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Letter to the Editor

Additional insights on COVID-associated mucormycosis

Sir,

The response letter by Arakeri et al was a good read.[1]

In the original paper, the authors mentioned that mucormycosis has been found to be linked to COVID-19 infections caused by the B.1.617.2 (Delta) variant.[2] The Delta-mucor hypothesis gained importance due to the unusual surge noticed during Indian's second wave; however, its scientific basis still needs to be established.[3] Direct Delta variant-associated immune dysregulation and metabolic dysfunction is a relatively minor mechanism in the absence of other potential contributors (evidenced by the low percentage of mucor cases seen in asymptomatic and untreated COVID patients).[4] Such cases form a unique subset and deserve deeper exploration.

The SARS-COV-2 virus may tend to infiltrate the pancreatic islets, leading to the genesis of hyperglycaemia and/or diabetes. However, we are unsure if there is any actual evidence that the Delta variant, in particular, has a significant adverse impact compared to other variants. If we show these comparative data on the pancreatic islets through cell-line or animal studies, we can more confidently explain why cases increased during the second wave.

More countries are showing mucor cases; however, the numbers in India greatly exceeded all other nations (>45000 cases). This means we should look for India-specific factors, ranging from the geographic distribution of mucor-causing organisms,[3] specific host factors, and even the medical management protocols deployed during that time. If we study the dosing of steroids during the first and second waves (through an analysis of medical prescriptions), our understanding could further improve.

Steam inhalation practice (rampant during the pandemic) could have also resulted in heat injury to the nasal epithelium, enabling infection with the ubiquitous mucor organisms. However, very few case reports exist on this topic. Furthermore, a recent pre-print shows a lack of association.[5] Another source of mucosal trauma could be repeated 'nasopharyngeal swabbing.' Although it seems unlikely, a pre-print indicates that this could be independently associated with a higher risk of COVID-associated mucormycosis (CAM).[5] Prolonged oxygen administration could be another important source of trauma to the protective mucosal barrier.[3]

The connection between mask behaviour and mucormycosis also deserves a more committed exploration. Due to financial issues and general difficulty associated with N-95 mask use, many relied on low-cost cloth and surgical masks and frequently reused them. The cloth masks, in particular, could serve as a reservoir of fungal spores.[5] Their mesh-like design could entrap and accumulate the free-floating spores that might eventually settle within the nasal passages during air exchange, and germinate once tissue conditions become conducive. A hyperglycaemic and immunosuppressive state induced by diabetes and/or high-dose and prolonged corticosteroid therapy constitute the favourable tissue milieu.

Alongside explorations into steroid use, mode of oxygen administration, comorbidities (eg, diabetes, renal disease), immunosuppressant use, future efforts must be strategically planned to address the role of viral variants, mask practices, steam inhalation, nasopharyngeal swabbing, exposure to gardening activities, and indoor/outdoor pollution (environmental fungal contamination). It is noteworthy that different contributors act simultaneously.

Conflict of interest

We have no conflicts of interest.

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Ethics statement/confirmation of patients permission

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