



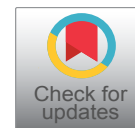
## REVIEW ARTICLE

# Black Fungus Development in SARS-COVID-19 Patients

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## Abstract

Mucormycosis refers to a fungal infection resulting from fungus that belong to the order Mucorales and was first described in 1885 by Paltauf. Being the third most prevalent opportunistic fungal infection after candidiasis and aspergillosis, it causes significant endothelial damage by invading the vascular wall. Multiorgan failure and sepsis develop owing to its spread toward the brain. It usually has poor prognosis and it is impacted by the time it takes to diagnose and most significantly the patient's overall condition. Severe acute respiratory syndrome Coronavirus disease 2019 (COVID-19) resulting from coronavirus 2 (SARS-CoV-2) is related to different fungal and bacterial opportunistic infections. Over the world, recently, in India in particular, numerous mucormycosis cases have been rapidly reported in COVID-19 patients. Taking corticosteroids to treat COVID-19 was observed in 76.3% of cases, followed by remdesivir (20.6%) and tocilizumab (4.1%). This retrospective study aims to analyze the association between SARS-COVID-19 and mucormycosis.

## Keywords

Black fungus, Mucormycosis, SARS-COVID 19, Treatment

glucose availability. It is assumed that asexual spore production is the source of infection in humans. Then, the microscopic spores become airborne and they land on nasal and oral mucosa in humans. Invading the vascular wall, it leads to significant endothelial damage, infarction, and thrombosis, causing deep tissue ischemia and necrosis, including fat and muscle. Consequently, multiorgan failure and sepsis develop. Perforation or palatal orbit is caused by the sinus infection which may easily spread to the mouth. It may spread toward the brain through the apex of the orbit, the plate, or blood vessels. It usually has poor prognosis and it is influenced by the time it takes to diagnose and most significantly the overall condition of the patient [1-14]. Nowadays, all over the world, but specifically in India, several mucormycosis cases were quickly reported in COVID-19 patients. Taking corticosteroids to treat COVID-19 was observed in 76.3% of cases, then remdesivir (20.6%) followed by tocilizumab (4.1%).

## Material and Methods

PubMed articles were retrospectively evaluated. Studies were evaluated from ... to .... A combination of medical subject heading (MeSH) terms and keywords was searched. Research inclusion criteria were "Black Fungus, Mucormycosis, SARS-COVID-19, Treatment". The primary outcome measure were "Covid-19 association, diagnosis and treatment". Two authors (DC, SL) analyzed the articles. Randomized controlled trials (RCTs), cohort studies, case-control studies, randomized studies, prospective and retrospective studies were searched. No search limits of languages and all languages were included. We excluded case reports, articles not focused on surgical management. The object

## Introduction

Mucormycosis denotes a fungal infection owing to fungus of the order Mucorales. In 1885, it was first described by Paltauf. It is the third most prevalent opportunistic fungal infection following candidiasis and aspergillosis. Mucormycosis results from Mucor, Lichtheimia, and Rhizopus, accounting for 70-80% of all cases. These saprophytic organisms can be detected in the pharyngeal mucosa, oral mucosa, nasal mucosa, and paranasal sinuses of asymptomatic people. They may also be found in the manure, starchy foods, soil, and fruits. In nearly 50% of mucormycosis patients, diabetes mellitus (DM) is a predisposing factor, comprising a high



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of this retrospective study is to analyze the association between SARS-COVID-19 and Mucormycosis.

## Results

Awadhesh Kumar Singh, et al. [15] systematically reviewed 101 mucormycosis cases in SARS-COVID-19-infected subjects, 82 of which are from India whereas 19 are from other countries. Mucormycosis was predominant in men (78.9%), in active (59.4%) people and those who recovered from Covid-19 (40%). 80% of cases had DM, whereas 14.9% had concomitant diabetic ketoacidosis (DKA) and 76.3% of cases reported corticosteroid intake for COVID-19 treatment. In 2019, Prakash, et al. [16] conducted a national multicenter study which confirmed or suspected 388 zygomycosis cases in India prior to COVID-19, and they found that 18% had DKA and 57% were out of control. I have found that it is DM.

Likewise, Patel, et al. [17] examined the data of 465 mucormycosis cases without COVID-19 in India and found that the common diseases among Indians include DM (73.5%), malignancies (9.0%), and organ transplantation (7.7%). Having DM significantly raises the chances of contracting Rhino-orbital-cerebral by a factor of 7.5, as Bala, et al. [18] proved in their prospective study in India prior to the COVID-19 pandemic. John, et al. [19] reported the results of 41 confirmed mucormycosis cases in COVID-19-infected subjects, of which 93% of cases had DM, whereas most cases (80%) received corticosteroids.

## Discussion

Severe acute respiratory syndrome Coronavirus disease 2019 (COVID-19) resulting from coronavirus 2 (SARS-CoV-2) is linked with many fungal and bacterial opportunistic infections. Recently, worldwide, particularly in India, several mucormycosis cases have been rapidly reported in people with COVID-19. Phycomycosis or zygomycosis was first introduced in 1885 by Paltauf [2]. Then, in 1957, Baker [20] called it mucormycosis. Mucormycosis is a rare yet fatal fungal infection usually impacting immunocompromised people. It is an angio-invasive disease caused by molds of the genera *Rhizomucor*, *Mucor*, *Rhizopus*, *Cunninghamella*, and *Absidia* of order Mucorales, class Zygomycetes [21]. The global spread of mucormycosis is between 0.005 and 1.7 per million population, but it is nearly 80 times higher (0.14 per 1000) in India than in developed countries Cause resulting in high glucose levels in Mucorales spores (first-time hyperglycemia, diabetes, and steroid-induced hyperglycemia) (metabolic acidosis, DKA, decreased leukocyte phagocytic activity (WBC) because of SARS-CoV-mediated suppression Long-term hospitalization with or without a ventilator seems be a contributing factor to the cause [22,23]. The most common organs associated with mucormycosis were the nose and sinuses (88.9%), followed by the rhino-orbit-

al (56.7%) and cerebral sites (22%). Continued use of corticosteroids has been linked to many opportunistic fungal infections, which include aspergillosis and mucormycosis. These findings need to be revisited Cortisone-Therapy in the context of the COVID-19 pandemic, where corticosteroids are largely used [24-26]. Reports of mucormycosis/series of cases are increasing quickly, particularly between COVID-19 patients in India and in other countries. It is very rare for mucormycosis to occur in healthy people. However, some immunological conditions predict it, including uncontrolled DM with or without DKA, hematological and other medical conditions, long-term neutropenia, organ transplantation, iron overload or hemochromatosis, immunosuppression and corticosteroid therapy, deferoxamine. Includes therapy, severe burns, acquired immunodeficiency syndrome (AIDS), malnutrition, intravenous drug abuse, and openness Post-traumatic injury [27]. Microbiological identification of hyphae based on diameter, presence or absence of septum, bifurcation angle (right or acute bifurcation), and pigmentation distinguishes it from other pre-proven fungal infections in the journal. Mucormycosis can include the nose, axillary, sinuses, central nervous system (CNS), lungs (pulmonary), gastrointestinal tract (GIT), skin, heart, joints, kidneys, jaw bones, and mediastinum (invasive type), but e Rhino-orbital-cerebral is the most commonly observed in clinical practice around the world [27]. The standard treatment for mucormycosis is antifungal therapy with amphotericin B at a dose of 1-1.5 mg/kg/day. The removal of necrotic tissue supports the elimination of invasive fungi that systemic antifungals cannot reach [28].

## Conclusions

The presence of DM causes a higher risk of mucormycosis and DM is usually linked to the COVID-19 severity. Uncontrolled hyperglycemia and DKA precipitation are more frequent because of corticosteroid intake. Low pH mucor spores are fertile medium for germination owing to acidosis. Steroid intake contributes to reducing the WBCs' phagocytic activity. Frequently, COVID-19 leads to endothelialitis, endothelial damage, lymphopenia, thrombosis, and a decrease in CD4+ and CD8+ levels, which causes secondary or opportunistic fungal infections. Corticosteroids overuse in the background of diabetes mellitus, COVID-19, seems to increase Mucormycosis. Efforts are needed to ensure fair usage of only the best glucose and corticosteroids in those with COVID-19. A history of taking corticosteroids for the treatment of COVID-19 was noted in 76.3% of cases, then remdesivir (20.6%) and tocilizumab (4.1%). To mitigate the fatal outcome of this aggressive and invasive disease, a combination of sinus debridement, blood sugar control, and antifungal treatment, is needed [28].

## Declaration of Interest

Nothing to declare for all authors.

## Funding

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## Author's Contribution

AKS conceptualized the study, performed the literature search, and wrote the first draft; RS conducted the tables, the data analysis, and the first draft's revision, and SRJ and AM edited the final draft. All authors mutually agreed to submit this study for publication.

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