Indian J Otolaryngol Head Neck Surg
https://doi.org/10.1007/s12070-021-02801-8

OTHER ARTICLES

# Mucor Alert: Triad of COVID-19, Corticosteroids Therapy and Uncontrolled Glycemic Index

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Received: 20 May 2021 / Accepted: 1 August 2021


**Keywords** COVID-19 · Mucormycosis · Diabetes mellitus · Immunocompromise

## Dear Sir,

We read the recent article titled "Paranasal Mucormycosis in COVID-19 Patient" by Saldanha M et al. [1] with great interest. The authors did a fantastic job highlighting the importance of a fatal disease at this crucial time. We would like to draw attention to a spike of mucormycosis in COVID-19 suffered or recovered patients. Immunocompromised COVID-19 patients are vulnerable to rhino-orbital-cerebral mucormycosis, which is a life-threatening opportunistic invasive fungal infection caused by mucoromycetes [2, 3]. The mortality rate even with the treatment is around 50% [4]. A high index of suspicion, a low threshold for diagnosis, immediate and accurate management with aggressive surgical debridement and systemic antifungal therapy remains the standard of care. The targeted points for attention are described below which might be helpful for the halt of this epidemic.

### At-Risk Population

Those with uncontrolled diabetes mellitus and diabetic ketoacidosis**,** history of treatment with corticosteroids therapy [5], organ or bone marrow transplant, other forms of metabolic acidosis, neutropenia [6], increased serum iron levels [7], deferoxamine or iron chelation therapy in patients of hemodialysis [8], and malignant hematologic disorders [8].

### COVID-19 Related Immunosuppression

This viral infection causes significant immunosuppression due to lymphopenia, reduced CD4 and CD8 T cells [9–11]. There is a huge inflammatory cytokine surge, increased neutrophils, and endotheliolitis [11]. It induces a prothrombotic state by directly invading the endothelium and causing diffuse endothelial inflammation [10–12]. It also induces pre-diabetic state [13].

### Corticosteroids Related Immunosuppression

They are the mainstay in COVID-19 management and are used for immunomodulation-related lung damage. Being no definitive treatment for COVID-19, only systemic corticosteroids have shown improved survival [14], but at the cost of an exhausted immune response. It induces hyperglycemia [15] with impaired neutrophil migration and phagolysosome fusion [16, 17]. According to Indian guidelines moderate cases should get systemic methylprednisolone 0.5-1 mg/kg/day or dexamethasone 0.1–0.2 mg/kg for three days within 48 h of admission, if inflammatory markers are raised or need for mechanical ventilation is present. Severe cases should get systemic methylprednisolone 1-2 mg/kg/day or dexamethasone 0.2–0.4 mg/kg for 5–7 days [12].

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Published online: 08 August 2021

### Uncontrolled Gycemic Index

Those with diabetes are at an increased risk of complication and mortality than non-diabetics [18]. A rapid diagnosis can result in lowering mortality. Impaired neutrophil function causes defective chemotaxis, transmembrane migration, and reduced superoxide production [19]. Reduced binding of transferrin to iron in acidotic conditions favors the growth of mucor [20]. Increased expression of endothelial receptors GRP-78 will result in dysfunction of polymorphonuclear cells leading to defect in chemotaxis and intracellular apoptosis [21]. Increase GRP-78 mediates invasion and damage of human endothelial cells by Rhizopus oryzae [22]. Structural and functional modifications of platelets results in defective membrane properties and alterations of nitric oxide metabolism [23]. Active ketone reductase system in uncontrolled diabetes favors growth in the acidic and glucose-rich environment [24].

### Preventive Measures

Judicious use of corticosteroids, antifungals, and broad-spectrum antibiotics is recommended. One should not initiate early and high-dose corticosteroid therapy. They are recommended at titrated doses with strict sugar monitoring. The target to control hyperglycemia during the management of COVID-19 and after recovery should be kept in mind. Stringent follow-up is necessary in high-risk COVID-19 patients [12]. Drugs like tocilizumab should be discouraged as they reduce immunity [25]. High-risk patients should be advised to wear a mask all the time after recovery and change it regularly, avoid dusty and soil areas, gardening and maintain personal hygiene. A separate set of instruments and endoscope for the debridement of mucormycosis. Adequate sterilization of endoscope, instruments, and operating room to prevent cross-infection.

### Measures for Early Detection

An extensive examination of COVID-19 patients and not ignoring the red flag symptoms that can detect the dreaded disease at the earliest. Diagnostic nasal endoscopy and biopsy for KOH smear in high-risk patients such as those admitted in ICU, on steroids therapy, more than 50 days of hospital stay, on mechanical ventilation, or high levels of IL6 and ferritin [26]. The high-risk patients when undergoing HRCT thorax may be advised for added scans of the nose, paranasal sinuses, and brain for early detection.

### Alarming Signs of Mucormycosis

Development of nasal obstruction, nasal crusting, foul or bloody nasal discharge, unilateral facial or orbital pain, facial palsy, facial numbness, blackening of nose or cheek, headache, toothache, loosening of tooth, palatal eschar, periorbital swelling, diplopia, blurred vision, ptosis, proptosis, reduced vision, focal seizures [27].

### Goals of Management of Mucormycosis

A delay of even 6 days in beginning the treatment raises the mortality from 35 to 66% [12]. To minimize the mortality, the three main goals are reversal of the underlying immunosuppression. Aggressive debridement to reduce fungal load and for faster penetration of antifungal therapy. Systemic antifungals are paramount in the management with surgical debridement [12].

Finally, I thank the authors and hope that they and readers find some of this information useful.

**Acknowledgements** This manuscript is original and it, or any part of it, has not been previously published; nor is it under consideration for publication elsewhere. There exists no conflict of interest among the authors and there are no financial disclosures to be made. Being a Letter to the Editor, it is exempted from the ethical requirements of the institutional review board.

**Author contributions** BS Conceptualization of the article and revising it critically for important intellectual content. MC Conception and drafting of article, formal analysis and final approval of the version. NS Manuscript preparation and update the references, final approval of the version.

**Funding** Nil.

**Declarations**

**Conflicts of interest** Nil.

**Ethical Approval** This manuscript is exempted from the ethical requirements as it does not contain any human or animal research.

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