Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Commentary

Fostering a deeper understanding of COVID-19-associated mucormycosis – A commentary on "The mucormycosis coinfection in the context of global COVID-19 outbreak: A fatal addition to the pandemic spectrum" (Int. J. Surg. 2021:106031)

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Dear Editor,

We read with great interest the article by Devnath et al. on the catastrophic repercussions of mucormycosis coinfection caused by the angioinvasive saprophytic fungi in COVID-19 patients [1]. The authors accentuated that *voriconazole* prophylaxis for non-mucor fungal infections is a risk factor for mucormycosis. In stark contrast, they specified *voriconazole*—in the line of amphotericin B, posaconazole, or itraconazole—as one of the effective anti-mucor drugs. Indeed, a case-control observational study demonstrated that voriconazole prophylaxis is a risk factor for mucormycosis [2]. Besides, voriconazole causes fatal breakthrough mucormycosis in immunocompromised patients with hematologic malignancies [3]. This evidence strongly advocates that voriconazole is a predisposing factor for mucormycosis.

Devnath et al. accentuated that "early diagnosis" of mucor infection is highly imperative to forestall belligerent fungal invasion, prevent/mitigate extensively disfiguring surgery, and improve patient survival rates [1]. Diagnosis through both conventional (histopathological or direct microscopic investigation and culture) along with novel molecular (fungal internal transcribed spacer (ITS) region sequencing) approaches might be helpful. However, the conventional diagnostic method is slow, invasive, and insensitive [4], while the ITS region sequencing technique has standardization concerns due to various in-house-developed probes and primers [5]. Besides, there is no robust evidence to directly link this diagnostic factor (i.e., ITS region) with any "targeted" anti-mucor therapy.

In this line, a seminal study by Soliman et al. in Nature Microbiology showed that mucoricin, a pivotal toxin in the pathogenesis of mucormycosis, is released by both *dead* and living fungal hyphae [6]. This evidence explains why antifungal treatment alone is insufficient and why frequent surgical debridement of the infected tissue is imperative for mucormycosis management. Interestingly, the authors proposed that the development of mucoricin "targeted" antibody therapeutics might reduce the surgical requirement and augment the antifungal treatment outcome. Perhaps, quantification of mucoricin toxin level might be an attractive tool for "early diagnosis" of mucor infection, which ultimately might prevent/mitigate the need for radical surgery.

The incidence of post-operative mucormycosis recurrence is still a grave concern. According to a recent report from the Sassoon General Hospital, a large state-run hospital in India, the incidence of recurrent mucormycosis cases requiring revision surgery is about 20% [7]. Recurrence of mucormycosis might be due to incomplete debridement of the infected tissues—especially in the frontal sinus, skull base, or other clinically difficult-to-access anatomical sites like pterygopalatine fossa. Besides, inadequate post-operative cleaning and care, neglected immune-boosting adjunct therapies, and incomplete antifungal courses might fuel the incidence of breakthrough mucormycosis infection [7,8].

Prevention is better than cure. A recent analysis revealed that 86% of the mucor cases were unvaccinated, while 8% of mucor cases received both doses of COVID-19 vaccine [9]. Although this evidence favors the hypothesis that COVID-19 vaccination is a preventive strategy against mucormycosis infection, a recent report by the U.S. Centers for Disease Control and Prevention (CDC) revealed that three-fourth (74%) of the fully vaccinated persons were tested positive for COVID-19 [10]. Hence, clinicians should not rule out the possibilities of mucormycosis infection in fully (COVID-19) vaccinated persons.

Psychiatric support is an often-overlooked approach in the comprehensive management of mucormycosis. Sudden vision loss, extensive facial disfigurement, or amputation [11] due to aggressive surgical management of mucormycosis might be a traumatizing experience for most patients. A recent study revealed that oral and maxillofacial surgery might precipitate mental illness, including post-traumatic stress disorder (PTSD), anxiety, and depression [12]. Notably, post-surgical facial disfigurement and reduced social support might dwindle psychosocial adjustment and ultimately elicit psychological distress [13].

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Hence, counseling the mucormycosis patients and their kin is imperative to mitigate post-surgical physical disability, shock and consequent psychological/psychosocial issues. In this line, King Edward Memorial (KEM) Hospital in India is a pioneer in setting a dedicated ward with regularly visiting psychiatrists for counseling the mucormycosis patients and their kin [14]. However, the lack of widespread implementation of this approach is still a critical concern.

A deeper understanding of coronavirus disease-associated mucormycosis (CAM) immensely helps to mitigate morbidity and mortality risks and prevent CAM. With the resource limitations, lack of patient awareness, and paucity of diagnostics aids, it is quintessential to understand these causative and contributory factors for effectively combating the CAM syndemic.

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Declaration of competing interest

No conflicts of interest to declare.

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