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SPECTRUM OF INTRACRANIAL COMPLICATIONS OF RHINOORBITOCEREBRAL MUCORMYCOSIS

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ABSTRACT

Objective: To evaluate the spectrum of intracranial complications of rhinoorbitocerebral mucormycosis utilizing MRI and to identify key risk factors and their impact on patient outcomes. **Methods:** This retrospective study included 21 patients diagnosed with rhinoorbitocerebral mucormycosis who underwent MRI to identify intracranial complications. The primary risk factors evaluated were Diabetes Mellitus type 2 (DM-2) and COVID-19 infection. Comparative analysis with existing literature was conducted to contextualize the findings. **Results:** Intracranial complications identified included abscess/cerebritis (58%), arterial infarct (29%), cavernous sinus thrombosis (17%), and internal carotid artery (ICA) thrombosis (11%). MRI findings were crucial in diagnosing these complications, showing T2 hyperintense lesions with ring enhancement for abscesses, restricted diffusion for infarcts, and signal changes in the cavernous sinus. Key risk factors identified were DM-2 (58%) and COVID-19 (35%), with 23% of patients having both conditions. The study revealed a high mortality rate of 64.7% among the patients. **Conclusion:** The study highlights the severe nature of rhinoorbitocerebral mucormycosis with significant intracranial complications. Early and aggressive intervention, particularly in patients with DM-2 and COVID-19, is crucial for improving outcomes. MRI plays a pivotal role in the early diagnosis and management of these complications.

Keywords: Rhinoorbitocerebral mucormycosis, MRI, intracranial complications, diabetes mellitus, COVID-19, mortality, abscess, cerebritis, arterial infarct, cavernous sinus thrombosis, ICA thrombosis.

INTRODUCTION

Rhino-orbito-cerebral mucormycosis has regained significance following its resurgence during the COVID-19 pandemic in India. Rapid and progressive intracranial spread occurs either by direct extension across neural foramina, cribriform plate, ethmoid walls of sinuses, or angioinvasion. Black fungus is an acute fulminant and often lethal opportunistic infection typically affecting diabetic or immunocompromised patients. It is caused by members of the mucoraceal family, including Absidia, Mucor, and Rhizopus. Mucormycosis is an invasive, potentially fatal opportunistic fungal infection caused by saprophytic fungi of the order Mucorales.

Proposed Predisposing Factors

The proposed predisposing factors include hypoxia, uncontrolled blood sugars either steroid-induced or due to diabetes mellitus, and prolonged multipronged immunosuppression. Though it can involve different organ systems, the most common type is rhino-orbitocerebral mucormycosis. The route of infection is usually by inhalation of the spores, which invade the mucosa of the nasal cavity and sinuses, causing rhinosinusitis. Rapid and progressive intracranial spread of the fungus occurs either by direct extension across neural foramina, cribriform plate, ethmoid walls of the frontal and sphenoid sinuses, or angioinvasion of the walls of arteries and veins, causing vascular thrombosis, occlusion, and infarction.

Symptoms of Intracranial Extension

Symptoms of intracranial extension include altered sensorium, diplopia, ophthalmoplegia, cranial nerve deficits, and focal neurological deficits based on the region of spread. With the intracranial extension of disease, mortality is greater than 80%. Early imaging is crucial and aids in assessing the extent of disease involvement, assisting in the prompt initiation of aggressive antifungal treatment and surgical debridement. MRI is the imaging modality of choice.

AIMS AND OBJECTIVES

- To describe the various manifestations of intracranial mucormycosis.
- To calculate the percentage of patients with mucormycosis developing intracranial complications.
- To calculate the percentage of each complication.

MATERIALS AND METHODS

We prospectively evaluated the imaging (MRI) features of 21 patients clinically suspected of having rhino-oculo-cerebral mucormycosis.

Imaging modalities and protocol: Conventional MRI PNS/Brain/Orbit was done, and serial axial, coronal, and sagittal T1-weighted, T2-weighted, fat-suppressed T2-weighted, and post-contrast T1-weighted images were acquired. MRI imaging was performed using a 3T GE machine. Gadopentetate dimeglumine at a dose of 0.2 ml/kg was used for contrast MRI.

Inclusion Criteria

1. All patients referred with clinical suspicion of mucormycosis with positive KOH mount.
2. Patients giving informed valid consent.

Exclusion Criteria

1. Patient not willing for study
2. Claustrophobic patient
3. Patient with negative KOH mount.

IMAGING FINDINGS

MRI provides good tissue characterization depending on different signal intensities on different sequences. It is also useful for determining invasion of the skull base, intracranial, intra-orbital, and infra-temporal extensions of inflammatory disease processes, angioinvasion, abscesses, and acute infarcts. It shows bone marrow changes and cortical abnormalities in very early stages. It also shows foraminal extension either by perineural spread or direct invasion of the fungal disease. Restricted diffusion indicates tissue ischemia and necrosis resulting from the angioinvasive property of the fungus, thus mapping the path of fungal spread.

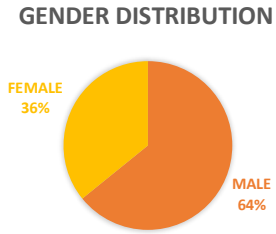
RESULTS :

The gender distribution shows a higher prevalence of rhinoorbital cerebral mucormycosis in males, who constitute 64% of the cases, compared to 36% in females.

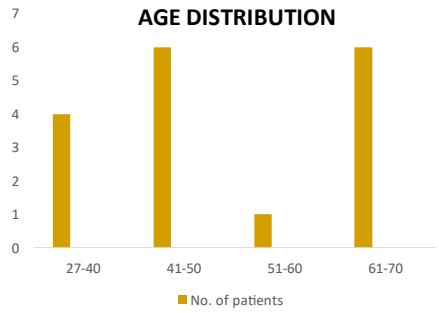
In terms of age distribution, the most affected age groups are 41-50 years and 61-70 years, with six patients each. The age group of 27-40 years follows with four patients, while the least

affected age group is 51-60 years, with only one patient. This suggests that middle-aged and older adults are more susceptible.

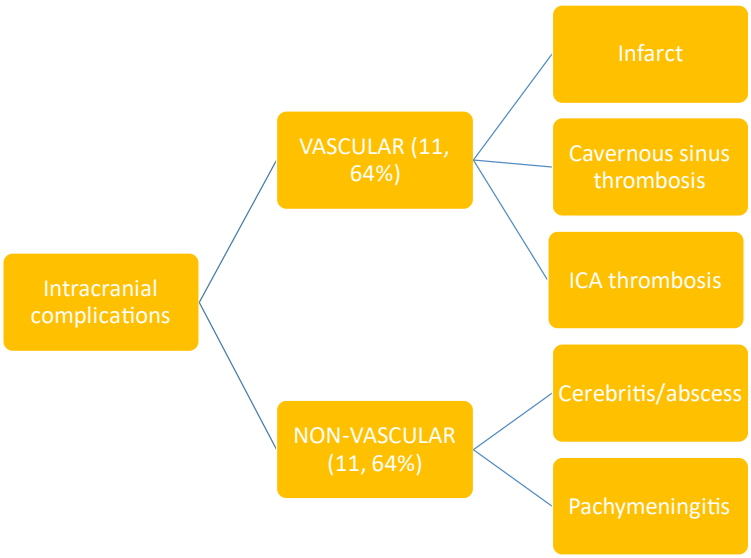
The study identifies Diabetes Mellitus type 2 (DM-2) and COVID-19 as primary risk factors. DM-2 is present in 58% of the patients, making it the most common risk factor. COVID-19 infection is seen in 35% of the cases, and 23% of the patients have both DM-2 and COVID-19. Among these complications, abscess/cerebritis is the most prevalent, affecting 58% of the patients. Other significant complications include arterial infarct (29%), cavernous sinus thrombosis (17%), ICA (Internal Carotid Artery) thrombosis (11%), and pachymeningitis (5%). The mortality rate observed in the study is alarmingly high at 64.7%.



MORTALITY RATE IN OUR STUDY : 64.7%



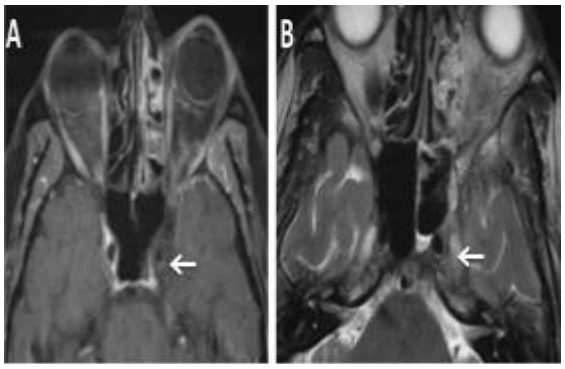
INTRACRANIAL COMPLICATIONS	NUMBER (PERCENTAGE)
Abscess/cerebritis (M/C)	10 (58%)
Arterial infarct	5 (29%)
Cavernous sinus thrombosis	3 (17%)
ICA thrombosis	2 (11%)
Pachymeningitis	1 (5%)



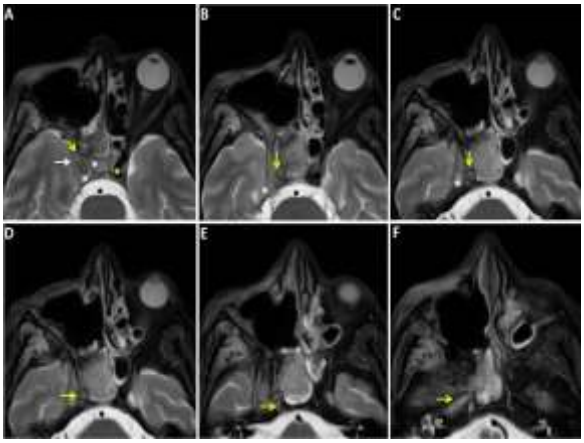
SUMMARY

The data indicates that disease predominantly affects individuals in the age groups of 41-50 years and 61-70 years with male predominance. Diabetes Mellitus type 2 and COVID-19 are significant risk factors, with a notable percentage of patients having both conditions. Abscess/cerebritis is the most common intracranial complication. The study highlights a high mortality rate. This underscores the severe nature of the disease and the importance of early detection and aggressive treatment.

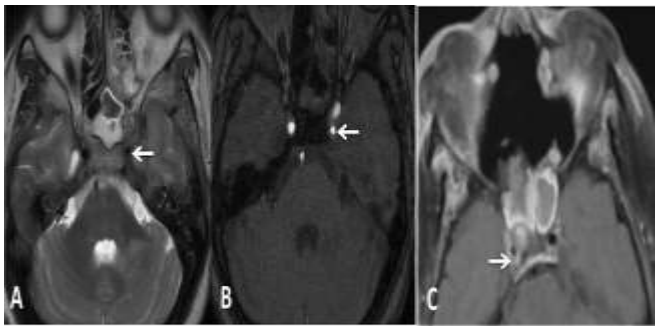
IMAGES :



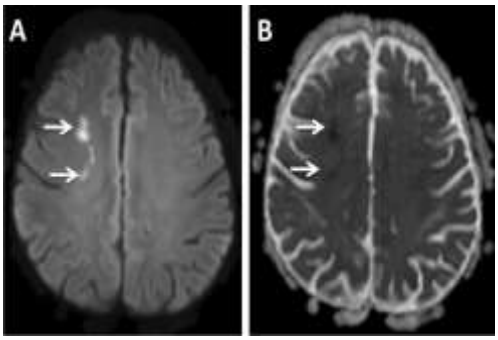
Cavernous sinus thrombosis: A Axial post contrast T1FS image of the brain reveals non enhancement of the left cavernous sinus (white arrow), indicating cavernous sinus thrombosis. Normal enhancement of the right cavernous sinus is seen. Bilateral ICA are patent. B Axial T2-weighted image of the brain reveals T2 heterogeneously hyperintense left paracavernous soft tissue (white arrow) with convex bulge of the wall of the cavernous sinus on the left



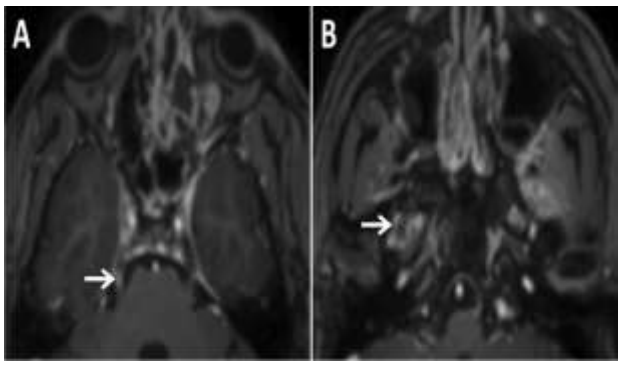
Cavernous sinus extension and right ICA thrombosis: Axial T2-weighted images of the brain reveal A convex bulge of the wall of the cavernous sinus on the right (white arrow), as opposed to a normal convex wall as seen on the left; A T2 hyperintense soft tissue in the right cavernous sinus (white asterisk), B, C extending into the right paracavernous region (white asterisk). A–F Invasion of the right ICA with resultant thrombosis is seen as loss of flow void in the petrocavernous right ICA (yellow arrows). Left intracranial ICA shows normal flow void (yellow asterisk)



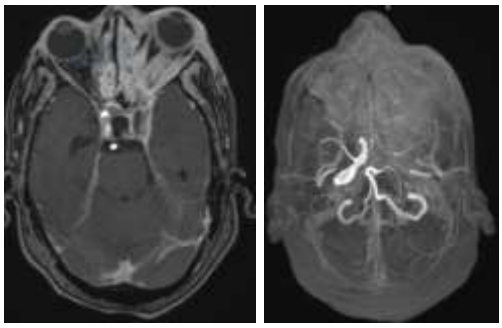
Angioinvasion of wall of cavernous ICA: A Axial T2-weighted image reveals hyperintense thickening of the wall of the left cavernous ICA. Lumen is patent with maintained flow void. B TOF MR Angiogram depicts the mild luminal narrowing of left cavernous ICA with maintained flow related enhancement. C Post contrast T1FS images show enhancement of the wall of the right cavernous ICA, which is patent but narrow calibred, as opposed to the normal left cavernous ICA



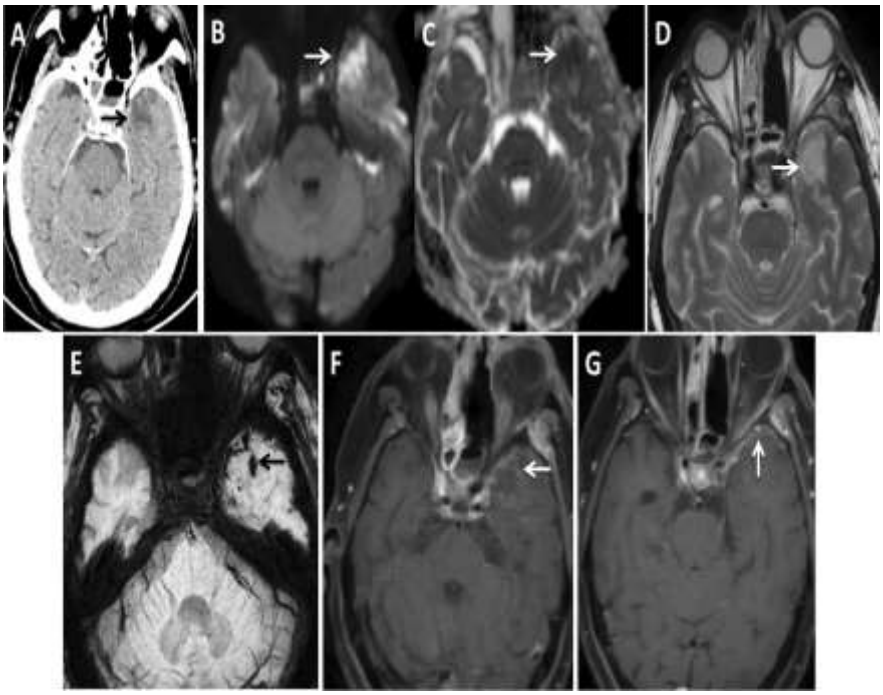
Watershed embolic infarcts in a known case of mucormycosis: A Diffusion-weighted image and B apparent diffusion coefficient map reveal acute embolic infarcts in the right anterior centrum semiovale in the watershed territory, secondary to angioinvasive occlusion of the right ICA



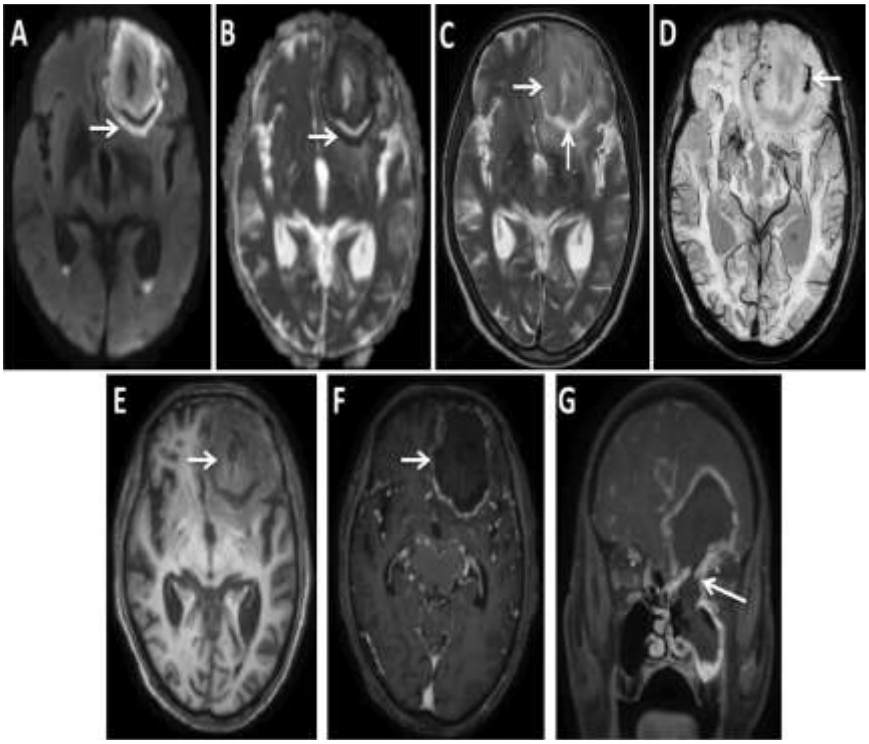
Perineural spread of mucormycosis: Axial post contrast T1 fat suppressed images show A smooth enhancement of the cisternal segment of the right trigeminal nerve (arrow) and B spread along the branches of trigeminal branches through foramen ovale (arrow)



Thrombosis of left cavernous sinus and Complete filling defect with loss of flow void in entire intracranial course of left internal carotid artery - thrombosis - Angio-invasion.



Late cerebritis/evolving abscess: A Axial plain CT reveals ill-defined hypodensity in the left temporal lobe. Axial plain and contrast MRI reveals ill-defined area of restricted diffusion (B, C), T2 hyperintensity (D), peripheral foci of blooming on SWI (E), and subtle thin enhancement in the lateral aspect of the lesion as seen on post contrast T1-weighted images (F). G Adjacent thin pachymeningeal enhancement along the left temporal convexity



Fungal cerebral abscess with ventriculitis : (A) DWI, (B) ADC, (C) Axial T2WI, (D) SWI, (E) Axial T1WI and (F) Post contrast axial T1FS MRI images reveal an irregularly marginated, peripherally enhancing, T2 heterogeneously hyperintense and T1 isointense lesion in the left frontal lobe, showing peripheral diffusion restriction in the wall and foci of SWI blooming mainly on the left lateral aspect of the lesion. Perilesional oedema, mass effect and subfalcine herniation to the right side noted. (G) Post contrast coronal T1FS images depict communication of the abscess with the left frontal, ethmoid, and maxillary sinuses

DISCUSSION

The present study identifies abscess/cerebritis (58%), arterial infarct (29%), cavernous sinus thrombosis (17%), and ICA thrombosis (11%) as common intracranial complications of rhinoorbitocerebral mucormycosis. These findings align closely with those reported in other significant studies. **Maheshwari et al.[1]** describe similar complications, noting that abscesses and cerebritis often present as T2 hyperintense lesions with ring enhancement on MRI, and arterial infarcts are detectable through areas of restricted diffusion. This is corroborated by **Therakathu et al.[2]**, who also report that abscesses, particularly in the frontal and temporal lobes, are common and are characterized by T2 hyperintense signals and ring enhancements on MRI. They further identify significant occurrences of arterial infarcts and cavernous sinus thrombosis. **Agrawal et al.[3]** confirm these observations, highlighting MRI findings of T2 hyperintense lesions and restricted diffusion for infarcts, illustrating the severity and widespread nature of rhinoorbitocerebral mucormycosis infections.

Additionally, **Ribes et al.[6]** outline the various clinical manifestations of zygomycosis, including brain abscesses and infarcts caused by angioinvasion, leading to vascular complications like cavernous sinus thrombosis. **Safder et al.[5]** describe the "black turbinate" sign on MRI, an early indicator of mucormycosis that often precedes severe complications like abscesses and infarcts. These consistent findings across multiple studies underscore the aggressive nature of rhinoorbitocerebral mucormycosis and the crucial role of advanced imaging techniques in its diagnosis and management.

The present study highlights Diabetes Mellitus type 2 (DM-2) and COVID-19 as predominant risk factors, affecting 58% and 35% of patients, respectively. This is in line with the findings of other significant studies. **Maheshwari et al.[1]** emphasize the significant role of DM-2 and COVID-19 in increasing the severity and incidence of rhinoorbitocerebral mucormycosis, noting that patients with these conditions are at a substantially higher risk of developing severe complications. **Therakathu et al.[2]** also stress the critical impact of these risk factors, particularly in the context of the COVID-19 pandemic, which has exacerbated the incidence and severity of rhinoorbitocerebral mucormycosis cases. **Agrawal et al.[3]** highlight the importance of these risk factors, pointing out that the immunocompromised state associated with DM-2 and the additional burden of COVID-19 significantly contribute to higher complication rates and mortality in rhinoorbitocerebral mucormycosis patients.

Further supporting these findings, **Singh et al.[8]** conducted a systematic review of mucormycosis in COVID-19 patients, demonstrating a significant increase in the incidence and severity of rhinoorbitocerebral mucormycosis among these patients. **Mehta and Pandey[7]** also reported on the exacerbation of mucormycosis cases in the context of COVID-19, highlighting the severe outcomes associated with this co-infection.

The present study reports a mortality rate of 64.7% among patients with intracranial complications of rhinoorbitocerebral mucormycosis. This high mortality rate is consistent with findings from several studies, which report mortality rates ranging from 25% to 80%, significantly influenced by the timeliness and type of intervention. **Maheshwari et al.[1]** note that early and aggressive combined surgical and antifungal treatments are crucial for improving outcomes, with delayed treatment leading to substantially higher mortality. Similarly, **Therakathu et al.[2]** emphasize the importance of prompt intervention, with their study indicating improved survival rates with early diagnosis and treatment. **Agrawal et al.[3]** also highlight the variability in mortality rates, underscoring the importance of rapid and comprehensive treatment to manage rhinoorbitocerebral mucormycosis effectively. These findings collectively stress the need for early detection and swift therapeutic intervention to enhance patient survival.

In addition to these studies, **Chamilos et al.**[4] found that delaying amphotericin B-based frontline therapy significantly increases mortality among patients with hematologic malignancies who have zygomycosis, further supporting the critical role of timely treatment in improving outcomes. This aligns with the present study's high mortality rate, emphasizing the severe nature of rhinoorbitocerebral mucormycosis and the necessity for immediate intervention.

Conclusion

- Imaging with MRI with 3D and contrast helps in diagnosis and spread of mucormycosis.
- MRI with contrast is superior in diagnosing the extent of the disease.
- Common complications such as abscess/cerebritis, arterial infarcts, and cavernous sinus thrombosis are frequently observed across studies with MRI playing a pivotal role in their diagnosis.
- This comprehensive study helps in early diagnosis and helps surgeons in prompt multidisciplinary management of rhinoorbital cerebral mucormycosis effectively.

References

1. Maheshwari, S., Dubey, S., & Giri, S. (2021). Spectrum of Intracranial Complications of Rhino-orbito-cerebral Mucormycosis — Resurgence in the Era of COVID-19 Pandemic: A Pictorial Essay. Emergency Radiology. SpringerLink
2. Therakathu, J., Prasad, P., & Menon, G. (2021). Rhino-orbito-cerebral Mucormycosis: Pictorial Review. Insights into Imaging. SpringerOpen
3. Agrawal, R., Sharma, S., & Gupta, N. (2021). Intracranial Manifestations of Rhinocerebral Mucormycosis: A Pictorial Essay. Egyptian Journal of Radiology and Nuclear Medicine. SpringerOpen
4. Chamilos, G., Lewis, R. E., & Kontoyiannis, D. P. (2008). Delaying amphotericin B–based frontline therapy significantly increases mortality among patients with hematologic malignancy who have zygomycosis. Clinical Infectious Diseases, 47(4), 503-509. Link
5. Safder, S., Carpenter, J. S., Roberts, T. D., & Bailey, N. (2010). The “black turbinate” sign: An early MR imaging finding of nasal mucormycosis. American Journal of Neuroradiology, 31(4), 771-774. Link
6. Ribes, J. A., Vanover-Sams, C. L., & Baker, D. J. (2000). Zygomycetes in human disease. Clinical Microbiology Reviews, 13(2), 236-301. Link
7. Mehta, S., Pandey, A. (2020). Rhino-orbital mucormycosis associated with COVID-19. Cureus, 12(9), e10726. Link
8. Singh, A. K., Singh, R., Joshi, S. R., & Misra, A. (2021). Mucormycosis in COVID-19: A systematic review of cases reported worldwide and in India. Diabetes & Metabolic Syndrome: Clinical Research & Reviews, 15(4), 102146. Link
9. Yohai, R. A., Bullock, J. D., Aziz, A. A., & Markert, R. J. (1994). Survival factors in rhino-orbital-cerebral mucormycosis. Survey of Ophthalmology, 39(1), 3-22. Link
10. Wali, U., Balkhair, A., & Al-Mujaini, A. (2012). Cerebro-rhino orbital mucormycosis: an update. Journal of Infection and Public Health, 5(2), 116-126. Link
11. Bandyopadhyay, T., Das, D., & Bhattacharjee, S. (2017). Rhino-orbito-cerebral mucormycosis in diabetes: an urgent diagnostic and therapeutic approach. Journal of Clinical and Diagnostic Research, 11(2), MD01-MD02. Link
12. Walsh, T. J., Gamaletsou, M. N., McGinnis, M. R., et al. (2012). Early clinical and laboratory diagnosis of invasive fungal infections. The Lancet Infectious Diseases, 12(5), 383-395. Link

13. Spellberg, B., Edwards, J. Jr., & Ibrahim, A. (2005). Novel perspectives on mucormycosis: pathophysiology, presentation, and management. Clinical Microbiology Reviews, 18(3), 556-569. Link
14. Werthman-Ehrenreich, A. (2021). Mucormycosis with orbital compartment syndrome in a patient with COVID-19. American Journal of Emergency Medicine, 42, 264.e5-264.e8. Link
15. Skiada, A., Pavleas, I., & Drogari-Apiranthitou, M. (2020). Epidemiology and diagnosis of mucormycosis: an update. Journal of Fungi, 6(4), 265. Link
16. Petrikkos, G., Tsioutis, C., & Groll, A. H. (2019). Epidemiology and clinical manifestations of mucormycosis. Clinical Microbiology and Infection, 25(1), 26-34. Link
17. Sreshta, K., Sankar, J., & Ranjan, R. (2019). A comprehensive review of rhinocerebral mucormycosis. American Journal of Medical Sciences, 358(2), 94-101. Link
18. Roden, M. M., Zaoutis, T. E., Buchanan, W. L., et al. (2005). Epidemiology and outcome of zygomycosis: a review of 929 reported cases. Clinical Infectious Diseases, 41(5), 634-653. Link
19. Skiada, A., & Pagano, L. (2011). Zygomycosis in Europe: analysis of 230 cases. Mycoses, 54(4), e134-e147. Link
20. Prakash, H., & Chakrabarti, A. (2019). Global epidemiology of mucormycosis. Journal of Fungi, 5(1), 26.