

## Mucormycosis- A Post Covid Challenge in India

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### Abstract

In 2019, an unknown virus known as Covid-19 was discovered in Wuhan, China. The first case of Covid-19 was discovered in India on January 30, 2020. In March 2020 it was declared as a global pandemic by World Health Organization. In 2021 India faced the 2<sup>nd</sup> wave of Covid-19. Among the patients recovered from Covid19, few developed opportunistic infection with Black fungus also known as Mucormycosis. Diabetes Mellitus was found to be a risk factor in mucormycosis. The main aim of this article is to conduct a detailed review of mucormycosis infection.

**Keywords:** Mucormycosis; Covid 19; Steroids; Diabetes Mellitus

### Introduction

Covid 19 is a very severe contagious respiratory disease caused due to SARS Cov2 and it is associated with many bacterial and fungal infections. Many persons who recovered from covid 19 experienced signs of mucormycosis [1]. Mucormycosis is a fungal infection that progresses very rapidly in humans, it begins with the nose and paranasal air sinuses, as it enters arteries, it forms thrombi and causes necrosis of soft tissues [2]. Mucormycosis is the third most fungal infection in humans after candidiasis and aspergillosis and usually affects immunocompromised patients especially those who were using steroids for a long time [3]. Patients who were on steroids during treatment of Covid19 were more seen to be affected by mucormycosis [4]. Mucormycosis has a very low incident

rate about 0.0005 to 1.7% per million population whereas it has an 80% higher rate in the Indian population which is 0.14% on 1000, Its fatality rate is 46% but may increase in immunocompromised patients up to 80%. The information was gathered from scholarly literature search found on Google Scholar and Pub Med Central [7]. All data was collected until June 20<sup>th</sup>, 2021. The goal of the study is to conduct a systematic review of types, characteristic, diagnosis and treatment choices of mucormycosis.

### Mucormycosis causative agents

Mucorales are saprophytic fungi that can be discovered in decaying organic materials and soil samples. In a study of *Mucorales* in Indian soils, pathogenic species such as *Rhizopus*, *Lichtheimia*,

*Cunninghamella*, *Rhizomucor* and *Apophysomyces* were isolated. In a community and hospital environment in India, aeromycological investigation revealed the identification of pathogenic Mucorales in air samples. Mucorales taxonomy is still changing; 11 genera and 27 species have been identified as mucormycosis causal agents [8].

**Types of mucormycosis**

There are 5 types of diseases caused by mucor infection.

**Rhinocerebral**

This is the most common form, usually seen in patients with ketoacidosis diabetes mellitus. This form presents with sinusitis, facial and eye pain, proptosis, and even progressing to signs of orbital structural involvement. 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 [5,6,8,13].

**Pulmonary**

Only form is frequently seen in patients with neutropenia, such as those with leukemia or lymphoma. This form presents with fever, dyspnea and possible hemoptysis [5,6,8,13].

**GI tract**

This form is seen in severely malnourished patients, with kwashiorkor and also among patients with amoebic colitis and typhoid. The stomach, ileum, and colon are usually involved, mimicking intra-abdominal abscess [5,6,8,13].

**Cutaneous**

This form can follow minor trauma, insect bites, wounds, burns and the use of non-sterile dressings. Necrotic lesions occur on the epidermis that is painful and hardened, usually with a blackened central area. These lesions can progress into the dermis and even muscle [5,6,8,13].

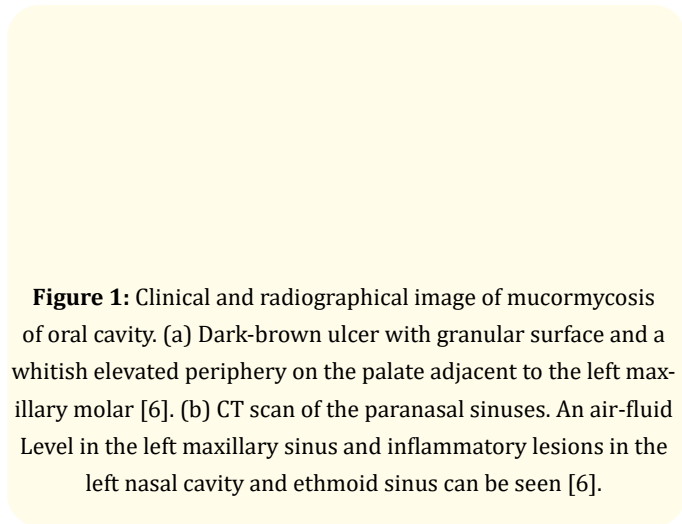
**Disseminated**

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 [5,6,8,13].

**Mucormycosis of oral cavity**

Mucormycosis in the oral cavity can be characterized by granular necrosis or ulceration on the hard palate near to maxillary molar region.

Mucormycosis of the oral cavity: Differential diagnosis, characteristics, clinical and radiographic images.



**Figure 1:** Clinical and radiographical image of mucormycosis of oral cavity. (a) Dark-brown ulcer with granular surface and a whitish elevated periphery on the palate adjacent to the left maxillary molar [6]. (b) CT scan of the paranasal sinuses. An air-fluid level in the left maxillary sinus and inflammatory lesions in the left nasal cavity and ethmoid sinus can be seen [6].

| Diagnosis   | Characteristics   |
|---|---|
| <b>Infections</b><br>Necrotizing ulcerative gingivitis and stomatitis (mostly anaerobic bacteria) | Painful ulceration, non-indurated, well-defined irregular border, with or without variegated surface  |
| Invasive fungal infections (mucormycosis, aspergillosis)  | Painful, dark-brown ulceration, well-defined irregular raised border, invasive down growth (the central surface of the ulcer is lower than the border), variegated necrotic surface, fast progression |
| Chronic granulomatous infections (tuberculosis, tertiary syphilis)                                | Mildly painful ulcer and/or palatal perforation, ill-defined irregular border, variegated surface, chronic course   |
| <b>Malignant diseases</b><br>Melanoma   | Mildly painful, dark-brown or black ulcer, ill-defined irregular border, variegated surface, may alternate with nodules or exophytic growths, relatively chronic course                               |
| Squamous-cell carcinoma   | Mildly painful, reddish ulcer, ill-defined irregular and indurated raised border, variegated surface, relatively chronic course   |
| Extranodal lymphoma   | Mildly painful ulcer, ill-defined irregular and indurated border, variegated surface and/or exophytic growth, relatively chronic course   |
| Plasmacytoma-multiple myeloma   | Mildly symptomatic swelling, with or without surface ulceration, ill defined border, relatively chronic course  |
| Salivary gland adenocarcinomas  | Mildly symptomatic swelling, with or without surface ulceration, relatively chronic course  |
| <b>Other benign and reactive oral lesions</b><br>Necrotizing sialometaplasia                      | Mildly painful swelling progressing (within 2 - 3 weeks) to necrotic tissue, which sloughs off while pain subsides  |
| Peripheral giant-cell granuloma   | Pedunculated asymptomatic swelling, often pigmented, covering surface epithelium may be ulcerated   |

**Table 1:** Differential diagnosis and main clinical characteristics of palatal lesions of mucormycosis in oral cavity [6].

### Histopathological diagnosis

Histopathology of mucormycosis species reveals fungi with broad, nonseptate hyphae showing right angle branching which can be readily differentiated from *Aspergillus* which shows regular, septate, and acute angle branching hyphae type [7].

### Treatment for mucormycosis

The line of treatment for mucormycosis is Amphotericin B, but subsequently, posaconazole and isavuconazole are also prescribed if mucormycosis is detected otherwise surgical excision of the affected region must be done. The major issue in the treatment modality of mucormycosis in India is the lack of financial support in people as most of the people are not able to afford Liposomal Amphotericin B [9]. Adjunctive hyperbaric oxygen can also be given in this infection as many studies show a good prognosis as the use of adjunctive hyperbaric oxygen can reduce the hypoxia of the local tissues and also enhances the neutrophil and macrophage killing ability [10]. If the prognosis is poor in any case then there should be surgical excision of that affected area should be done. If there is the involvement of oral cavity with Patient exhibiting symptoms like facial cellulitis, paraesthesia over the face, nasal discharge, necrotic turbinates, fever and headache. Tooth extraction is the mode of treatment in case of early diagnosis, whereas it results in jaw resection when diagnosis comes late [12]. If there is delayed healing or non-healing of the tooth socket, of a patient, the doctor must be alerted for severity and management of infection [11].

### Discussion

Mucormycosis is a lethal fungal infection, even though occurrence rare, effects mainly among immunocompromised and patients with malignancies like leukemia etc. Uncontrolled diabetes can reduce the immunity of a person and thus he can be more vulnerable to mucormycosis. This fungal infection starts from paranasal air sinuses and then it invades the patient's blood vessels and then it spread through other organs like the brain, lungs, eyes, etc. which can be more dangerous [12]. Dentist plays crucial role in diagnosis and treatment of mucormycosis infection since majority of site of infection is rhino cerebral or rhinomaxillary area involving facial tissues, palate, alveolar bone, and mandibular bone. The need of early diagnosis with detailed case history and thorough inspection of lesion will be the best clinical approach to be followed at the earliest [13].

The mortality rate of this infection is very high and is up to 70%. Death can happen in 2 weeks after the infection if there is unsuccessful treatment. Majority of cases have permanent effects like

blindness, cranial nerve defects, and surgical disfigurement so this infection cannot be taken lightly [14]. We should be very careful while assessing the risk factors and type of mycosis infection in patient for proper treatment [15,16]. Mucormycosis is fatal fungal infection which spreads quickly and becomes extensive before patient attends the clinic with characteristic symptoms.

Mucormycosis therefore is a disease with a poor prognosis, and thus it's important to stay watchful about host populations, risk factors, epidemiology, and early management for a positive outcome [16]. The growth in mucormycosis cases in industrialised nations is connected to immunosuppression in patients with haematological malignancies and transplant recipients. With the emergence of novel risk factors and causative agents, the epidemiology of mucormycosis has shifted in recent years. Therefore, need for more population based research [17-19].

### Conclusion

The exact reason for the occurrence of post covid mucormycosis in the Indian population is still unknown. Though its prevalence in India is higher than in Western countries, this is owing to the presence of Mucorales in the environment, which is linked to a lack of hygiene in a few communities and medical environments. Diabetic patients are more vulnerable to this infection. A patient who has recently recovered from Covid 19 and was on corticosteroids should make every attempt to maintain the blood sugar level. As the disease progresses into the cranial vault it may lead to blindness, lethargy, seizures, and death. The mortality rate in India is high because of due to lack of early diagnosis and management of already advanced cases. Even though Liposomal Amphotericin B shows good treatment results, increased treatment cost and number of doses prevents low socioeconomic patients from receiving this line of treatment. To conclude, this review paper points out that Mucormycosis even though rarest among fungal infection, is fatal and therefore highlights the role of dentists and need of early diagnosis and prompt treatment to reduce mortality and morbidity among patients.

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