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Outbreak of Black Fungus in COVID-19 patients: An emerging issue

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To the Editor,

Mucormycosis, commonly called black fungus, is an airborne infection of the respiratory tract caused by fungi Mucorales. The most common genus associated with mucormycosis is Rhizopus. The spectrum of mucormycosis is wide and it ranges from cerebral, cutaneous, and pulmonary to fatal disseminated infections (1).

The coronavirus disease 2019 (COVID-19) pandemic is inciting consternation on several grounds. Several new strains of coronavirus have been identified; the ultimate trajectory of the disease is still undetermined. These variants may impact immunity, vaccine effectiveness and are more contagious. Recently, a double mutant variant of SARS- CoV-2, officially called B.1.617 has drawn attention as it can evade immunity resulted from the exposure with earlier strains (2). This B.1.617 variant in India, which was first identified in the United Kingdom, is a serious health concern, account for the deadly second wave of coronavirus. In India, COVID-19 cases dropped in September 2020 but now began to rise from March 2021 and the last peak was considered as “ripple in a bathtub” as compared to the current one (3).

Furthermore, an outbreak of black fungus in India is another unwelcome surprise brought on by the COVID-19 pandemic, as patients reported in the country to die from black fungus who were earlier infected with the B.1.617 variant of COVID-19. The second wave of COVID-19 in India along with the surge of mucormycosis is an emergency, as almost 9,000 cases of this fungal infection have been detected in past one month, with 1500 cases from Maharashtra state of India (4).The epidemic of mucormycosis in India has worsened the complications of COVID-19; moreover, cases have now started to report from neighboring countries as well.COVID-19 patients have compromised immune systems and are more prone to superimposed infections. Black fungus is more frequently seen in immune-compromised patients with hematological malignancies, comorbidities, trauma, and solid organ transplant (5).

India accounts for nearly one out of every six diabetics worldwide (6). According to the survey from India, 80% of the patients of COVID-19 with mucormycosis are of the known case of diabetes. Patients with diabetes are generally immune-compromised, as unmanaged blood sugar levels create

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an acidic medium, as seen in diabetic ketoacidosis, and are ideal for the black fungus to grow (7).

Corticosteroids have a potent anti-inflammatory property that can prevent lung damage in COVID-19 patients. Dexamethasone is considered the drug of choice, and when unavailable Prednisone, Methylprednisolone, and Hydrocortisone can be put to use (8). According to National Institutes of Health COVID-19 treatment guidelines, pharmacologic management for severe infection require 6mg of Dexamethasone once daily for 10 days or until discharge. Such patients also require supplemental oxygen, high-flow oxygen therapy, non-invasive or invasive ventilation. The mortality rate in COVID-19 patients may reduce with corticosteroids but the safety of the drug for the treatment of COVID-19 has not been evaluated absolutely as patients receiving high dose steroids have an increased risk of superimposed infections (7). Surveys have also proved long-term ventilation to lower immunity, and the fungus is likely spread by humidifier water mixed with oxygen.

Ergosterol is a phytosterol, analog to cholesterol in mammals. It is found most abundantly in fungal cell membranes. The process of sterol biosynthesis is affected by oxygen concentration. Fungal cells cannot synthesize ergosterol under hypoxic conditions and absorb sterols from the external culture environment (9). COVID-19 patients experience a low level of oxygen in the blood with the common symptoms of oxygen deprivation and exhaustion. The ability of the fungal cells to grow by absorbing pre-formed sterols from the external culture environment in the absence of oxygen might be the cause of mucormycosis infection in such patients. The sterols not only adapt for their biosynthesis but have also enabled the eukaryotes to build a defense mechanism against oxidative stress. Oxygen therapy is recommended for patients infected with COVID-19 which can cause oxidative stress.

To further establish the significance of ergosterol adaptation, Amphotericin B, currently is the recommended drug for the treatment of mucormycosis in COVID-19 patients (10). It is in the polyene class of antifungal drugs, binds irreversibly to ergosterol, resulting in the rapid disrupted cell membrane and cell death.

The mucormycosis in the COVID-19 pandemic is the emerging issue of the current time. We suggest that healthcare researchers should look into the role of diabetes and corticosteroid medications in the surge of black fungus in COVID-19 patients. The correlation of imbalance between production and destruction of reactive oxygen species (ROS) due to oxidative stress in COVID-19 patients and evolvement of sterols further needs to be investigated.

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Conflicts of Interest

The authors declare no conflict of interest.

Authors' Contributions

I.U, S.S and M.J.T conceived the idea, S.S, F.S, and A.J performed a literature review and wrote the initial manuscript. I.U, M.J.T, and A.J reviewed the manuscript and critically revised it to the final form. All authors read and approved the final version of the manuscript.

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