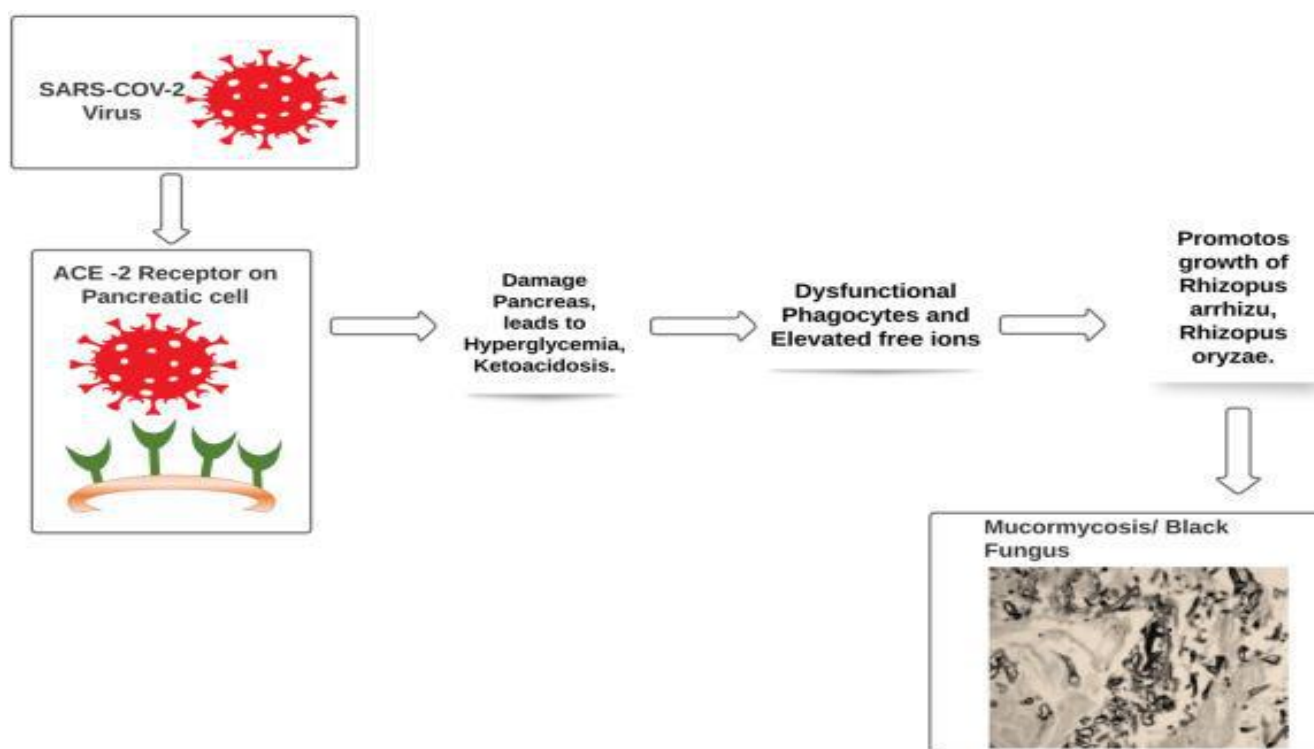
**Disseminated:** Dissemination can occur, mainly from the pulmonary form, to the heart, brain, bones, kidney, and bladder. Dialysis patients on deferoxamine therapy are predisposed to this form.

**Mucormycosis:** An opportunistic pathogen during COVID-19

The pandemic of coronavirus disease 2019 (COVID-19) still remains on an upsurge trend. The second wave of this disease has led to panic in many countries, including India and some parts of the world suffering from the third wave. As there are no proper treatment options or remedies available for this deadly infection, supportive care equipment's such as oxygen cylinders, ventilators and heavy use of steroids play a vital role in the management of COVID-19.[2] In the midst of this pandemic, the COVID-19 patients are acquiring secondary infections such as mucormycosis also known as black fungus disease. Mucormycosis is a serious, but rare opportunistic fungal infection that spreads rapidly, and hence prompt diagnosis and treatment are necessary to avoid high rate of mortality and morbidity rates. [4,5]



Mucormycosis is caused by the inhalation of its filamentous (hyphal form) fungi especially in the patients who are immunosuppressed. Recent studies have documented alarming number of COVID-19 patients with mucormycosis infection.



The entry of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is possible via spike protein available on the envelope which binds with angiotensin converting enzyme 2 (ACE 2), which are available at pancreatic beta cells, lungs, kidney and small intestine. It is possible that entry of virus into pancreatic cells may damage beta cells and leads to insulin deficiency. Patient with hyperglycemia and ketoacidosis are more susceptible to get attacked by Mucormycosis moulds.[9]

Treatment of Covid-19 patient with immunosuppressant having uncontrolled diabetes mellitus and ketoacidosis are also at major risk for Mucormycosis as it leads to dysfunctional phagocytes causes impaired intracellular killing by oxidative and non-oxidative mechanism.

## LABORATORY DAIGNOSIS

### Specimens:

Scrapings from the lesion

Pus

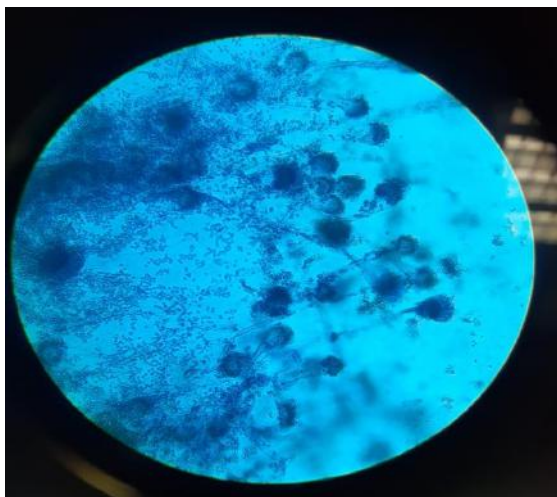
Sputum

Nasal discharge

### Direct microscopy:

It depends on demonstration of characteristic appearance of broad, nonseptate hyphae with right-angled branches in the specimen by microscopy. KOH mount of discharge scrapings may show broad, irregularly set hyphae with right-angled branches in case of rhinocerebral zygomycosis. [10]

Histological sections stained with H&E stain reveal the presence of hyphae.



### Culture.

Culture on SDA medium without antibiotics is dense and hairy. The LPCB preparation of the colony shows coenocystic nature of the hyphae and characteristic sporangia that contain sporangiophores. Fungal cultures are frequently negative. The fungi are difficult to culture because they are a single and very long cells and damage to any part of the cell prevents them to grow.



Since culture often fails to show growth, histopathology of affected tissue is very useful to confirm the diagnosis. Fungal stain of biopsy material obtained from the affected tissue showing non septate hyphae with broad, irregular branches that form more or less at right angles confirms the diagnosis. [6,8,]



## TREATMENT

Once diagnosis has been established, correction of hypoxia, acidosis, hyperglycemia, and electrolytic imbalance needs to be undertaken.[3] Steroids, anti-metabolites, and immunosuppressive drugs should be discontinued, if possible. Aggressive surgical debridement is usually undertaken, along with high dose intravenous amphotericin B therapy (5mg/kg IV daily).[5]

Treatment is continued until remission is achieved. Liposomal amphotericin B may be more effective and less toxic. Resistance to amphotericin B has been observed with prolonged therapy. Local irrigation and packing to aid delivery of amphotericin B to necrotic and poorly perfused tissues has been tried as an adjunct to therapy. This could help prevent disfiguring surgery [4].

## PROGNOSIS

The survival rate in patients with uncontrolled diabetes mellitus suffering from the rhino cerebral form is very grave. Patients with leukemia or lymphoma suffering from the pulmonary form usually die from the infection. The GI tract infection is usually diagnosed on autopsy.[6] The overall mortality is high, usually 30% to 70%.6,8 Death usually results in 2 weeks if untreated or unsuccessfully treated. The survival rate lowers as the diagnosis to treatment interval increases. Seventy percent of survivors have permanent residual effects, including blindness, cranial nerve defects, and surgical disfigurement.

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