

# Imaging spectrum, associations and outcomes in acute invasive fungal rhino-ocular-cerebral sinusitis in patients with COVID-19 pneumonia

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## ABSTRACT

**Background:** Coronavirus Disease 2019 (COVID-19) has been speculated to enhance mucormycosis infection due to its immune-altering pathophysiology. Early identification of high-morbidity conditions is crucial for optimal treatment and improved outcomes. **Methods:** A retrospective study was conducted on 63 patients with clinical and microbiological evidence of rhino-ocular-cerebral mucormycosis, who had a history of COVID-19 infection. The clinical, demographic, and imaging data were retrieved and analyzed. Descriptive statistics (mean [SD] and frequency [%]) were used to describe important characteristics across audit cycles. **Results:** Out of 63 patients, 54 (85.71%) patients had associated comorbidities, with diabetes mellitus being common comorbidity and all patients had received injectable and/or oral corticosteroids. Imaging showed nasal and paranasal sinus, perisinus, maxillary alveolar arch, and hard palate involvement in 62 (98.41%), 33 (52.38%), 5 (7.94%) and 5 (7.94%) patients, respectively. Orbital involvement was seen in 24 (38.10%) patients. Skull base involvement was seen in 11 (17.46%) patients, and intracranial extension of disease was present in 11 (17.46%) patients. A total of 16 patients were on mechanical ventilation, of whom 3 succumbed. The mean (standard deviation [SD]) intensive care unit (ICU) stay was 13.2 days (6.8) for 5 patients who succumbed and 6.4 days (4.6) for 30 patients who survived ( $P$  value = 0.008). **Conclusion:** Cross-sectional imaging not only provides the extent of disease spread but also plays a vital role in providing a surgical roadmap to treating surgeons and in predicting prognosis in patients with invasive fungal infections.

**Keywords:** Black turbinate, corticosteroids, COVID-19, diabetes mellitus, guitar pick sign, MRI, mucormycosis, orbital compartment syndrome, orbital exenteration

## Introduction

Ever since its outbreak was reported from Wuhan, China, in December 2019, the Coronavirus Disease 2019 (COVID-19) clinical spectrum has long drawn out, with initial presentations of only a dry cough and high-grade fever to further involvement of various organ systems causing generalized malaise, shortness of breath, anosmia, ageusia, diarrhea, acute cardiac injury, vascular and

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**How to cite this article:** Patel VB, Patel A, Mishra G, Shah N, Shinde MK, Musa RK. Imaging spectrum, associations and outcomes in acute invasive fungal rhino-ocular-cerebral sinusitis in patients with COVID-19 pneumonia. *J Family Med Prim Care* 2023;12:1055-62.

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Received: 02-06-2022

Revised: 07-09-2022

Accepted: 09-09-2022

Published: 30-06-2023

### Access this article online

Quick Response Code:



Website:  
<http://journals.lww.com/JFMPC>

DOI:  
10.4103/jfmprc.jfmprc\_1189\_22

gastrointestinal tract complications, and superimposed secondary infections. Although COVID-19 cases were rapidly surging across the globe, there was another challenge that was faced especially in developing countries, which included the varied patterns of various opportunistic infections. Case reports/case series and institutional experiences across India have documented the association of COVID-19 infection with mucormycosis after the country experienced a surge in cases of mucormycosis infection in patients recovered from COVID-19 during the “second wave”.

COVID-19 has been speculated to enhance mucormycosis infection due to its role in altering ferritin levels, serum iron, free radical-induced endothelitis, hepcidin activation by viral mimicry, and the upregulation of glucose receptor protein. *Rhizopus*, *Mucor* and *Rhizomucor*, *Cunninghamella*, *Lichtheimia*, and *Apophysomyces* have been noted to cause human infection. Mucormycosis is an invasive fungal infection most often affecting immunocompromised patients. Early identification of these high-morbidity conditions is crucial for optimal treatment and improved outcomes.<sup>[1]</sup>

It is known that underlying comorbid conditions such as diabetes, systemic steroid therapy, neutropenia, haematological disorders, and immune-compromised status predispose to poor outcomes due to altered acquired immune defenses.<sup>[2,3]</sup> Moreover, treating these patients as suggested in treatment guidelines with corticosteroids acts as a double-edged sword, which has its benefits as well as limitations.<sup>[4]</sup> COVID-19 itself has also been responsible for impaired cell-mediated immune response leading to a drop in CD4<sup>+</sup>T and CD8<sup>+</sup>T cell counts.<sup>[5]</sup> A complex interaction of all these factors together makes the COVID-19-infected patient more vulnerable to opportunistic infections. A few publications indicate the association of these opportunistic infections in severely ill or immunocompromised patients; however, there is a lack of substantial evidence of associated co-morbidities as well as other factors, which may have an association providing a window for these opportunistic infections to flare up. Although *Aspergillus* is associated with the infection without tissue invasion, mucormycosis is an angioinvasive fungus leading to necrotic and ischemic changes within the tissues and causing a rapid spread of the disease with a reported fatality rate of 46%.<sup>[6]</sup> A few studies have shown the relationship between diabetes, especially uncontrolled diabetes, and steroid therapy in a patient with fungal infections and associated COVID-19 infections.<sup>[7]</sup>

Being a tertiary referral center, we observed an increasing number of referrals for computed tomography (CT) and magnetic resonance imaging (MRI) to evaluate the extent of rhino-ocular-cerebral infections in COVID-19-infected patients. A literature search showed limited reports of fungal infections and COVID-19 association in non-diabetics who received steroids as well as diabetics who did not receive steroid therapy or patients with COVID-19 who were immunocompetent and received steroid therapy and developed rhino-ocular-cerebral manifestations (ROCM). This makes it difficult to establish a

cause–effect relationship between COVID-19 and ROCM during the disease process. We intended to analyze the various comorbid factors and their relationship with COVID-19 disease as well as evaluate the imaging features to know the extent of the disease to predict the treatment outcome. This will not only help the treating physicians to understand the evolving disease pattern but also modify timely treatment strategies based on the extent of disease evident on imaging.

## Materials and Methods

This retrospective study was conducted in the Department of Radiodiagnosis at a tertiary care rural teaching hospital in western India, after the approval of the Institutional Ethics Committee (IEC/BU/2021/Ex.24). A total of 63 patients with clinical and microbiological evidence of rhino-ocular-cerebral mucormycosis, who had a history of COVID-19 infection (nasopharyngeal swab/reverse transcriptase-polymerase chain reaction [RT-PCR] confirmed) and had undergone contrast-enhanced CT and/or MRI scan of the head, orbit, and paranasal sinuses from April 2021 to October 2021 were included in the study. The clinical, demographic, and imaging data were retrieved and analyzed [Table 1]. Imaging (Multidetector CT [MDCT]/MRI) of the paranasal sinuses, orbit, and brain was performed to assess the disease extent. MDCT scan with contrast was performed with clinical suspicion of disease limited to the nasal cavity and paranasal sinuses, and contrast-enhanced MRI (CEMRI) was performed in patients with clinical suspicion of orbital and intracranial extension as well as with equivocal CT imaging findings.

Imaging findings were recorded for paranasal sinus and oral cavity involvement, skull base and bony involvement, orbital involvement, and intra-cranial involvement [Table 2]. The patients were staged based on the clinical proposed staging of rhino-ocular-cerebral mucormycosis (ROCM).<sup>[7]</sup>

All patients were treated with an aim of urgent management of acute invasive fungal rhino sinusitis (AIFR) and associated comorbid conditions by a multidisciplinary team. They were administered intravenous amphotericin B (5 mg/kg/day) for 4 weeks or intravenous posaconazole with a loading dose of 300 mg every 12 h on the first day, followed by a maintenance dose of 300 mg every 24 h thereafter up to 6 weeks depending on availability.

Serum electrolytes and renal function tests were monitored for all patients and the doses were titrated accordingly.

Surgical debridement depended on the extent of the disease. Stage 1 and 2 diseases were treated via endoscopy and included turbinectomy, wide middle meatal antrostomy, ethmoidectomy, and sphenoidotomy. Palatal necrosis required maxillectomy or palatectomy depending on the extent of necrosis. Orbital extension of disease had a few surgical approaches, which included endoscopic subperiosteal abscess evacuation, orbital decompression, orbitotomy, and orbital exenteration.

**Table 1: Demographic and clinical details**

Variable	Category	Frequency (%)		
Age	Mean (SD)	55.90 (12.4)		
Sex	Female	17 (26.98)		
	Male	46 (73.02)		
COVID status	Current COVID-19	5 (7.94)		
	Recent history of COVID-19	58 (92.06)		
Clinical presentation	Eye	Pain	14 (22.22)	
		Swelling	11 (17.46)	
		Vision impairment	6 (9.52)	
		Redness	13 (20.63)	
		Proptosis	5 (7.94)	
	Cheek	Swelling	14 (22.22)	
		Pain	40 (63.49)	
		Redness	13 (20.63)	
	Nasal	Nasal discharge	37 (58.73)	
		Nasal crusting	15 (23.81)	
		Nasal blockage	6 (9.52)	
	Oral cavity		6 (9.52)	
	Comorbidities	Diabetes	Known case	40 (63.49)
			Recent	13 (20.63)
	Cardiovascular		2 (3.17)	
Hypertension		28 (44.44)		
Others	Multiple myeloma	1 (1.59)		
	Rheumatoid arthritis	2 (3.17)		
	Autoimmune hemolytic anemia	1 (1.59)		
	Hypothyroidism	4 (6.35)		

A postoperative specimen was sent for fungal culture, sensitivity, and histopathology.

Patients were discharged on oral posaconazole (200 mg twice a day) to be continued until two negative samples were evident on microbiology tests. Follow-ups were planned with imaging and endoscopy as and when needed.

### Statistical analysis

Descriptive statistics (mean [SD] and frequency [%]) were used to describe important characteristics across audit cycles. A Chi-square test was performed to look for the association between imaging characteristics and patient outcomes. A *P* value of less than 0.05 was considered significant. Statistical analysis was performed using STATA (14.2) software.

### Results

The mean (SD) age of patients was 55.90 (12.33) years (range 25 years to 80 years) with 73.02% (*n* = 46) males and 26.98% (*n* = 17) females. Recent history of COVID-19 infection within the last 6 weeks of presentation with symptoms of AIFR was observed in 58 (92.06%) patients, and 5 (7.94%) had COVID-19 infection at the time of presentation with AIFR [Table 1]. In 27 patients, the date of RT-PCR-positive data was available, which showed that most patients developed AIFR within 31 days. Out of 63 patients, 54 (85.71%) patients had associated comorbidities with diabetes

**Table 2: Imaging manifestations and extent of disease**

Variable	Category	Frequency (%)	
Imaging extent	Nasal and paranasal sinus involvement	Sinusitis 61 (96.83%) Erosion and thinning of the paranasal sinus wall 34 (53.97%)	
		Turbinates 35 (55.56%) Nasal septum 3 (4.76%) Erosion of the nasal wall 1 (1.59%)	
Perisinus involvement	Sphenopalatine	9 (14.29%)	
	Pterygopalatine fossa	20 (31.75%)	
	Pterygo-maxillary fissure	22 (34.92%)	
	Infratemporal fossa	20 (31.75%)	
	Pre-maxillary region	23 (36.51%)	
	Maxillary alveolar arch	Erosion	5 (7.94%)
		Hard palate	Erosion 5 (7.94%)
	Orbital involvement	Invasion	18 (28.57%)
		Proptosis	11 (17.46%)
		Optic neuritis	12 (19.05%)
Medial canthus		8 (12.70%)	
Nasolacrimal duct		8 (12.70%)	
Lamina papyracea		6 (9.52%)	
Inferior orbital fissure		9 (14.29%)	
Foramen rotundum		3 (4.76%)	
Foramen ovale		3 (4.76%)	
Vidian canal		3 (4.76%)	
Skull base involvement	Foramen lacerum	3 (4.76%)	
	Carotid canal	1 (1.59%)	
	Cribriform plate	5 (7.94%)	
	Sclerosis	5 (7.94%)	
	Lysis	2 (3.17%)	
	Clivus	5 (8.06%)	
	Intracranial involvement	Pachymeningeal enhancement	5 (7.94%)
		Fungal encephalitis	1 (1.59%)
		Intracranial abscess	5 (7.94%)
		Meningitis	1 (1.59%)
Cavernous sinus		5 (7.94%)	

mellitus being a common comorbidity. A significant number of patients (*n* = 40) had a history of diabetes before COVID-19 infection and 13 were detected during admission for COVID infection. Out of this, 53 patients with diabetes, 40 patients were on oral hypoglycemic drugs, and 13 patients were on insulin treatment. Other comorbidities included hypertension in 28 (44.44%) patients, coronary artery disease in 2 (3.18%) patients, multiple myeloma in 1 (1.59%) patient, rheumatoid arthritis in 2 (3.17%) patients, autoimmune hemolytic anemia in 1 (1.59%) patient, and hypothyroidism in 3 (6.35%) patients. All patients in the present study had received injectable and/or oral corticosteroids during the COVID-19 infection tenure and two patients 2 (3.17%) had received tocilizumab and 53 (84.12%) had received remdesivir.

Eye-related complaints were present in 14 (22.22%) patients, cheek-related complaints were present in 41 (65.08%) patients, and nasal symptoms were present in 41 (65.08%) patients.

Imaging showed nasal and paranasal sinus involvement in 62 (98.41%) patients, perisinus involvement in 33 (52.38%) patients, maxillary alveolar arch involvement in 5 (7.94%) patients and hard palate involvement in 5 (7.94%) patients. Orbital involvement was seen in 24 (38.10%) patients. Skull base involvement was seen in 11 (17.46%) patients, and intracranial extension of disease was present in 11 (17.46%) patients [Table 2]. Out of 63 patients, 61 (96.83%) had involvement of the ethmoid group of sinus air cells, 31 (49.20%) had maxillary sinus involvement, 13 (20.63%) had sphenoid sinus involvement, and 3 (4.76%) had frontal sinus involvement, which was less common. Based on the proposed staging of rhino-orbito-cerebral mucormycosis (ROCM)<sup>[7]</sup>, 1 (1.59%) patient had stage I disease, which is a disease limited to the nasal cavity and minimal fat stranding along the medial canthus; 34 (53.97%) had stage II disease, which includes disease extension to paranasal sinuses; 10 (15.87%) had stage III disease with additional involvement of the orbit; and 18 (28.57%) had stage IV disease with intracranial involvement. Out of 18 patients with stage IV disease, 4 did not have orbital involvement; however, the disease extended directly to intracranial spaces.

Out of 24 patients who had orbital involvement, 10 patients had a stage III disease and 14 had stage IV disease. Orbital exenteration was performed in eight patients, out of which six had stage III disease and two had stage II disease at the time of diagnosis; however, the disease progressed and therefore exenteration was performed.

Good recovery post-treatment was observed in 52 (82.54%) patients, 2 (3.17%) patients had to be discharged against medical advice, and 9 (14.29%) succumbed to death. The mean age of those who survived was 55 years (12.1%) and those who succumbed was 61 years (13%). No statistically significant difference was observed in the age of those who survived and succumbed. Of the nine patients who succumbed to their disease, subgroup analysis revealed that all had diabetes and six had stage IV disease and three had stage III disease. A total of 16 patients were on mechanical ventilation, of which 3 succumbed. In total, 35 patients required ICU admission, out of which 5 succumbed. The mean (SD) ICU stay was 13.2 days (6.8) for 5 patients who succumbed and 6.4 days (4.6) for 30 patients who survived ( $P$  value = 0.008).

Overall, patients' outcome with involvement of the orbit, skull base, and intracranial extension was poor as compared to those with the disease limited to nasal and paranasal sinuses.

## Discussion

The impact of various fungi in the present era has led us to intensify our understanding of these varied species to hitch their extraordinary potential to evade capture and thus leading to devastating health conditions.

In the recent pre-COVID era estimate of 2019–2020, the prevalence of mucormycosis varied from 0.005 to 1.7 per million

population globally; however, its prevalence in India was about 80 times higher.<sup>[8]</sup>

Prakash *et al.*<sup>[9]</sup> in 2019, in a nationwide multicenter study of 388 cases of mucormycosis, concluded that 18% of patients with mucormycosis in India had diabetic ketoacidosis (DKA) and 57% had uncontrolled diabetes. Notwithstanding, India has the second highest population of diabetes, thus making the Indian diabetic population the most vulnerable to secondary infections by this pathogen.<sup>[10]</sup>

The incidence of COVID-19 patients developing secondary infection was reported to be 8% in one of the studies with *Candida* and aspergillosis reported as the most common pathogens.<sup>[11]</sup> In the present study, mucormycosis was the most common fungi followed by *Aspergillus* and a combination of *Aspergillus* and *Candida*.

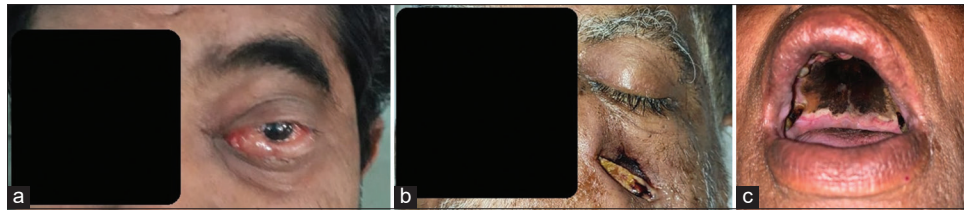
Factors contributing to its pathogenesis include its ability for rapid growth, utilization of the host iron for growth, adherence to the endothelial surface, and downregulation of host immune response defense genes. The role of ketoacidosis, high blood sugar, and altered iron metabolism in the host have been noted as contributing to the pathogenesis of mucormycosis.<sup>[1]</sup>

It has been postulated from various case reports that pre-existing commodities such as diabetes mellitus, use of systemic steroids, immunosuppressive agents, and antiviral agents in the management of COVID-19 may also predispose an individual to angioinvasive mucormycosis infection.<sup>[12-14]</sup> In the present study, the most commonly associated comorbidity was diabetes in 84.13% of patients, followed by hypertension in 44.44%. Other associated comorbidities were hypothyroidism, coronary artery disease, multiple myeloma, rheumatoid arthritis, and autoimmune hemolytic anemia in a few cases. In the present study, 40 patients had a previous history of diabetes and 13 had new-onset diabetes detected during the COVID-19 infection. Nair *et al.*,<sup>[15]</sup> in their retrospective study, found that 13/127 patients developed new-onset diabetes with uncontrolled sugar levels during COVID disease.

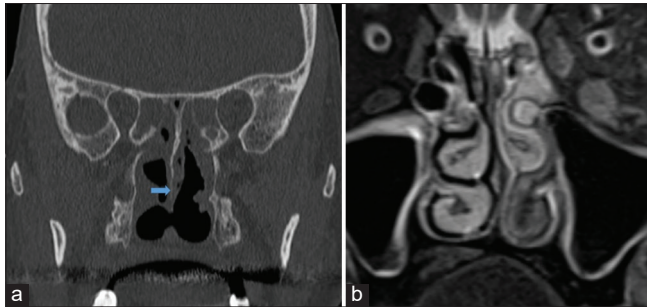
It is known that long-term use of corticosteroids is often associated with various opportunistic fungal infections including aspergillosis and mucormycosis; however, there are a few case reports where even a short course of corticosteroids has been linked to mucormycosis, especially in people with DM.<sup>[16]</sup>

Most patients in the present study had received a short course of corticosteroid therapy during the COVID illness and most patients (85.71%) had associated commodities, with diabetes being the most common association.

In the present study, 23 patients' ferritin levels were available, which were elevated; however, the mean (SD) of ferritin values was comparable across all stages of the disease ( $P$  value 0.189). Dallalzadeh *et al.*,<sup>[17]</sup> additionally postulated that mechanical



**Figure 1:** Different clinical presentations. (a) Left-sided periorbital oedema, conjunctival chemosis, and proptosis. (b) Left oculomotor palsy with discoloration and ulceration in the left maxillary region. (c) Discoloration of the palate



**Figure 2:** (a) Coronal CT image shows mucosal thickening along the ethmoid sinuses and nasal cavity with nasal septal perforation/erosion (blue arrow). (b) A black turbinate sign shows a lack of normal enhancement of turbinate due to necrosis on the post-contrast T1W image

ventilation and COVID-19-induced immunosuppression are also additional risk factors for opportunistic fungal infection in COVID-19 patients. In the present study, 55.5% ( $n = 35$ ) had a history of ICU stay, of which 25.2% ( $n = 16$ ) had a history of mechanical ventilation.

The warning signs include nasal stuffiness, foul smell, epistaxis, nasal discharge, nasal mucosal-erythema, inflammation, discoloration, ulcer, eschar, eyelid edema, periorbital edema, facial discoloration, regional pain, headache, proptosis, sudden vision loss, facial paresthesia, sudden ptosis, ocular motility restriction, diplopia, facial palsy, fever, altered sensorium, paralysis, and focal seizures [Figure 1].

Clinico-radiological features, with microbiological confirmation on direct microscopy or culture or histopathology with special stains or molecular diagnostics, are essential to prove ROCM.

In the present study, all 63 patient’s microbiology tests confirmed the presence of *Mucor*, *Aspergillus*, and *Candida* fungi, as depicted in Table 3.

Honavar<sup>[18]</sup> proposed a simple staging system that follows the general anatomical progression of ROCM from the nasal mucosa to the paranasal sinuses, orbit, and brain, with sub-staging based on the severity in each of these anatomical locations.

The role of imaging in acute invasive fungal rhino sinusitis (AIFR) lies primarily in documenting the extent of the disease. Although CEMRI is the imaging modality of choice, especially for suspected intracranial and intraorbital disease, CT is more

**Table 3: Microbiologic results of 27 patients**

Pathogen	Patient no. (%)
<i>Mucor</i>	16 (59.26)
<i>Aspergillus</i>	5 (18.52)
<i>Candida</i>	2 (7.40)
<i>Aspergillus + Candida</i>	1 (3.70)
<i>Mucor + Aspergillus</i>	3 (11.11)

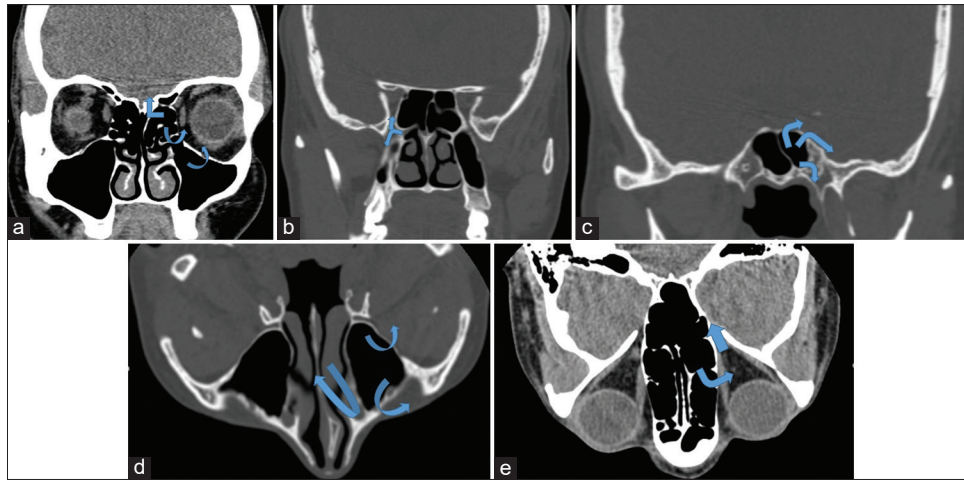
appropriate for bony involvement. Infected soft tissues, which are vascular, suggest an unsalvageable fungal infection and these are the regions that need to be surgically debrided until bleeding tissue is encountered. Contrast enhancement on MRI imaging is an indicator of vascular tissue, and enhancement represents necrosis. Thus, it has been proposed that it can navigate a surgeon decide the extent of resection.

During the initial stage of the disease, nasal involvement may be seen as a mucosal thickening and/or bone erosions of the nasal wall, nasal septum, middle turbinate, inferior turbinate, or ostium of the nasolacrimal duct [Figure 2a]. On CEMRI, a lack of mucosal enhancement may be seen, and in turbinates lack of enhancement, it is termed the “black turbinate sign,” which represents necrosis [Figure 2b]. This is followed by paranasal sinus involvement seen as a sinonasal mucosal thickening, partial or complete opacification of the sinuses, bone erosions, and extra sinus spread.

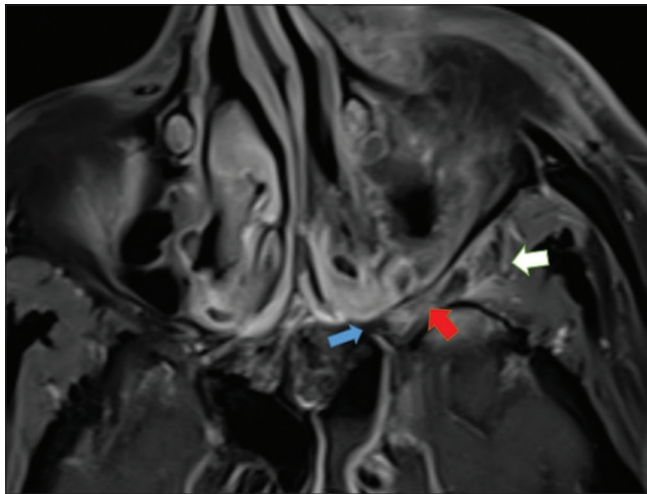
In the present study, the ethmoid sinus was the commonest Paranasal sinus (PNS) to be involved, followed by the maxillary sinus as was observed in another study by Sharma *et al.*<sup>[7]</sup>

The pathways of the spread of the disease are predominantly by direct tissue invasion [Figure 3]. It may extend through natural bony defects or along natural gateways such as the nasolacrimal duct, pterygopalatine fossa [Figure 4], lymphatics, and neurovascular bundles or by bony destruction. Vigilant evaluation of these anatomical locations on MRI/CT is needed to evaluate the disease extent.

Extrasinus spread may occur with intact bony walls via microvascular channels in the bone. Perisinus spread may occur in the anterior perianal space, posterior perianal space, buccal space, nasopharynx, sphenopalatine foramen, pterygomaxillary fissure, pterygopalatine fossa, and infratemporal fossa. The disease may also spread to the palate or oral cavity with the formation of oronasal or oroantral fistulae [Figure 5].



**Figure 3:** Pathways of spread: Coronal image (a) direct extension from ethmoid and maxillary sinuses to orbit or intracranial compartment (b) disease from the nasal cavity via sphenopalatine foramen to the pterygopalatine fossa, which is a crossroad for extension into infratemporal fossa and cavernous sinus (c) disease from the sphenoid sinus may extend to the skull base, cavernous sinus, and brain. Axial image (d) disease from maxillary sinus may extend to premaxillary fascial and retro-antral soft tissue as well as along the nasolacrimal duct (e) disease in the orbit may extend to the orbital apex and cavernous sinus



**Figure 4:** Contrast-enhanced T1 axial image shows disease extension from the left sphenopalatine foramen (blue arrow) to the pterygopalatine fossa (red arrow) and into the infratemporal fossa (white arrow)

Early orbital involvement may be seen as an inflamed nasolacrimal duct, sac, or thickening of the medial rectus muscle, which may be followed by the involvement of the rest of the extraocular muscles. Retro-orbital fat stranding, patchy enhancement along a medial and inferior wall, erosion of lamina papyracea, and orbital wall inflammation at superior and inferior orbital fissures have been observed. Severe inflammatory edema and/or orbital compartment syndrome may be seen as uveoscleral thickening or tenting of the posterior pole of the globe. Orbital compartment syndrome is an ophthalmic emergency, potentially resulting in ischemia and loss of vision. It requires urgent surgical intervention to decompress the orbit and relieve the pressure. Delay in care can lead to permanent blindness. On imaging, there is posterior globe tenting also called a guitar pick sign [Figure 6]. Significant proptosis stretches the optic nerve and causes damage with a posterior angle of <120

degrees. Disease in the orbital apex may lead to cavernous sinus invasion [Figure 7], which may appear bulky with internal hypo enhancement, sometimes associated with a dilated superior ophthalmic vein. The intra-orbital extension was observed in 38.09% of the patients in the present study, which is similar to the study by Sharma *et al.* Although in the present study, skull base involvement was seen in 17.46% of cases, the intracranial extension was seen only in 18% of the patients, which is more as compared to the study by Sharma *et al.*<sup>[7]</sup>

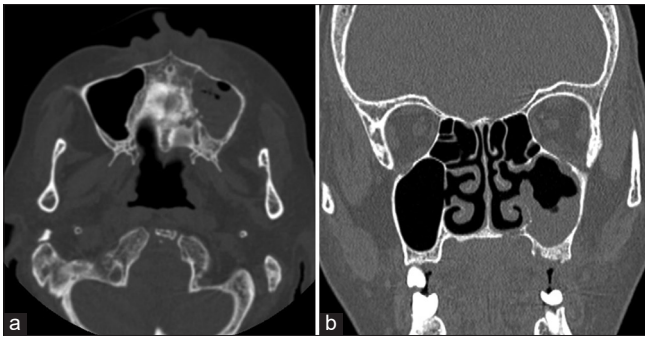
Skull base erosions [Figure 8a] and intracranial complications, such as leptomeningitis, cerebritis, encephalitis, and intracranial abscess [Figure 8b], may occur due to the spread via the skull base. *Mucor* may cause arterial narrowing or arteritis with an aneurysm, especially in the cavernous portion of the internal carotid artery, sometimes leading to arterial infarcts.

AIFR requires prompt and aggressive medical management and debridement.<sup>[19]</sup>

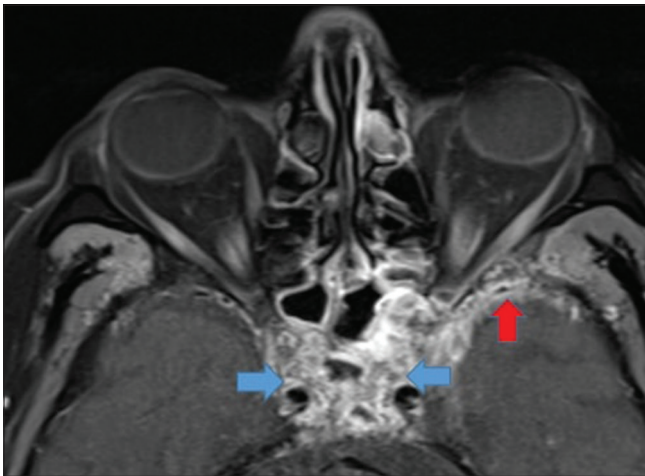
In the present study, the intracranial extension was evident as pachymeningeal enhancement in 7.94%, fungal encephalitis in 1.59%, intracranial abscess in 7.94%, and cavernous sinus involvement in 7.94%.

In the present study, all patients were administered intravenous amphotericin B (5 mg/kg/day) for 4 weeks or intravenous posaconazole with a loading dose of 300 mg every 12 h on the first day, followed by a maintenance dose of 300 mg every 24 h and thereafter up to 6 weeks depending on availability.

Surgical debridement depends on the extent of the disease. Stage 1 and 2 diseases may be treated via endoscopy and may include turbinectomy, wide middle meatal antrostomy,



**Figure 5:** Plain CT (a) axial and (b) coronal image show erosion along the left side of the hard palate

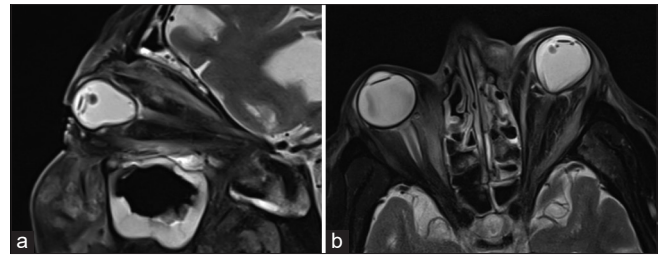


**Figure 7:** Contrast-enhanced T1 axial image showing involvement of both cavernous sinuses (blue arrows) and pachymeningeal enhancement along the left temporal region (red arrow)

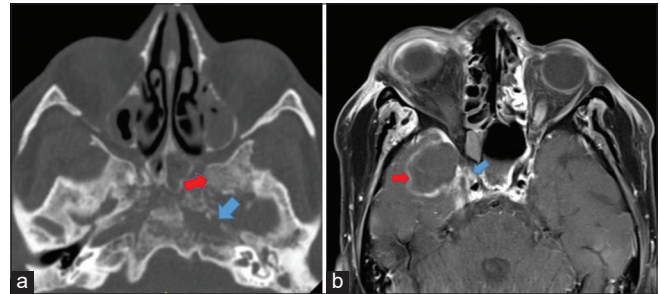
ethmoidectomy, and sphenoidotomy. Palatal necrosis requires maxillectomy or palatotomy depending on the extent of necrosis. Orbital extension of disease has a few surgical approaches, which include endoscopic subperiosteal abscess evacuation, orbital decompression, orbitotomy, and orbital exenteration.<sup>[19]</sup>

In the present study, surgical intervention was performed in 54 (85.71%) patients, limited endoscopic surgical debridement was performed in 40 (60.32%) patients, extensive surgical debridement with fronto sphenoidectomy in 1 patient, extensive endoscopic surgical debridement with orbital exenteration in 8 (12.7%) patients, extensive endoscopic surgical debridement with extended maxillectomy in 4 (6.35%) patients, and extensive endoscopic surgical debridement with orbital exenteration and maxillectomy in 1 (1.59%) patient.

There are a few limitations to the present study, which include a few lacking important details such as baseline HbA1c (glycated hemoglobin), ferritin levels, and history of use of immune-modulating drugs. Secondly, the true estimation of the incidence of mucormycosis could not be made due to a lack of control.



**Figure 6:** (a and b) Sagittal and coronal MRI T2 images show posterior globe tenting, also called a guitar pick sign, in orbital compartment syndrome as well as the involvement of the premaxillary region



**Figure 8:** (a) CT axial image showing extensive erosion of the greater wing of the sphenoid more on the left side (red arrow) as well as erosion along the left carotid canal (blue arrow). (b) Post-contrast T1 axial image shows disease within the right cavernous sinus (blue arrow) with adjacent intracerebral rim enhancing abscess (red arrow)

Increasing cases of mucormycosis in India in COVID-19 patients can be attributed not only to the disease-modulating immune system but also to other factors, leading to a complex interplay between diabetes, widespread use of corticosteroids, elongated hospital stay, and mechanical ventilation. Cross-sectional imaging not only provides the extent of disease spread but also plays a vital role in providing a surgical roadmap to the treating surgeon and in predicting the prognosis.

## Conclusion

Despite the early diagnosis, combined with aggressive medical and surgical management, the prognosis for recovery from AIFR is guarded. All efforts should thus be made to maintain a high level of clinical suspicion, optimal diabetic control, and prudent use of corticosteroids in patients, especially who are immunocompromised and in the present era with COVID-19 infection, to reduce the disastrous morbidity of fatal mucormycosis.

## Acknowledgments

We thank Dr. Mehel Patel for his intellectual input and Ms. Jaishree Ganjwale for her help in statistical analysis.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

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