

# The risk of cutaneous mucormycosis associated with COVID-19: A perspective from Pakistan

Dear Editor,

During the recent pandemic, the increase in the cases of mucormycosis confronts the possibility of a double pandemic that could completely overwhelm healthcare systems. Pakistan is one of the countries that is severely affected countries by the COVID-19 outbreak, with 1,063,125 confirmed cases of COVID-19 and 23,797 deaths as of 09 August 2021.<sup>1</sup>

Mucormycosis is an emerging fungal infection that can be classified into six forms namely: rhino-orbital-cerebral, pulmonary, cutaneous, gastro-intestinal, disseminated and mucormycosis of other sites. Of these, cutaneous mucormycosis is the third highest clinical presentation, caused by opportunistic fungi of the phylum *Glomeromycota*, which tends to infect individuals with a deficient immune response.<sup>2</sup> Susceptible populations include diabetics, malnourished individuals, cancer and organ transplant patients, and those with active tuberculosis, human immunodeficiency virus (HIV), AIDS, or a history of chronic respiratory diseases, asthma, and liver disease.<sup>3,4</sup>

The clinical presentation of primary cutaneous mucormycosis may have a gradual or insidious onset. Eschars are the most prevalent cutaneous finding, but it also includes targetoid lesions, tender nodules, ulcers and purpuric lesions. Secondary cutaneous mucormycosis manifestations are more frequent than primary manifestations. They usually result from a rhinocerebral or disseminated infection, and have an acute onset with high mortality.<sup>5</sup>

According to global epidemiological surveillance, infections of mucormycosis have been on the rise, with a particular increased incidence in Asian countries.<sup>3</sup> Although there is no thorough data available to assess the exact burden of fungal diseases in Pakistan, the country reported high rates of mucormycosis infections (14/100,000) even prior to the onset of the COVID-19 pandemic.<sup>6</sup> Corresponding to the trend in its neighbouring country, India,<sup>4,7</sup> several cases of mucormycosis, also known as black fungus-related deaths, are now being identified among COVID-19 patients at various hospitals across Pakistan.<sup>8</sup> The use of steroids leaves the COVID-19 patients immunocompromised, and the viral infection, added to a prolonged admission in intensive care in severe cases provides ideal conditions for mucormycosis to infect patients. Furthermore, it was reported that an increasing majority of COVID-19 patients took corticosteroid medications especially during the second COVID-19 wave in Pakistan, which explains the recent increment in mucormycosis cases in the country.<sup>9</sup>

Additionally, severe COVID-19 disease leads to increased levels of pro-inflammatory markers, including IL-1, IL-6 and tumor necrosis alpha, and decreased levels of CD4 interferon-gamma, CD4 and CD8 cells; which augments the chances of microbial infections including mucormycosis. Usage of low-quality industrial-grade oxygen cylinders, unclean and humid environment of the hospital facility, tap water in humidifiers and antibiotic overuse may also trigger the mucormycosis infection.<sup>5</sup>

The diagnosis of cutaneous mucormycosis is difficult because of its non-specific findings. It mainly relies on polymerase chain reaction and fungal culture. Since it is a highly fatal disease, rapid diagnosis and multidisciplinary measures are key to improve mortality rates.<sup>10</sup> However, as with many other developing countries that are experiencing concomitant infectious epidemics in addition to COVID-19 such as Zika virus in Brazil, Yellow Fever in Africa, the diversion of medical supplies and personnel to COVID-19 will prove to be a considerable challenge for Pakistan in prioritizing mucormycosis surveillance, diagnosis and management alongside a robust COVID-19 response.<sup>11-13</sup> The

struggle of developing countries against cutaneous mucormycosis is further compounded due to suboptimal laboratory facilities and lack of expertise, which is a major hindrance in keeping accurate disease records.

To successfully contain the outbreak of mucormycosis in the country, the first step is the development of context-specific management guidelines in order to deter the side effects of the antifungals required for its treatment. Second, the use of corticosteroids in COVID-19 patients must be exercised with extreme caution and in accordance with WHO's recommendations, which specifically warn against their use in mild, moderate or asymptomatic COVID-19 infections.<sup>14</sup> Since a delay of mere 6 days in the inception of treatment for COVID-19 associated mucormycosis results in a twofold increase in the mortality rate,<sup>15</sup> laboratory facilities should be enhanced and rapid diagnostic kits must be expedited. It is also crucial to reinforce the public health capacity in Pakistan and improve the physician to patient ratio which currently stands well below the WHO standards. Infection control practices must be updated in a stringent capacity in all healthcare facilities to provide protection against both mucormycosis and COVID-19.

A handful of population-based studies have been conducted to calculate the prevalence of mucormycosis in the western world. However, the findings from such studies are not relevant in developing countries, as the high-risk groups and interventions differ considerably. In developing countries, a rise in the incidence of mucormycosis can be attributed to the excessive burden of diabetes mellitus, while in developed countries, it is commonly found in immunosuppressed individuals or those receiving transplants. The advent of latest risk factors and etiological agents, such as post-tuberculosis, chronic renal failure, and stay in ICU, warrants population-based studies in countries like Pakistan with a high incidence of vulnerable populations to understand the epidemiology of the disease.<sup>3</sup>

Thus, the added burden of highly fatal re-emerging infectious diseases such as mucormycosis puts the public health security at significant risk. In the wake of the COVID-19 pandemic, it is crucial to expand laboratory-testing capacities, invest in robust technologies to improve epidemiological surveillance, and institute awareness and preventive measures to alleviate the burden on our health services.

## KEYWORDS

COVID-19, cutaneous mucormycosis, Pakistan, public health

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Not applicable.

## CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests.

## ETHICS STATEMENT

The present study includes printed and published information; therefore, the formal ethical clearance was not applicable for this study.

Sucharu Asri<sup>1</sup>

Muhammad Rizwan Akram<sup>2</sup>

Mohammad Mehedi Hasan<sup>3</sup> 

Fatima Muhammad Asad Khan<sup>4</sup>

Nida Hashmi<sup>5</sup>

Fareha Wajid<sup>6,7</sup>

Irfan Ullah<sup>8</sup> 

<sup>1</sup>Faculty of Medicine and Health Sciences (FMHS), Shree Guru Gobind Singh Tricentenary Medical College, Haryana, India

<sup>2</sup>Sheikh Zayed Medical College and Hospital, Punjab, Pakistan

<sup>3</sup>Department of Biochemistry and Molecular Biology, Faculty of Life Science, Mawlana Bhashani Science and Technology University, Tangail, Bangladesh

<sup>4</sup>Dow University of Health Sciences, Karachi, Pakistan

<sup>5</sup>Karachi Medical and Dental College, Karachi, Pakistan

<sup>6</sup>Jinnah Sindh Medical University, Karachi, Pakistan

<sup>7</sup>California Institute of Behavioral Neurosciences and Psychology, Fairfield, California, USA

<sup>8</sup>Kabir Medical College, Gandhara University, Peshawar, Pakistan

### Correspondence

Mohammad Mehedi Hasan, Department of Biochemistry and Molecular Biology, Faculty of Life Science, Mawlana Bhashani Science and Technology University, Tangail, 1902, Bangladesh.

Email: [mehedi.bmb.mbstu@gmail.com](mailto:mehedi.bmb.mbstu@gmail.com)

### DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

### ORCID

Mohammad Mehedi Hasan  <https://orcid.org/0000-0002-3871-889X>

Irfan Ullah  <https://orcid.org/0000-0003-1100-101X>

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