

COVID-19 and mucormycosis syndemic: double health threat to a collapsing healthcare system in India

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Summary

In addition to the overwhelming and uncontrollable second wave of COVID-19 in India, the country is also dealing with an outbreak of mucormycosis, a deadly fungal infection, which is affecting thousands of COVID-19 patients. With the increasing number of cases of mucormycosis and a fatality rate of 50%, many Indian states and union territories have declared an epidemic of black fungus due to its unprecedented emergence, which has adversely affected the already debilitated health system of the country. The advent of the new fungal epidemic in the country is due to the overdosage, panic and injudicious use of corticosteroids among COVID-19 patients, as well as their pre-existing medical history of diabetes, given that India is the diabetes capital of the world. Thus, there is an urgent need to address this public health concern by having nationwide surveillance, diagnostic and management system of the disease, along with public awareness and education to combat the syndemic of COVID-19 and mucormycosis in the country.

keywords black fungus, COVID-19, mucormycosis, pandemic, syndemic

Sustainable Development Goals: Good health and well-being

India is experiencing a detrimental surge of coronavirus disease 2019 (COVID-19) cases during its second wave with a total of 28 996 949 cases and 351 344 deaths as of 7 June 2021, which is increasing with every passing day [1]. This sudden rise of COVID-19 cases has been an interplay of various factors, such as the appearance and arrival of variants of concern including B.1.617.2, B.1.1.7, B.1.351 and P.1, breach of standard public health protocols such as hand washing, wearing a mask and social distancing, and hosting of mega-events like the *Kumbh Mela* festival and rallies which attracted huge masses [2].

Along with COVID-19, India is also experiencing an outbreak of mucormycosis, a deadly fungal infection, which is affecting thousands of COVID-19 patients. Also known as black fungus, this disease is caused by opportunistic fungi in the *Mucorales* family, which is commonly found in the ecosystem and often associated with rotting organic matter. Humans can be infected by inhaling and consuming spores in food or drugs, or contaminating wounds with spores [3]. Patients with

immunocompromised conditions, including those with COVID-19, are mostly affected. Immune function can be repressed by immunosuppressive medications, such as corticosteroids, and a variety of immunocompromising illnesses, such as cancer, diabetes and retroviral disease, as well as patients who have undergone transplant surgeries [3].

With an overall case fatality rate of 50%, black fungus has emerged as a public health concern in India, especially among COVID-19 patients [4]. Due to this unfortunate scenario and possible underreporting of cases, the central government declared mucormycosis as a notifiable disease in accordance with the Epidemic Diseases Act of 1897. As of 7 June 2021, there are more than 28 200 reported cases of mucormycosis in the country [4]. Due to this alarming situation, many Indian states and union territories, including Rajasthan, Telangana, Odisha, Karnataka, Tamil Nadu, Gujarat and Chandigarh, have declared black fungus an epidemic [5]. Public health authorities and medical specialists claim that this new epidemic was exacerbated by the overdosage of

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corticosteroids among COVID-19 patients, as well as panic use among individuals who fear for their lives due to the increasing COVID-19-related deaths.

In September 2020, the World Health Organization (WHO) recommended the use of corticosteroids to patients with severe and critical COVID-19. On the other hand, corticosteroids should not be used in treating patients with asymptomatic, mild and moderate COVID-19 symptoms, unless they are taking them for another disease [6]. Following this recommendation, many Indian physicians included corticosteroids in treating severe and critical COVID-19 cases, such as patients who are on a ventilator or requiring supplemental oxygen.

However, the WHO recommendation on daily dosage was not followed. The WHO suggested 32 mg of methylprednisolone per day while the Indian Directorate General of Health Services advised a daily dose of 1–2 mg/kg, approximately 70–140 mg of methylprednisolone for a severe COVID-19 patient with an average weight of 70 kg [6,7]. Several COVID-19 patients became immunocompromised as a result of the high doses of corticosteroids, making them more susceptible to fungal infections. Furthermore, the general public, mostly with mild and non-severe COVID-19 symptoms, also took corticosteroids out of panic and anxiety without medical advice leading to emergence of the black fungus epidemic. Intake of corticosteroids for COVID-19 treatment was observed in 76% of mucormycosis cases [8].

Another potential factor of the mucormycosis outbreak among Indian COVID-19 patients is their pre-existing diabetes. Given that India is the diabetes capital of the world, the indiscriminate usage of steroids for patients with diabetes potentially led to a surge of mucormycosis cases in the country. 94% of patients with COVID-19-associated mucormycosis have a history of poorly controlled diabetes [9]. Other pre-disposing factors include prolonged stay in intensive care units and comorbidities like malignancy or post-transplant status [10].

Clinical features of COVID-19-associated mucormycosis include symptoms like nasal blockage and discharge, pain and/or redness around eyes or nose, headache, fever, shortness of breath, coughing, hematemesis and altered mental status [10]. Mucormycosis may affect the lungs, but nose and sinuses are the most frequent infection sites. It can then spread to the eyes, causing blindness, or to the brain, causing headaches and seizures [10]. Thus, the most common form is rhino-orbito-cerebral mucormycosis, followed by pulmonary mucormycosis. Regarding the diagnosis, the mean duration between diagnosis of COVID-19 and onset of mucormycosis symptoms was 15.6 ± 9.6 days. A delay of even 6 days in initiating treatment doubles the 30-day mortality from 35% to

66% [10]. Therefore, early diagnosis and management may prevent further progression of the disease or even mortality. However, despite being one of the largest pharmaceutical hubs globally, there is a shortage of Amphotericin B, the current treatment for mucormycosis, in India due to the increasing cases of black fungus [11].

The Centers for Disease Control and Prevention and the All India Institute of Medical Sciences enumerated important factors such as control of blood sugar level, steroid monitoring and dosage variance according to the severity of COVID-19 infection. Inappropriate steroid consumption raises the blood sugar level and weakens the immune system, a condition that favours fungal infection. Medical procedures include rapid control of diabetic ketoacidosis, reduction or discontinuation of steroids and immunomodulating drugs, antifungal prophylaxis, radioimaging and clinical monitoring of fungal progression [12]. Surgical removal of necrotic tissue, debridement and enucleation of the eye, if involved, have also proved to be life-saving. Other clinical interventions include proper cleaning and sterilisation of humidifiers and ventilators, utilisation of disposable or disinfected personal protective equipment, and proper hygiene maintenance.

Even though measures have been declared, a wide gap between various schemes and policy implementation still persists. The lacunae in policy execution might have galvanised the crisis of fungal outbreak. The wide disparity in doctor-to-patient ratio (8 physicians per 10 000 population) often leads to poor prognosis, negligence and inadequate medical supplies [13]. Dearth of medical supplies and medicines, such as Amphotericin B, and shortage of beds in hospitals (8.5 hospital beds per 10 000 population) have caused widespread unavailability of prompt treatment leading to death of patients [13,14]. Another challenge with mucormycosis is the requirement of interdisciplinary management guidelines, as it does not fall under one speciality owing to its widespread involvement. The necessity to treat mucormycosis long-term with nephrotoxic drugs that can further burden the healthcare system with increasing demands of haemodialysis and hospitalisations due to renal failure should also be considered.

The government must address the shortage of medicines in the country, train an ample workforce and generate technical expertise in order to avert the spread of black fungus. Duty-free imports and relaxation of domestic taxes should be implemented to ensure an adequate supply chain of drugs, as pharmaceutical manufacturers are overwhelmed with the exponential demand [14]. Epidemiological surveys in hospitals and COVID-19 care units must be introduced to prevent onset of damp areas that might be a breeding ground for mucormycosis.

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Physicians and patients should occasionally be screened for the presence of the black fungus. Awareness about the fungal infection through various media should be ensured to create a healthy atmosphere among the population. Mass vaccination will also ensure immunity towards the COVID-19 infection, which in turn will help in reducing complications. Thus, concerted efforts of revamping surveillance, diagnosis and management, along with public awareness and patient education, are the requisites for managing the COVID-19 and mucormycosis syndemic in India.

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