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

Mucormycosis coinfection in the context of global COVID-19 outbreak: A fatal addition to the pandemic spectrum

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Mucormycosis is an invasive fungal infection, often associated with extremely severe complications in immuno-compromised patients [1]. Such infections are caused by opportunist and ubiquitous fungi belonging to the order Mucorales, family Mucoraceae, which is also commonly known as the black fungus [2]. Generally, along with immunocompromised conditions, solid organ transplantations and neutropenia, haematological malignancies, stem cell transplantation, patients on steroids and voriconazole prophylaxis and individuals diagnosed with uncontrolled diabetes mellitus etc. serve essential risk factors for mucormycosis to develop [1,3].

Severe opportunistic infections such as oropharyngeal candidiasis, pneumonia, pulmonary aspergillosis, bloodstream candida infections, etc., in patients infected by SARS-CoV-2 or after the post infection period have been reported from all over the world [4,5]. Initially, China reported secondary fungal infections in critically-ill ventilated COVID-19 patients and later studies from Europe, and America also reported COVID-19 associated mucormycosis (CAM) such as rhinoorbital mucormycosis, pulmonary mucormycosis, invasive fungal sinusitis etc. In COVID-19 patients [1,6–8]. *Aspergillus fumigatus, Rhizopus microspores, Lichtheimia ramosa, R. arrhizus,* and other fungal pathogens were found as causative agents of such complications. Among Asian countries, Iran initially found 15 CAM, mainly rhino-orbital mucormycosis, during first wave of cases from April to September 2020 [9].

Recently, associations of mucormycosis/black fungus in increasing the mortality rate of critically ill and recovering COVID-19 patients in India were making headlines across the world [6]. The prevalence of mucormycosis (approximately 0.14 cases per 1000 population) in India is about 80 times higher than other developed countries [10]. Overall, India reported at least 40,845 cases of mucormycosis and 3129 fatalities from such fungal agents since April 2021. Out of the total number of mucormycosis patients in India, 34,940 had COVID-19, 26,187 had the co-morbidity of diabetes, and 21,523 were on steroids [11]. Several studies reported that COVID-19 is associated with substantial mortality in DKA (diabetes ketoacidosis) patients and concluded that DKA is common and severe in individuals hospitalized with COVID-19 [12,13]. A recent systematic review reported that 101 cases of mucormycosis in people with COVID-19 have been reported worldwide, of which 82 cases were from India among which18 (out of total 31) expired due to several complications [14]. Singh et al., also reported that 80% of the patient were having pre-existing diabetes mellitus (DM) with concomitant DKA in 14.9% [14]. According to Lin et al., India is the second leading country with most diabetic burden with highest death due to the disease, which may be one of the major factors for increasing the number of deaths in patients with CAM [15].

Apart from India, Asian countries like, Iran, Pakistan and Nepal have also reported CAM cases. Pakistan reported also at least 22 cases of CAM, among them 4 succumbed to death [16]. In June month of this year apart from Pakistan, Iraq also reported 5 CAM cases and one death so far [17]. Nepal also reported 14 CAM cases and encountered really high mortality rate with six deaths so far [18].

Bangladesh also reported first CAM case on May 8 and another on May 23, both were male aged 45 and 60 years old [19]. According to DGSH (Directorate General of Health Services), later a 65 years old person was also diagnosed with the disease and became first reported death due to the fungal infection. The expired patients had diabetics and kidney problems [20]. Another 45 years old patient was also recently diagnosed with mucormycosis in Dhaka [21].

Proper management guidelines to control and treat such infections are urgently needed by countries encountering black fungus in COVID-19 patients. Hence, first of all early diagnosis can be obtained by fungal detection via histopathology or direct microscopic examination and culture, along with molecular methods such as sequencing common DNA region of fungi known as internal transcribed spacer (ITS) region which is recommended as a best method for species level identification of Mucorales [10]. Secondly, proper management and treatment of patients with CAM. Physicians can follow India or other countries who successfully treated patients with mucormycosis. The standard management of mucormycosis consists of proper removal of the infected hard and soft tissue by surgery, and parenteral antifungal therapy with Amphotericin B.5 or antifungal drugs like Posaconazole, Voriconazole and Itraconazole which have been found useful against mucor infection [22]. Overall, control of hyperglycemia, early treatment with liposomal amphotericin B, and surgery are found successful for CAM management and reducing the associated mortality rate [23].

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However, it has been found that use of several steroids in patients with COVID-19 compromises the immunity of patients and consequently secondary infection can developed. Patients with COVID-19 have been administered variety of steroid drugs (dexamethasone, methylprednisolone) which weakens the immune system, as long term use of steroid found has been found to be associated with mucormycosis or aspergillosis [14]. Moreover, steroids increase blood sugar levels, such as in 101 CAM cases, diabetes mellitus was reported in 93% of cases, while 88% were receiving corticosteroids [9] and these lead to the chances of acquiring fungal infections and developing invasive mucormycosis due to rise in blood sugar. Maintaining adequate hygiene and sanitation measures, controlling diabetic levels, judicious use of steroids, addressing immunocompromised status of patients altogether help in alleviating the risks of getting fungal infection while appropriate treatment after timely diagnosis aid in improving survival rates of mucormycosis patients. Thus administration of several drugs should be critically revised thinking about fungal co-infections, for example, substantial thoughts should be given before administering drugs targeting immune systems such as tocilizumab.

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Popy Devnath - conceptualization, manuscript writing.
Kuldeep Dhama – conceptualization, manuscript writing and editing.
Abu Montakim Tareq - conceptualization, manuscript writing.
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Declaration of competing interest

Authors declare that they have no conflicts of interest.

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Popy Devnath[a]
[a] *Department of Microbiology, Faculty of Sciences, Noakhali Science and Technology University, Noakhali, 3814, Bangladesh*
E-mail address: popydn.mbg@nstu.edu.bd.

Kuldeep Dhama[b,**]
[b] *Division of Pathology, ICAR-Indian Veterinary Research Institute, Izatnagar, Bareilly, 243122, Uttar Pradesh, India*

Abu Montakim Tareq[c]
[c] *Department of Pharmacy, International Islamic University Chittagong, Kumira, Chittagong, 4318, Bangladesh*
E-mail address: montakim0.abu@gmail.com.

Talha Bin Emran[d,*]
[d] *Department of Pharmacy, BGC Trust University Bangladesh, Chittagong, 4381, Bangladesh*

** Corresponding author. Division of Pathology, ICAR–Indian Veterinary Research Institute, Izatnagar, Bareilly, Uttar Pradesh, 243122, India.

* Corresponding author. Department of Pharmacy, BGC Trust University Bangladesh, "BGC Biddyanagar", Kanchannagar, 4381, Chandanaish, Chittagong, Bangladesh.
E-mail address: kdhama@rediffmail.com (K. Dhama).
E-mail address: talhabmb@bgctub.ac.bd (T.B. Emran).