

# Dreadful Rise of Mucormycosis in Diabetic Patients during COVID Era – A Case Series Analyzing Various Aspects

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## Abstract

Novel coronavirus infection has been sweeping across the globe since 2019. Various clinical manifestations are seen in coronavirus disease 2019 (COVID-19) patients and there has been a notable rise in the incidence of invasive fungal infections like mucormycosis. The prevalence of mucormycosis in India is being approximately 0.14 cases per 1000 population which is about 80 times the prevalence in developed countries. Conditions causing immunosuppression are closely associated with the development of any fungal infection including mucormycosis and in India, the most important risk factor for developing mucormycosis is diabetes mellitus. Since mucormycosis lacks stereotypical clinical features, it may show resemblances to other diseases affecting the bone and the oral mucosa and early diagnosis is crucial as the infection is rapidly progressive and fatal. The mortality of this infection remains high ranging from 32 to 70% and one of the patient mentioned in this case series died within 2 weeks after diagnosing mucormycosis. Here, we are reporting three cases of mucormycosis in diabetic patients reported during COVID-19 outbreak.

**Keywords:** Coronavirus disease 2019, Diabetes mellitus, Fungal infections, Maxillary sinus, Mucormycosis.

## INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 infection was first reported in Wuhan (China) and was announced by the World Health Organization in December 2019. Records shows that more than 386 million people are affected worldwide and as of February 2022, 5.7 million people have lost their lives.<sup>[1]</sup>

Patients with coronavirus disease 2019 (COVID-19) are more vulnerable to fungal infection because of the compromised immune system with low CD4 and CD8 lymphocytes, associated conditions such as diabetes mellitus and the use of immunosuppressive agents like steroids for the management of moderate-to-severe cases.<sup>[2]</sup> The country has recorded 28,252 cases of mucormycosis from 28 states as of June 7, 2021 and 17,601 cases had diabetes mellitus history and 24,370 cases had history of COVID-19.<sup>[3]</sup> A meta-analysis involving 52,916 COVID-19 patients showed that COVID associated mucormycosis incidence is 50 times higher (seven cases per 1000 patients) compared to the highest known incidence of mucormycosis cases (0.14 cases per 1000 patients).<sup>[4]</sup> In this case series, we discuss the various aspects of increased incidence of mucormycosis in diabetic patients during COVID-19 era.

## CASE DESCRIPTION AND RESULTS

### Case 1

A 45-year-old male patient presented with pain in the right upper back tooth region since 20 days. He was a known case of diabetes mellitus and was under medication for past 6 years.. Patient had COVID-19 infection 1 month back and was under medication for the same. Due to the use high dose of systemic steroid, patient's glycemic control was poor following COVID-19 infection. On physical examination, there is mild diffuse swelling in the right side of the face extending from the infraorbital region to the lower third of the face. Patient's right eye had proptosis with orbital cellulitis. Crustations were present on the right nostril and nasal cavity appeared reddish (Figure 1a). On palpation tenderness was present in relation to the right maxillary region. Intraorally, an ulcerative lesion covered with yellowish slough present in relation to the right

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**Figure 1:** (a) Patient with orbital cellulitis and crustations around nostril. (b) NCCT PNS showing mucosal thickening of the right frontal sinus, bilateral maxillary sinuses, sphenoidal sinus, and bilateral ethmoidal sinuses with obliteration of bilateral osteomeatal complex

side of the palate. Lesion involved adjacent vestibule and exposed the underlying bone.

NCCT PNS showed mucosal thickening of the right frontal sinus, bilateral maxillary sinuses, sphenoidal sinus, and bilateral ethmoidal sinuses with obliteration of bilateral osteomeatal complex. There is thinning and focal erosion of the floor of the left maxillary sinus (Figure 1b).

Operative procedure included endoscopic debridement of the osteomeatal complex and the bilateral maxillary sinus debridement.

### Case 2

A 70-year-old male patient presented with head ache and pain in the left side of the face since 5 days. He was a known case of diabetes mellitus and hypertension and was under medication for the same for the past 3 years. He had fever 10 days back and tested positive for COVID-19. On extra oral examination, diffuse swelling was seen on the left side of the face involving nose. Orbital cellulitis was also seen on the same side. The nasal cavity appeared reddish and few erythematous spot were observed on the lower lip. On intraoral examination, ulcerative lesion was observed on the middle third of the palate and upper lip (Figure 2a) Edematous and erythematous gingiva seen in relation to 26, 27 and these teeth were tender on percussion.

Nasal endoscopy showed Grade 1 changes in the right side and Grade 2 changes in the left side of the nasomeatal complex.

Screening sinus computed tomography (CT) of paranasal sinuses showed polypoidal mucosa thickening in the bilateral maxillary, sphenoidal, ethmoid, and frontal sinus. Erosion was seen in the posterior wall of the maxillary sinus with pre-antral, post-antral, pterygopalatine fissure soft tissue. Nasal septum was deviated to the left side with compensatory inferior turbinate hypertrophy (Figure 2b).

Surgical management included endoscopic debridement of the nasal cavity and the maxillary sinus debridement.

### Case 3

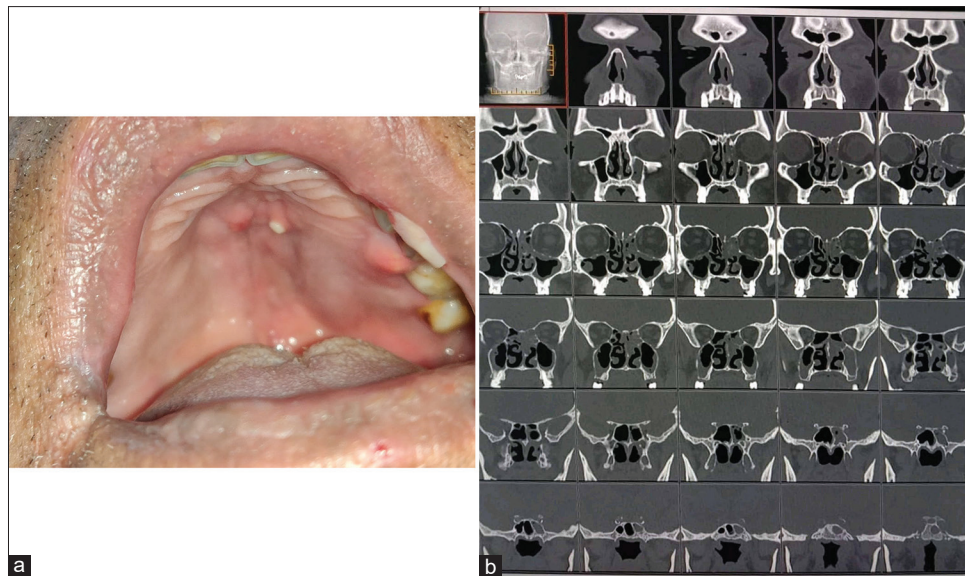
A 49-year-old female patient presented with numbness over the left side of the face for 12 days. She was a known case of diabetes mellitus and was under medication for the past 6 years. Patient had COVID-19 infection and pneumonia 1 year back. On clinical examination, patient was having diffuse swelling in the left side of the face with facial palsy and was unable to open the left eye (Figure 3a). Intraorally, ulcerative lesion covered with white slough seen on the left side of the palate. Tenderness on percussion presents in relation to 23, 24, 25, 26, and 27.

Magnetic resonance imaging (MRI) paranasal sinus (contrast) showed thickening in the left maxillary and ethmoidal sinuses with pre-antral and post-antral fat stranding. On contrast, there is an enhancement in the pre-antral region in the pterygopalatine fossa and infratemporal fossa with mild bulky pterygoid muscle on the left side. On contrast administration, there is multifocal non-enhancing areas in the left maxillary sinus (Figure 3b)

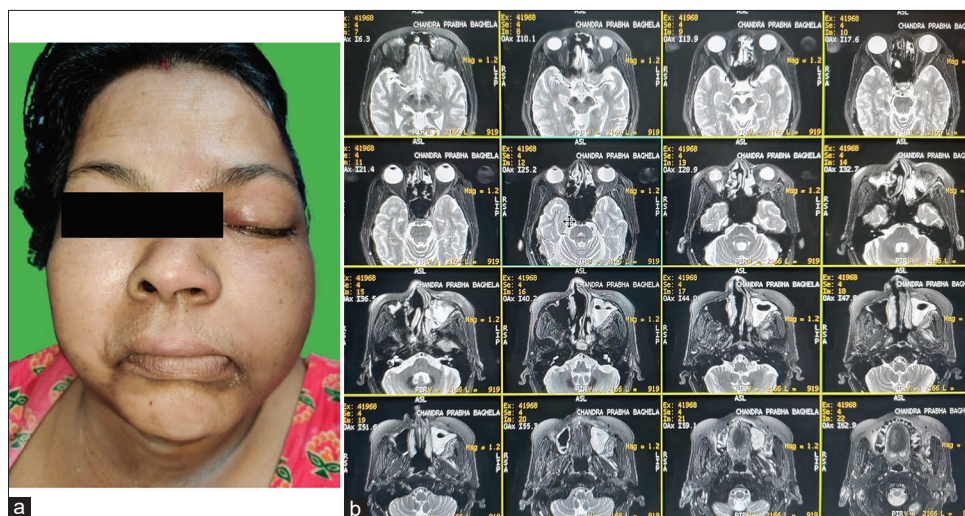
Surgical management included left maxillary sinus debridement and left orbital exenteration.

### DISCUSSION

Mucormycosis is a fatal fungal infection commonly seen in immunocompromised conditions.<sup>[5]</sup> Diabetes is the single most important risk factor for developing mucormycosis in India in contrast to the developed countries, where hematological malignancies predominate.<sup>[6]</sup> During this COVID-19 outbreak period, patients with moderate-to-severe COVID-19 are more susceptible to mucormycosis. There is always immunosuppression in COVID-19 patients with a decrease in CD4+ T and CD8+ T cells and there is higher chance of developing fungal co-infections in critically ill patients, like the patients who needs mechanical ventilation, or had a longer duration of hospital stays.<sup>[7]</sup> In all the cases reported above,



**Figure 2:** (a) Ulcerative lesion on the middle third of the palate and upper lip. (b) CT of paranasal sinuses showing polypoidal mucosa thickening in bilateral maxillary, sphenoidal, ethmoid, and frontal sinus. Note the erosion in posterior wall of maxillary sinus with pre-antral, post-antral, and pterygopalatine fissure soft tissue



**Figure 3:** (a) Diffuse swelling in the left side of face with facial palsy. (b) MRI paranasal sinus (contrast) showing thickening in left maxillary and ethmoidal sinuses with pre antral and post antral fat stranding

patients had diabetes mellitus and severe COVID-19 infection and it is the possible cause of immunosuppression.

Mucormycosis of the sinuses is characterized by initial involvement of the paranasal sinuses and turbinates. During this stage, it will be difficult to distinguish symptoms from those of more common causes of sinusitis. On examination, the nasal mucosa appears initially erythematous, then dark purple and black with the onset of tissue necrosis.<sup>[8]</sup> In the cases discussed above, two patients showed reddish nasal mucosa and one patient was presented with crustations around nostrils. Other clinical features are facial pain with swelling, epistaxis, headache, proptosis and orbital cellulites, ophthalmoplegia with blindness, hemiplegia or stroke, and

decreased mental function.<sup>[9]</sup> In all the cases discussed, headache and facial edema were commonest clinical finding and one of the patient was presented with orbital complications including complete loss of vision in the left eye and underwent orbital exenteration.

Mucormycosis of sinus is seen as non-specific nodular mucosal thickening on MRI and CT and this finding was observed in all the cases discussed above. The “black turbinate” sign on contrast MRI may be helpful in differentiating mucormycosis from bacterial sinusitis.<sup>[8]</sup>

Treatment recommendations of mucormycosis were recently updated by the European Confederation of Medical Mycology. The first-line drug in mucormycosis therapy is

liposomal amphotericin B (L-AmB). Isavuconazole and new posaconazole formulations have been added to the guidelines but in second-line treatment following L-AmB due to some remaining issues.<sup>[5]</sup>

The prognosis of the infection is poor with the overall mortality ranging between 33.3 and 80%<sup>[10]</sup> and one of the patient mentioned in this series died within 2 weeks after diagnosing mucormycosis.

## CONCLUSION

There is exponential rise of mucormycosis cases during this COVID period. Early diagnosis is very important as the infection is rapidly progressing and fatal in nature. Like any other fungal infection, conditions which cause immunosuppression are closely associated with the rise of mucormycosis. As diabetes mellitus is a common condition causing immunosuppression, there is high chance of developing mucormycosis infection in these patients. As steroids are integral part of COVID-19 patients treatment, all patients should be monitored closely for sequelae of immunosuppression for months following treatment.

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## CONFLICTING INTEREST

None.

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