



## COVID-19 and Black Fungus: New Insights Explaining the Pathogenicity of the Disease

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**Abstract**

The latest outbreak of COVID-19 has been associated with black fungus. In this study, the author reviewed the literature regarding the black fungus and its coexistence with COVID-19. Literature indicated several risk factors such as being diabetic and immunocompromised. We added our new insights to the pathogenesis of fungi through the results of our previous studies in which we demonstrated that fungi express estrogen receptor, BCL2 protein, and p53. These biomarkers imply that fungi benefit from the microenvironment if estrogen exists. However, if patients under steroid treatments, they are likely to develop secondary infections such as black fungus.

**Keywords:** Black Fungus; COVID-19; p53; BCL2; Estrogen Receptor

**Introduction**

Corona virus disease (COVID-19) transmission is a human-to-human disease that has been labeled a global pandemic, killing more than half a billion people worldwide and causing serious respiratory problems for more than five million individuals. There is injury to the alveolar with severe inflammatory exudation, in addition to lower acute respiratory syndrome. COVID-19 patients had lower levels of immunosuppressive CD4+ and CD8+ T cells and most patients in intensive care units (ICU) require mechanical breathing, resulting in a prolonged hospital stay. It has been observed that these patients have fungal co-infections. COVID-19 individuals get mucormycosis, a severe black fungus illness that causes vision and hearing loss, as well as death. This chapter will cover mucormycosis, a black fungus that develops as a result of post-covid problems [1].

In immune-compromised hosts, a fungus pathogen known as *Aspergillus* causes catastrophic disease. Due to the fungus's air-

borne nature, these hosts include haematological malignancies, which ruin the lungs' first defense. The prevalence of severe viral lung infections has increased, giving rise to pulmonary aspergilliosis (IPA). Most cases are IPA, with mortality rates ranging from 7 to 23 percent [2]. This IPA is comparable to triple strain corona, which causes havoc in the lower respiratory tract and causes acute respiratory distress syndrome (ARDS).

Patients in need of ICU have a high level of triple strain corona, which makes them more susceptible to mucormycosis. As a result, the fatality rate is thought to be significant [3].

Black fungi are a polyphyletic collection of organisms that includes polyextremotolerant and oligotrophic varieties. The development and buildup of melanin in the cell walls of these ascomycetes is the most obvious adaptation. Melanin is a dark pigment that shields cells and helps them survive a variety of harmful situations such as radiation and oxidative stress [4,5]. Black fungi can

biosynthesize other defensive chemicals such mycosporines and mycosporine-like amino acids (MAAs) in addition to melanin [4].

Mucormycosis, sometimes known as black fungus, is a kind of mucormycosis [1]. It is a dangerous fungus illness that affects persons who have a weak immune system [6]. Symptoms vary depending on where the infection develops in the body [7]. It affects the nose, sinuses, eye and brain, causing runny nose, one-sided face edema and pain, headache, fever, impaired vision, swollen and bulging eye, and tissue death [7]. Other diseases can infect the lungs, stomach, and intestines, as well as the skin [8]. It is spread by mold spores of the order Mucorales, most commonly through inhalation, contaminated food, or contamination of open wounds [9]. These fungi are common in soils, decomposing organic matter (such as rotting fruit and vegetables), and animal manure, but they rarely harm humans [10]. It is not passed down from person to person [7]. Diabetes with persistently high blood sugar levels or diabetic ketoacidosis, low white blood cells, cancer, organ transplant, iron overload, kidney problems, long-term steroids, or immunosuppressant use, and, to a lesser extent, HIV/AIDS are all risk factors [6,11].

### COVID-19 and black fungus

During the COVID-19 pandemic in India, the disease is causing yet another major health crisis. As of May 25, 2021, the Indian government reported that over 11,700 people were receiving treatment for mucormycosis. Because of the black discoloration of dead and dying tissue caused by the fungus, many Indian media outlets dubbed it “black fungus”. Even before the COVID-19 pandemic, it was estimated that mucormycosis rates in India were roughly 70 times higher than the rest of the world [12]. Many Indian state governments have declared it an epidemic due to the rapidly increasing number of cases [13]. During the COVID-19 pandemic in India in 2020 and 2021, several cases of mucormycosis, aspergillosis, and candidiasis were linked to immunosuppressive treatment [14]. In early 2021, one review relating to the association of mucormycosis and COVID-19 reported eight cases of mucormycosis; three from the United States, two from India, and one each from Brazil, Italy, and the United Kingdom [15]. Diabetes was the most common underlying medical condition [15]. Most had been in the hospital with severe breathing problems caused by COVID-19, had recovered, and then developed mucormycosis 10 - 14 days later. Five had abnormal kidney function tests, three had sinus, eye, and

brain involvement, three had lungs, one had gastrointestinal tract involvement, and one had widespread disease [15]. Mucormycosis was diagnosed postmortem in two of the seven deaths [15]. Because none of the three had traditional risk factors, the authors questioned the use of steroids and immunosuppressive drugs [15]. However, there were cases where there was no diabetes or use of immunosuppressive drugs. There have been reports of cases in children as well [16].

### Molecular bases of fungal pathogenesis: Perspectives from our studies

We have previously conducted two studies in candida and aspergillus. In the first study, we demonstrated that *Candida albicans* expressed both estrogen receptor and BCL2. This in turn, facilitates the formation of the hyphae, the pathologic form [17]. In another study, we found that *Aspergillus* is localized in lung tissues taken from human autopsies [18]. According to these findings, we think that fungi have molecular bases to facilitate their pathogenicity if the microenvironment is optimal. The mechanism by which Fungi expresses such biomarkers implies the contribution to autoimmunity, the other side of diseases such as COVID-19.

### Conclusion

COVID-19 is associated with black fungus. Fungi is provided with molecular mechanisms that increase their pathogenicity and may contribute to autoimmunity as another side of COVID-19.

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