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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Editorial

The recent mucormycosis storm over Indian sky

The spectre of the COVID-19 pandemic still looms large over India. People lucky enough to survive infection by COVID-19, now face the danger of acquiring the dreaded fungal infection, mucormycosis. This fungal infection is not unusual in India, as the case-rate in pre-Covid era was estimated at 70 times to the developed world [1]. However, the present rise of cases is unprecedented. The disease has been declared notifiable in India. Over 31,000 cases have already been reported in government portal by June 13, 2021. Even during first wave of COVID-19 infection, we observed over two times increase in mucormycosis cases compared to previous year [2].

1. Why this surge?

To answer this question, we may refer to our multi-centre retrospective study conducted during September to December 2020. The study reported that 60.4% patients of Covid associated mucormycosis (CAM) had uncontrolled diabetes, 78.1% had received steroids and 60.3% of them had inappropriate steroid therapy either steroid prescribed to patients with normal oxygen saturation on room air or at inappropriately high dose [2]. The study claimed uncontrolled diabetes, inappropriate steroid therapy as predominant risk factors for CAM. While 32.6% patients had no diabetic history, 79% of them received steroid therapy. The unprecedented number of mucormycosis cases at present possibly requires more explanations.

Without having any published descriptive epidemiology study during the second wave, we may rely on indirect evidences including the personal narrative of treating doctors, ecology of Mucorales in India, behaviour of COVID-19 virus, and evidences brought out in last year's study [2]. The four major issues may be highlighted to explain the present situation: diabetes, steroid, COVID-19, and environment. Large number of patients came to the hospitals with COVID-19 infection during the second wave. The existing healthcare infrastructure crumbled causing crisis of hospital beds, oxygen and manpower. Doctors did not have time for thorough examination of any patient. Glycaemic control of diabetic patients was neglected, and to compensate oxygen crisis, doctors prescribed higher dose of steroids for longer period. The steroid deranges blood sugar metabolism, and also lowers immunity of the patient by impairing neutrophil migration, and macrophage phago-lysosomal fusion [3]. The COVID-19 virus also deranges glucose metabolism by damaging beta cell of pancreas [4], alters iron metabolism leading to 'Hyper ferritinemic syndrome', which damages the cells and allow free iron in circulation. Iron is good food for Mucorales. The virus also causes 'endothelitis' allowing Mucorales to enter in the circulation through severe vascular endothelial injury. Hyperglycaemia and acidemic state induce upregulation of endothelial receptor glucose regulated protein (GRP78), which allows increased adhesion and penetration of Mucorales through receptor protein homologs (Cot H) [3,4]. It is not known how far immune dysregulation due to the virus affects anti-Mucor immunity. The fourth factor is environmental prevalence for Mucorales in India. Mucorales spores had been detected at 0.68–1.12 cfu/cubic meter in indoor and 0.73–8.60 cfu/cubic meter in outdoor air of India with predominance of main pathogenic species *Rhizopus arrhizus*. These high spore count in air allows the entry of spore in the respiratory tract of vulnerable patients causing mucormycosis [1].

2. How can we control the storm?

As mucormycosis is a devastating disease, certain strong measures are immediately required: a) good glycaemic control during management of COVID-19, b) judicious use of steroid at 0.1mg/kg/day dexamethasone for 5–10 days only in patients with oxygen desaturation, and absolutely no steroid in patients with normal oxygen saturation on room air, c) use of masks by vulnerable population to reduce exposure to Mucorales even at home and avoidance of construction sites, d) as majority of the patients manifest the disease after discharge from COVID-19 facility [2], patients may be advised to seek immediate medical attention on development of early symptoms and signs of the disease, e) post-COVID clinic should have ENT surgeon and ophthalmologist to pick up the disease early, f) training of healthcare workers on the diagnosis and management of mucormycosis.

3. Unresolved research questions

Though uncontrolled diabetes, inappropriate steroid therapy and high Mucorales load in the environment explain the surge to certain extent, additional factors may be responsible and require further studies: a) Is any other risk factor responsible for surge, which may be resolved by case-control study? b) Is there any mucor-specific immunity disturbance during COVID-19 induced immune dysregulation? c) Do the new variants alpha and delta cause higher mucor-specific immunity disturbance? d) Is there any genetic susceptibility for mucormycosis in Indian population? e) Whether the present prevalent *Rhizopus arrhizus* strains are more virulent than previous strains? f) Is there any environmental factor responsible?

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