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**Original Research Article**

# Management of rhino-orbital-cerebral mucormycosis: our experience

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## ABSTRACT

**Background:** Mucormycosis is a rapidly progressive, angio-invasive fungal infection caused by the fungus belonging to mucoraceae family that has predilection for the paranasal sinuses and adjacent mucosa. Of all the forms of mucormycosis, rhino orbital cerebral (ROCM) is the most common and most aggressive. Our aim is to study the diagnosis, investigation, medical and surgical management of ROCM.
**Methods:** A retrospective study of 273 patients was conducted at the department of ENT, government medical college and hospital, Nagpur between March 2021 to August 2021. Data was collected and analysed.
**Results:** Total 273 patients of mucormycosis were included in this study. There was total 197 (73%) males and 76 (27%) females, patient belonged to age group between 16 to 74 years. Diagnosis was made on the basis of clinical presentation and typical radiological and histopathological findings. On radiography, disease may be limited to a single sinus or involve multiple sinuses. In our study maxillary sinus was most commonly involved sinus 265 (97.06%) followed by ethmoid sinus 258 (94.50%), sphenoid sinus 209 (76.55%), frontal sinus 88 (32.23%). Extension to pterygomaxillary and infratemporal fossa was seen in 160 (58.60% patients), frontal bone involvement in 7 (2.56%), intra-orbital extension 67 (24.54%), intracranial extension 43 (15.75%), mandibular erosion 4 (1.46%).
**Conclusions:** Rhino orbital cerebral mucormycosis is a life-threatening fungal infection, with very high mortality. Interprofessional management typically consists of intervention from an infectious disease specialist, otorhinolaryngologist, microbiologist, ophthalmologist, and paramedical staff, all working hand in hand for better achievement of results. Early diagnosis and intervention surely achieve better prognosis.

**Keywords:** Mucormycosis, Endoscopic sinus surgery, Amphotericin B, Posaconazole

## INTRODUCTION

Mucormycosis is a rapidly progressive, angio-invasive fungal infection caused by fungus belonging to mucoraceae family that has predilection for the paranasal sinuses and adjacent mucosa. Of all the forms of mucormycosis, rhino orbital cerebral (ROCM) is the most common and most aggressive.[1] It mainly affects the immuno-compromised hosts. Management of ROCM specifically after the second wave of COVID-19 had been proven very challenging for the treating ENT Surgeons. From May 5 to July 12, 2021, 41512 cases and 3554 deaths were attributed to this rare, but life-threatening fungal infection in India.[2] This prompted the Central government of India to declare mucormycosis as an epidemic on May 10, 2021.[2] Diagnosis is often delayed because of non-specific presentation in patients that initially mimic like a sinusitis or just a dental problem. Rapid destructive growth of mucormycosis, severity of underlying risk factors, results in poor outcomes. Diagnosis is based on typical clinical features, nasal endoscopy, radiological, histopathological examination and culture of the scrapings from affected tissue. Microscopy and culture are the cornerstones of diagnosis. Histopathology allows differentiation of mucormycosis from aspergillosis. Upon suspicion of mucormycosis

appropriate imaging is strongly recommended to document the extent of the disease and is followed by strongly recommended surgical intervention.[3] Antifungals is the treatment modality of choice for mucormycosis and surgical debridement aids in reducing necrotic tissue and local fungal load, thus providing more surface for the antifungal to act. Depending upon severity of involvement of tissues surgical debridement is planned and repeated surgical procedures are recommended to achieve local control and improve outcome. Primary in vitro resistance to several antifungal drugs limits therapeutic options.[4] Facial disfigurement after aggressive surgical debridement requires a constant psychological support.

### *Aims*

The aim of the study was to study the diagnosis, investigation, medical and surgical management of rhino orbital cerebral mucormycosis.

## METHODS

This is a retrospective study of 273 cases who were diagnosed with ROCM after second wave of COVID-19. This study was carried out in the department of ENT, government medical college and hospital, Nagpur from March 2021 to August 2021.

### *Inclusion criteria*

Patients suspicious of ROCM with nasal swab KOH mount showing fungal elements and patients suspicious of ROCM with nasal endoscopy showing necrotic tissue or mucopurulent discharge were included in the study.

### *Exclusion criteria*

Patients with symptoms of sinusitis with KOH negative for fungal elements and patients following up on OPD basis with already completed treatment for mucormycosis were excluded from the study.

### *Sampling technique*

The study sample was determined as per universal sampling technique and all the patients enrolled for ROCM treatment who satisfied the inclusion criteria during this period have been included in this study. A total of 273 patients are included in this study.

Detailed history was taken and clinical examination was done to arrive at the diagnosis. Previous history of infection with COVID-19, and other risk factors were noted. Radiological investigations like contrast enhanced computed tomography (CECT) and magnetic resonance imaging (MRI) of paranasal sinuses, brain and orbit was done. CT scan finding showed soft tissue edema (enhancement) within the nasal mucosa, mucoperiosteal thickening, bony erosions and orbital and brain invasions. CT is advantageous over MRI due to its ability to detect bony erosions while MRI proved helpful in clearly delineating early vascular invasion, intracranial spread. Nasal endoscopy was done in all cases to look for necrotic tissues, or any mucopurulent discharge within the nasal cavity. Histopathological examination including tissue biopsy from necrotic debris along with KOH mount study preoperatively and postoperatively was done. Depending on the number of sinuses involved surgical debridement was planned accordingly. Limited disease involving one or two sinuses were debrided endoscopically. Extensive involvement of disease reaching to posterior wall of the maxilla, pterygopalatine fossa, infratemporal fossa, pterygoid plates, zygomatic bone, intra-orbital extension, mandibular erosion required open surgical debridement. Orbital exenteration were done in cases with severe orbital cellulitis, extensive tissue necrosis and vision loss. Only vision loss with limited tissue necrosis is not the criteria for orbital exenteration. Post operative bony defects in hard palate and orbit were advised reconstruction with prosthesis after 3 months of completed medical and surgical management. Facial disfigurement following an open debridement was common in patients, which constantly required a psychological support from the family. Antibiotic coverage along with antifungal therapy in the form of liposomal Amphotericin B was given. Treatment duration depended upon the patient's clinical improvement, endoscopic and radiological resolution of the disease. Patients were shifted to oral posaconazole 300 mg OD for 3 months as a step-down therapy. Patients with intracranial involvement were started on both liposomal amphotericin and posaconazole. Correction of the underlying risk factors (like uncontrolled diabetes, diabetic ketoacidosis) were also managed simultaneously. Craniotomy was done in cases of intracranial involvement. A multidisciplinary approach was used to manage the patients. Patients were kept in follow up with endoscopic examination at each visit to look for disease residual/recurrence. In suspected cases of recurrence, radiological investigations were advised.

Prerequisites for diagnosis are a high index of suspicion, recognition of risk factors, and prompt assessment of clinical manifestations. Microscopy and culture of scraping from necrotic tissues were helpful in diagnosis. Hyphae of mucorales are non-septate or pauci-septate and show an irregular, ribbon like appearance. Appropriate imaging like contrast enhanced computed tomography (CECT) and magnetic resonance imaging (MRI) of paranasal sinuses, orbit and brain was strongly recommended to document the extent of disease which can further help us to decide the plan of surgical debridement of the involved areas.

### *Statistical tool*

Data collected from the study subjects was entered in MS excel software and hence using the software, percentages and frequencies were calculated accordingly.

## RESULTS

Total 273 patients of mucormycosis were included in the study. There were total 197 (73%) males and 76 (27%) females, patients belonged to the age group between 16 to 74 years. Diagnosis was made on the basis of clinical presentation and typical radiological and histopathological findings. On radiography, disease may be limited to a single sinus or involve multiple sinuses. In our study Maxillary sinus was most commonly involved sinuses 265 (97.06%) followed by ethmoid sinus 258 (94.50%), sphenoid sinus 209 (76.55%), frontal sinus 88 (32.23%). Extension to pterygomaxillary and infratemporal fossa was seen in 160 (58.60% patients), frontal bone involvement in 7 (2.56%), intra-orbital extension 67 (24.54%), intracranial extension 43 (15.75%), mandibular erosion 4 (1.46%).

**Table 1: CT and MRI findings.**

| Extent of disease | N | Percentage (%) |
|---|---|---|
| **Maxillary sinus** | 265 | 97.06 |
| **Ethmoid sinus** | 258 | 94.50 |
| **Sphenoid sinus** | 209 | 76.55 |
| **Frontal sinus** | 88 | 32.23 |
| **Pterygomaxillary/ Infratemporal fossa** | 160 | 58.60 |
| **Frontal bone** | 07 | 2.56 |
| **Intra-orbital** | 67 | 24.54 |
| **Intracranial** | 43 | 15.75 |
| **Mandibular erosion** | 04 | 1.46 |

**Table 2: Surgical management.**

| Variables | N | Percentage (%) |
|---|---|---|
| **Endoscopic debridement/ FESS** | 209 | 76.55 |
| **Maxillectomy** | | |
| Total | 27 | 9.89 |
| Partial | 51 | 18.68 |
| **Orbital exenteration** | 17 | 6.22 |
| **Plastic reconstruction** | 02 | 0.73 |
| **Mandibular curettage/ mandibulectomy** | 04 | 1.46 |
| **Craniotomy** | 03 | 1.09 |
| **Frontal sinus exploration (external approach)** | 06 | 2.19 |

**Table 3: Death values.**

| Variables | Male | Female | Total | Percentage (%) |
|---|---|---|---|---|
| **Pre-op** | 05 | 03 | 08 | 2.93 |
| **Intra-op** | 00 | 00 | 00 | 00 |
| **Post-op** | 12 | 09 | 21 | 7.69 |
| **Total** | 17 | 12 | 29 | 10.62 |

**Figure 1: Right orbital exenteration.**

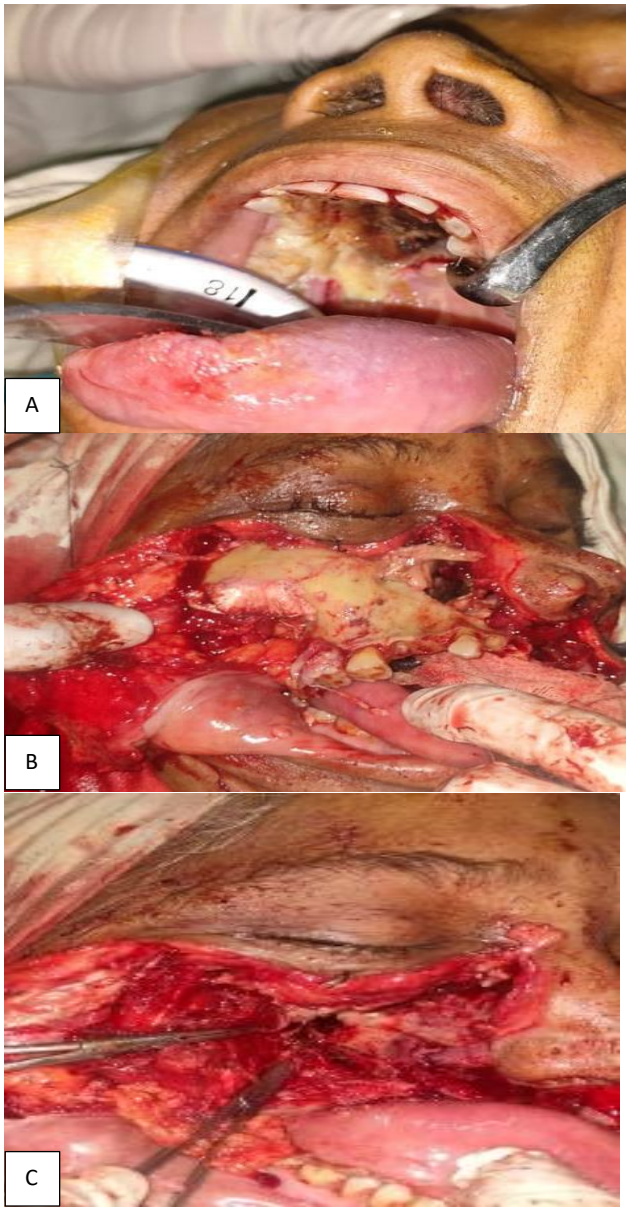


**Figure 2 (A-C): Right total maxillectomy.**

Depending upon the number of involvement of sinuses, surgery was sometimes limited to endoscopic approach only or an extensive open debridement was required. Ophthalmology review for assessment of ophthalmoplegia and optic neuropathy was done depending upon which orbital decompression or exenteration was done. Orbital exenteration was done (Figure 3) in about 17 (6.22%) patients for whom prosthesis was required after 3 months of treatment commencement. In case of open debridement, maxillectomy was done, partial or total depending upon the extent of the disease (Figure 1). Intracranial extension required craniotomy, and rarely mandible erosion was seen in 4 patients for which mandibular curettage was done (Figure 2). Table 2, shows the surgical management methods in our study. 80 patients (29.30%) patients required multiple settings of debridement. Mortality rate was 10.62% with preoperative mortality of 2.93% and postoperative mortality of 7.69%. At the end of 3 months follow up 89.37% patients were disease free.

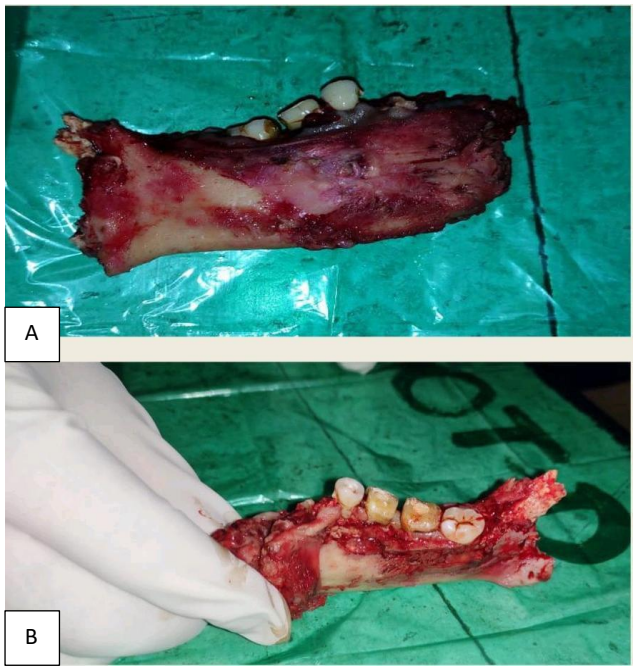


**Figure 3 (A and B): Right segmental mandibulectomy.**

In addition to surgery, timely initiation of antifungal therapy is important. First line treatment with high dose liposomal amphotericin B is strongly recommended (5-10 mg/kg). IV Amphotericin B was given for at least 2 weeks and for 6 weeks in patients with intracranial and cavernous sinus involvement after that we stepped down to oral Posaconazole for 3 months.

## DISCUSSION

Rhino orbitocerebral mucormycosis often occurs in patients who are immunocompromised, most commonly secondary to diabetes mellitus, hematologic malignancy, or iatrogenically following organ transplantation. Mucormycosis is difficult to diagnose having high morbidity and mortality.[3] It is essential for the clinician to maintain a high index of suspicion in populations at risk, as early diagnosis can be life-saving. Standard management of mucormycosis requires early diagnosis, a reversal of risk factors and underlying illness, surgical debridement and prompt administration of intravenous antifungals, usually amphotericin-B. Diagnosis delayed due to non-specificity of symptoms and disease tends to progress more rapidly involving deeper and major structures around the paranasal sinuses. Early diagnosis and prompt antifungal therapy remains the cornerstone of mucormycosis management.[5] Clinical suspicion can be done by characteristic clinical and endoscopic findings. Definite diagnosis is arrived by demonstrating the characteristics ribbon shaped asymmetrical non septate hyphae or pauciseptate, irregularly branching at right angle on culture of tissue specimens.[6] Study conducted by Asdaq et al showed there was a male preponderance with a mean age of 55 plus 15 years while our study also showed similar results.[7] As per study conducted by Anagha et al showed maxillary sinus involvement in all 25 patients, a total of 19, 08, and 10 patients were found to have involvement of ethmoid sinus, frontal and sphenoid sinus respectively.[8] In our study of 273 patients, maxillary sinus (265) was the most commonly involved sinus followed by ethmoid (258), sphenoid (209) and frontal sinus (88).

### *Limitations*

MRI study is a better imaging modality to study intracranial and intra-orbital extension of the disease. However, only few patients were able to get an MRI done due to unavailability of this imaging modality in our institute and due to unaffordability by many patients. Those patients who were operated somewhere outside but were admitted in mucor wards for only administration of Amphotericin-B were not included in this study, as they had a variable duration of stay because of which the entire course of the disease could not be studied in them

## CONCLUSION

Rhino orbito cerebral mucormycosis is a life-threatening fungal infection, with very high mortality. As a result, many doctors find it challenging to deal with. Interprofessional management typically consists of intervention from an infectious disease specialist, otorhinolaryngologist, hematologist, endocrinologist, microbiologist, ophthalmologist, and paramedical staff, all working hand in hand for better achievement of results. Early diagnosis and timely intervention surely achieve better prognosis.

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