

Early Diagnosis and Prompt Intervention with Liposomal Amphotericin and Surgery Prevents Morbidity and Mortality in Rhino-Orbito-Mucormycosis

Sudhir Halikar

Associate Professor, Department of ENT, Institute of Medical sciences & Research, JNU Jaipur, Rajasthan, India

Received: 01-04-2026 / Revised: 15-05-2026 / Accepted: 21-06-2026

Corresponding author: Dr. Sudhir Halikar

Conflict of interest: Nil

Abstract

Background: Rhino-orbito-cerebral mucormycosis is a life threatening, angioinvasive, opportunistic fungal infection often seen in immuno-compromised individuals. After the second wave of COVID-19, there was sudden upsurge of cases of Mucormycosis potentially due to associated Diabetes with very high blood sugar or ketoacidosis or steroid based treatment protocols. In the early part of epidemic, we came across cases of mucormycosis in advanced stage of disease like loss of vision, orbital involvement, intracranial extension, maxillary involvement with high morbidity and mortality.

Aim: The aim of the study is to emphasize the importance of early diagnosis and prompt intervention with empirical Amphotericin and surgical clearance of the disease.

Methods: In a retrospective analysis, 54 cases of mucormycosis in various stages of disease progression and complications presented to a tertiary care center over a period of 2 months between 1 April 2020 to 30 May 2020 during the second wave of COVID-19 were analyzed. Many cases of mucormycosis were diagnosed when the disease was limited to sinuses based on symptoms in patients suffering from COVID-19 and with diagnostic tools like diagnostic nasal endoscopy [DNE], CT and MRI imaging.

Results: Among 54 patients with COVID-19-associated mucormycosis, 81.4% were males and 90% had diabetes, with 89% demonstrating poor glycemic control. All patients had received corticosteroids for COVID-19 treatment, including 56% with irrational steroid use in mild non-hypoxemic disease. Twenty-four patients presented with early sinonasal disease and achieved 100% survival following FESS, whereas 30 patients had advanced disease with orbital, palatal, or cerebral involvement, resulting in a survival rate of 56.7% and significant postoperative morbidity. Extensive surgical procedures, including orbital exenteration, craniotomy, and maxillectomy, were frequently required in advanced-stage disease.

Conclusion: COVID-19-associated mucormycosis emerged as a significant epidemic with high morbidity and mortality, particularly among diabetic patients with poor glycemic control. Early recognition, a high index of suspicion, and prompt treatment with intravenous amphotericin B and surgical debridement while disease remains confined to the sinuses are critical for improving survival and reducing long-term disability.

Key words: COVID -19, Mucormycosis, Diabetes, Sinuses.

DOI: 10.25258/ijcpr.18.7.102

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Mucormycosis is an opportunistic fungal infection of the zygomycete family that can cause various types of infections. In most of the cases, there is pre-existing underlying condition that predispose the hosts to the infection.

As the fungi responsible are typical environmental organisms, they are usually non-pathologic in immunocompetent individuals, however in immunosuppressed patients, these otherwise innocuous organisms cause devastating and difficult-to-treat opportunistic infection [1].

Mucormycosis is characterized by tissue necrosis due to an invasion of blood vessels and subsequent thrombosis, which usually follows a rapid progression [3,7]. Its incidence in south East Asia is higher owing to the propensity of fungus to favour tropical climates and the high prevalence of DM in these areas [10].

The key to treatment is early and aggressive surgical debridement, along with high doses of intravenous antifungal therapy. The species most frequently isolated from patients are

Apophysomyces (*A. variabilis*), Cunninghamella (*C. bertholletiae*), Lichtheimia [*Absidia*] (*L. corymbifera* L. raosa), Mucor (*M. circinelloides*), Rhizopus (*R. arrhizus* (oryzae) *R. microsporus*), Rhizomucor (*R. pusillus*), and Saksenaea (*S. vasiformis*)[1,4]. The Rhizopus Oryzae is most common type and responsible for nearly 60% of mucormycosis cases in humans and also accounts for 90% of the Rhino-orbital-cerebral (ROCM) form. In patients with uncontrolled diabetics (particularly those with a history of diabetic ketoacidosis, transplant patients, HIV, patients on steroids or disease-modifying anti-rheumatic medication or other cancer patients), they can present with rapidly progressive necrotizing infection [1,2,5].

Histological features of mucormycosis include infiltration of fungus into mucosa, submucosa, blood vessels, thrombosis, and tissue infarction and haemorrhage [12]. Vascular and perineural invasion are the common pathological features of invasive mucormycosis [11,12].

In the pandemic of Corona virus disease 2019 [COVID-19] caused by severe acute respiratory syndrome corona virus 2 [SARS COVID -2], we witnessed an epidemic of mucormycosis particularly after the second wave of Covid in 2022 [6,8]. The primary reason that appears to have facilitated Mucorales spores to germinate in people with COVID-19 was an ideal environment of low oxygen (hypoxia), high glucose (diabetes, new-onset hyperglycaemia, steroid-induced hyperglycaemia), acidic medium (metabolic acidosis, diabetic ketoacidosis [DKA]), high iron levels (increased ferritins) and decreased phagocytic activity of white blood cells (WBC) due to immunosuppression (SARS-CoV-2 mediated, steroid-mediated or background comorbidities) coupled with several other shared risk factors including prolonged hospitalization with or without mechanical ventilators[4,6].

A multidisciplinary approach to rhino-cerebral-mucormycosis with ENT, NEURO, Ophthalmologist, Infectious disease and medical intensivists can help reduce mortality in an otherwise largely fatal disease [9]. Even despite these measures, outcomes remain poor and a high index of suspicion must be maintained in at risk population.

Material and Methods

This is a retrospective study comprising 54 cases who were diagnosed to be having mucormycosis during the second wave of COVID-19.

Inclusion criteria: All the patients who were histopathological confirmed to be having mucormycosis were included in this study.

All the 54 patients included in the study were based on tissue biopsy samples that came positive for mucormycosis from surgeries like Functional endoscopic sinus surgery -FESS, maxillectomy, orbital exenteration, intracranial excision of SOL and cutaneous lesions. Demographic data including age and sex of the patients, presenting complaints, comorbidities, imaging findings [CT and MRI], history of DM and use of corticosteroid treatment for COVID-19 were obtained. Sites of involvement by mucor and the types of surgeries performed were collected and analysed. Nasal endoscopy was done in all cases to look for necrotic tissue or any mucopurulent discharge within the nasal cavity; samples were collected on KOH mount to look for fungal hyphae. CT scan finding showed soft tissue enhancement within the nasal mucosa, mucoperiosteal thickening, bony erosion and brain invasions, while MRI proved helpful in delineating orbital soft tissue invasion and intracranial spread. Diagnosis was confirmed on histopathology from necrotic tissue collected during surgery.

Depending on the extent of the disease surgery was planned, a limited sinus disease required functional endoscopic sinus surgery -FESS [Image 1 and 2]. For extensive disease involving sphenopalatine fossa and infratemporal fossa Modified Denkers approach was utilised to open posterior maxillary wall.

Oral and Maxillofacial surgeons performed surgeries on maxilla, neurosurgeons performed brain surgeries and Plastic surgeons performed orbital exenteration. In some cases, endoscopic orbital debridement was done to avoid unnecessary disfigurement of eyes. Orbital exenteration was done in cases of severe orbital cellulitis, extensive tissue necrosis and particularly in cases with permanent vision loss after it was approved by Ophthalmologist.



Figure 1: Endoscopic surgical picture showing fungal colony on post wall of maxillary sinus as it appears on Petry dish. Early sinus disease



Figure 2: Endoscopic picture of fungal growth in maxillary sinus, FESS

Patients were categorised into two groups, group A comprised patients with early sinus disease and group B comprised patients in whom disease had spread in other organs from sinuses.

As 9 patients were referred to our centre in 2 days with advanced stage of disease and with reports coming from other centres suggesting sudden influx of patients of mucormycosis in covid positive patients, there was heightened awareness of this dark reality amongst consultants. This prompted them to look for early diagnosis of patients developing mucormycosis through a high index of suspicion in the admitted patients of COVID-19. All the covid positive patients were monitored for acute facial pain and oedema on face, swelling around eyes, blood stained nasal

discharge, signs and symptoms suggestive of sinus disease. With high index of suspicion, they all were started on empirical Amphotericin B and the drug was continued after histopathological reports came positive.

All the patients were treated with combination of surgical debridement and intravenous Amphotericin B and concomitant Posaconazole therapy. Because of sudden increased demand of Amphotericin in a short duration, Amphotericin was given as per availability both liposomal [3 - 5 mg/kg] and plane -deoxycholate form [0.25 to 0.5 mg/kg]. Amphotericin was prescribed for minimum 15 days in early sinus disease and for 4-6 weeks in advanced disease. Kidney function test was monitored in all the patients.

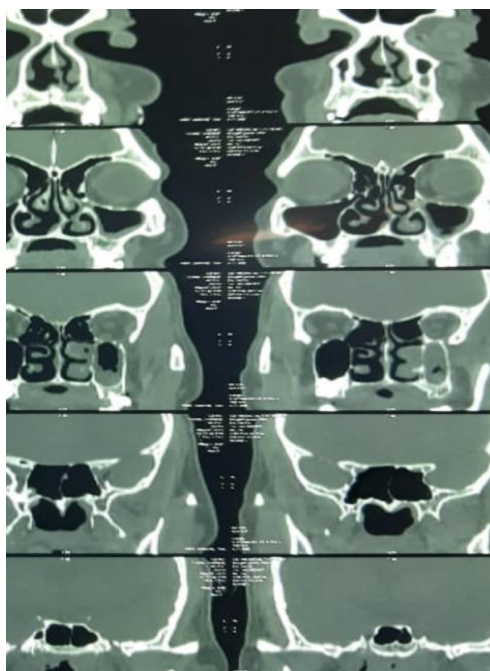


Figure 3: CT picture, early maxillary sinus mucosal disease

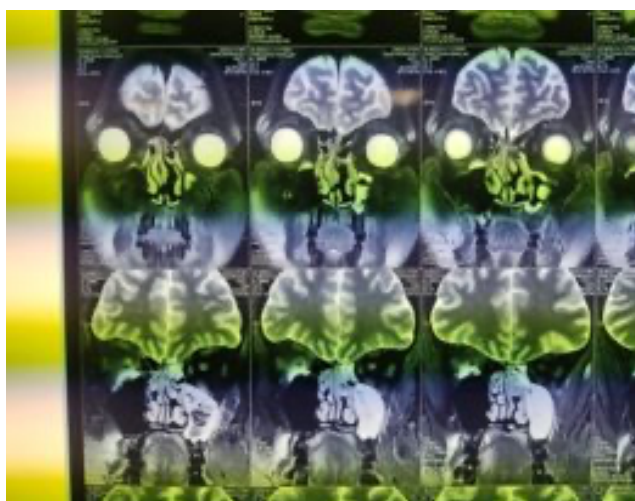


Figure 4: MRI picture, early sinus disease

Results:

Out of total 54 patients 44 [81.4%] patients were male, whereas 10 [18.5%] patients were females. The age group was from 24 yrs, the youngest to 76 yrs the oldest. Median duration from a positive COVID 19 PCR test to diagnosis of mucormycosis was 17 days. 90% of the patients were diabetic and 89% of those having uncontrolled sugar level [HbA1c more than 7.1]. All patients had received steroids during treatment of COVID 19; 56% patients were prescribed steroids for non-hypoxemic mild covid [irrational steroid therapy] while 9% patients were prescribed steroids in inappropriately high dose. The group A patients comprised cases in early sinus disease, where the disease was limited to sinuses and required limited surgical intervention -FESS [total 24]. The group B

patients comprised cases in advanced stage of disease with orbital, palatal or cerebral involvement [Total 30]. All the 24 patients in the early sinus disease group survived [100 % survival] whereas 13 out of 30 in the advanced stage disease group died [60% survival].

Only 2 out of 24 early sinus disease developed palatal or alveolar disease requiring maxillectomy, this was probably because of paucity of Amphotericin, as they received only Posaconazole in the first week, suggesting importance of Amphotericin. In the rest of early mucosal disease group there was no morbidity. Whereas the survivors in advanced stage group underwent multiple surgeries and landed with one or the other debilitating morbidity like loss of vision, loss of eye, loss of palate/maxilla etc. [Image 5]

KEY FEATURES OF DISEASE PRESENTATION		
Feature / Metric	Early Sinus Disease	Advanced Disease
Total Cases	24 cases	30 cases
Mortality Rate	0%	60%
Surgical Burden	Except for 2 cases (lack of Amphotericin); all cases required only 1 surgery	Multiple surgeries required (2–4)
Surgical Approach	FESS (Functional Endoscopic Sinus Surgery) was standard	Nasal endoscopic debridement , modified Denkers approach , maxillectomy , orbital exenteration , neurosurgery
Antifungal Therapy	Amphotericin required for 8–15 days	Amphotericin required for 4–6 weeks
Complications & Morbidity	No morbidity	morbidity like: Loss of vision, loss of maxilla/eye/palate, and neurological deficits

Figure 5:

Functional endoscopic sinus surgery [FESS] was the procedure of choice in 24 cases of early sinus disease group with only two requiring revision surgery as mentioned above. Whereas Endoscopic nose and sinus surgery with total turbinectomy, Modified Denker's approach to address pterygopalatine fossa and infratemporal fossa, Orbital exenteration [open or endoscopic] along with neurosurgery and/or partial or total maxillectomy based on extent of disease was the way to go in advanced stage cases. In 7 cases open exenteration of eye was done whereas in 3 cases endoscopic orbitotomy and clearance was done. 5 cases required craniotomy and 7 cases required maxillectomy.

Discussion

Rhino-orbito-cerebral mucormycosis often occurs in patients who are immunocompromised most commonly secondary to diabetes mellitus particularly those with very high blood sugar and ketoacidosis [9,10]. Steroid use is another common risk factor; it not only causes hyperglycaemia but its use is also associated with dysregulated immune response. Both DM and steroid use was postulated to be the driving force that led to an increase in COVID associated mucormycosis cases [6,7,10].

COVID-19 associated ROCM can be considered as sequel/complication of SARS-COVID 2 infection due to involvement of multiple factors like hyperferritinemia, altered glucose homeostasis, diabetes mellitus, lavish use of corticosteroids etc [6,7].

It is essential for the clinician to maintain a high index of suspicion in patients at risk, as early diagnosis can be lifesaving [8,9]. Standard management of mucormycosis requires early diagnosis, a reversal of risk factors and underlying illness and prompt initiation of antifungal like Amphotericin b and surgical debridement. Definitive diagnosis is arrived by histopathological evaluation demonstrating the non-septate, broad, ribbon like fungal hyphae on tissue specimens [10,12].

Our observation was patients who were mainly having maxillary sinus disease went on to develop pterygopalatine and infratemporal fossa spread along with orbital involvement partly through direct spread and mainly through sphenopalatine vasculature involvement. This was responsible for eye pain, orbital oedema, puffiness and swelling of cheeks, proptosis. Disease from maxillary sinus also spreads to involve palate, alveolus and maxilla

causing loose teeth and eventual loss of palate and maxilla. Disease from frontal sinus and ethmoids eventually have intracranial extension causing meningitis, cerebritis and cerebral SOL and abscess formation. While disease from sphenoid mainly involve cavernous sinus, optic nerve leading to ophthalmoplegia, vision loss. Intracranial involvement occurs by invasion through superior orbital fissure, ophthalmic vessels, cribriform plate, cavernous sinus, carotid artery and even perineural route [12]. Hence early diagnosis and prompt initiation of Amphotericin and surgical debridement remain cornerstone of therapy [4,9]. Intravenous Amphotericin B is drug of choice as an antifungal [4,10]. Liposomal form although is little expensive is preferred over deoxycholate form which has more nephrotoxicity. Prognosis remains poor even with aggressive surgery and intravenous fungal therapy, with reported mortality rates of 33.3-80% going up to 100 % in disseminated infections. Without early diagnosis and treatment, there may be rapid progression of disease with reported mortality rates from intracranial complications of 50 to 80 % [4,7]. In our study, the mortality was zero percent in the early sinus disease group whereas the mortality shot up to 60% in patients with advanced disease along with associated comorbidities and poor quality of life in the survivor group.

Conclusion

Every year around 3-4 cases of Rhino-orbito-cerebral mucormycosis are reported at tertiary care centres, but 54 cases in a span of 2-3 months at one centre sure is in line with the epidemic of mucormycosis in COVID 19. Given the high morbidity and mortality of mucormycosis, a comprehensive and efficient multidisciplinary approach is paramount. From Mucormycosis of COVID 19 experience, a message is clear 1] keep high index of suspicion in all cases of immunocompromised patients, particularly those with diabetes mellites with very high blood sugar with signs and symptoms suggestive of sinusitis and 2] Diagnose mucormycosis at the earliest when it is limited to sinuses only and do prompt intervention with initiation of iv Amphotericin and surgical intervention, that will prevent mortality and morbidity in this life threatening disease.

References

1. Hernández JL, Buckley CJ. Mucormycosis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026. Available from: StatPearls Publishing.
2. Saluja G, Bhari A, Pushkar N, et al. Experience on rhino-orbital mucormycosis from a tertiary care hospital in the first wave of COVID-19: an Indian perspective. *Med J Armed Forces India*. 2023;79(Suppl 1):S94-S101.
3. Samendra K, Deepak S, Khushboo C, et al. Rhino-orbito-cerebral mucormycosis and its resurgence during the COVID-19 pandemic: a review. *Indian J Ophthalmol*. 2022;70(1):39-56.
4. Pippal SK, Kumar D, Ukawat L. Management challenge of rhino-orbito-cerebral mucormycosis in the COVID-19 era: a prospective observational study. *Indian J Otolaryngol Head Neck Surg*. 2022;74:3485-3491.
5. Bhardwaj R, Sharma A, Parasher A, Gupta H, Sahu S, Pal S. Rhino-orbito-cerebral mucormycosis during the second wave of COVID-19: the Indian scenario. *Indian J Otolaryngol Head Neck Surg*. 2022;74:3492-3497.
6. Dravid A, Kashiva R, Khan Z, Halikar S, et al. Epidemiology, clinical presentation and management of COVID-19-associated mucormycosis: a single-centre experience from Pune, western India. *Mycoses*. 2022;65(5):526-540.
7. Sigera S, Denning DW. A systematic review of the therapeutic outcomes of mucormycosis. *Open Forum Infect Dis*. 2024;11(1)
8. Pawar R, Nitnaware A, Patel S, et al. Management of rhino-orbital-cerebral mucormycosis: our experience. *Indian J Otolaryngol Head Neck Surg*. 2022;74:223-227.
9. Paljiwala SK, Zangeneh T, et al. An aggressive multidisciplinary approach reduces mortality in rhino-cerebral mucormycosis. *Surg Neurol Int*. 2016;7(Suppl)
10. Gupta N, Shrinivas S, et al. Deoxycholate amphotericin B for management of mucormycosis: a retrospective cohort study from South India. *Mycoses*. 2022;65:432-439.
11. Mehta S, Wadia F, et al. Clinical characteristics, management and outcomes of post-COVID-19 mucormycosis: a retrospective analysis. *Indian J Otolaryngol Head Neck Surg*. 2024;76:388-391.
12. Sree Laxmi, Swapna Kumari B, et al. Histopathological study of mucormycosis in post-COVID-19 patients and factors affecting it in a tertiary care hospital. *Int J Surg Pathol*. 2023;31:56-63.