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# Preference and grading by operating surgeons for maxillectomies in mucormycosis cases: Original research

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***Abstract***---Aim: The purpose of the present research was to assess the preference as well as grading of maxillectomies in the Mucormycosis cases by operating surgeons. Methodology: An observational study

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conducted among 43 cases of confirmed CAM which included 35 males and 8 females, with an average age of 56 years. The surgical approach adopted in our cases included endoscopic surgical debridement with Denker's approach including mandatory pterygopalatine and infratemporal fossa exploration. All cases were intraoperatively scored using our designed intraoperative scoring assessment tool for mucormycosis. Postoperatively patient recovery was assessed using C reactive protein levels and weekly imaging. Results: Although an early observation in the post op period we observed higher mortality among cases reporting with high scores as per our intraoperative reporting system. At the end of 2 months of completed treatment we report 6 cases of mortality among whom 5 cases were found to have scores (>25) and one reported with a score of 18. Conclusion: This assessment helped to grade the disease severity and also gives an insight about the postoperative prognosis too.

***Keywords***---COVID-19, mucormycosis, fungal sinusitis.

## Introduction

Mucormycosis is an opportunistic fungal infection caused by group of filamentous moulds from the order Mucorales within the zygomycete family. They are involved in infections of different body parts, such as the nose and sinuses, eyes, brain, lungs, gastrointestinal tract and skin. They mainly affect individuals with underlying immunocompromised conditions. Only 6–10% of cases occur in subjects without underlying disease. The pathological feature of this infection is angio-invasion, thrombosis and subsequent necrosis of tissue. The treatment of mucormycosis is control of the immunosuppressive state, early and aggressive surgical debridement and antifungal therapy.[1-3] Chamilos et al. have reported a mortality rate of 46% in patients with mucormycosis.[4] The incidence of mucormycosis in the literature world-wide varies from 0.005 to 1.7 per million population.[5] Epidemiological studies have reported the prevalence in India to be 80 times higher in the pre-COVID era (0.14 per 1000).[6,7] An alarming increase in cases with rhino-orbito-cerebral mucormycosis (ROCM) and COVID 19 infection was seen especially during the second wave COVID-19 pandemic in India.

Numerous risk factors such as uncontrolled diabetes mellitus, immunocompromised states (due to administration of corticosteroids) and iron overload were considered responsible for this notifiable epidemic of COVID-19 associated ROCM. COVID-19 associated mucormycosis (CAM) is seen to be associated with a very high residual morbidity and mortality due to the angioinvasive property of the fungus, thereby causing vascular occlusion and consequently resulting in extensive tissue necrosis.[8] Mucormycosis causes blood vessel thrombosis and resultant necrosis with "dry gangrene "causing the drugs to become non penetrable and lacking efficacy. Therefore, debridement of the necrotic tissues may be a critical step aiding in complete eradication of the disease. However, the timing and extent of surgical debridement necessary to maximize outcomes of mucormycosis has never been clearly defined.

Rhinocerebral mucormycosis usually presents as noticeable blackish brown necrosed tissue over the nasal mucosa, palate, skin, orbit which is either evident clinically or radiologically.[9] Pterygoid fossa exploration is thus regarded as an essential step intraoperatively, as it may be the hidden source harbouring the infection, which might deceive the operating surgeon leading to high post op recurrences and poor prognosis.[10] Early diagnosis and prompt management is very crucial because it is fatal when it involves multiple systems. Amphotericin B is usually drug of choice, Hyperbaric oxygen therapy may act as an adjuvant in promoting wound healing and increasing phagocytosis. Stomatologists play an important role in early diagnosis thus reducing the mortality and morbidity associated with the disease. Interdisciplinary approach with Dental specialists such as Oral and Faciomaxillary surgeons, Prosthodontists, ENT surgeons, ophthalmologists and neurologist play an important role in the management of this debilitating disease.

**Aim of the present study**

The purpose of the present research was to assess the preference as well as grading of maxillectomies in the Mucormycosis cases by operating surgeons.

**Methodology**

43 patients who had covid 19 associated mucormycosis were included in the present study. Among all 43 cases, we found a male predominance (35 were males and 8 were females). The average age on presentation of patients was 56 years (28–80 years). Surgical debridement was carried out. In order to plan a complete clearance intraoperatively, we have designed a method for intraoperative scoring assessment. Through this assessment we made it a practice to mandatorily explore all areas of potential concerns such as the pterygopalatine fossa and infratemporal fossa in all the cases with CAM, even in those not having any evidence of disease radiologically. The goal of surgical debridement was (1) Disease control (2) Obtaining a histopathology and aiding in (3) Microbiological diagnostics. The surgical approach adopted in our cases included endoscopic Denker's approach with pterygopalatine and infratemporal fossa exploration. Endoscopic orbital decompression was done selectively in patients having orbital involvement. Total maxillectomy was chosen modality of treatment in patients with extensive disease which was not accessible endoscopically. Postoperatively patient recovery was assessed using C reactive protein levels and failure of the treatment was considered when CRP was elevated consecutively for 4 days which was further confirmed with postoperative imaging. All our patients were started on Inj liposomal amphotericin B (5–10 mg/kg) and later were continued on oral Posaconazole (600 mg on day 1 and then 300 mg per day from day 2) as per their disease remission with weekly assessment through imaging and alternate day renal function tests.[11]

**Results**

All 43 cases included in our study were confirmed with covid 19 associated mucormycosis. The average age on presentation of patients was 56 years (28–80 years). Out of the 43 cases included in our study (35 were males and 8 were

females). Each patient was assessed separately and each site of involvement was scored intraoperatively. The total intraoperative score was calculated out of 45 which was the maximum score as per our scoring system. The outcome was assessed by calculating CAM associated mortality post operatively and their intraoperative scores were compared. (Table 1) At the end of 2 months of completed treatment we report 6 cases of mortality among whom 5 cases were found to have scores (<25) and one reported with a score of 18. We also observed that patients with higher scores (>25) were mostly males 14.3% (5/35) and 1 female (12.5%).

Among the 6 patients we observed mortality with high intraoperative scores, 4 patients underwent endoscopic Denker's approach with pterygopalatine and infratemporal fossa clearance including endoscopic orbital decompression. We also observed that these patients had postoperative disease recurrence and required re-debridement which could have been a contributing factor for mortality. 2 out of 6 patients with high scores underwent total maxillectomy without orbital exenteration. An interesting observation made in our study was despite having no radiological evidence of disease extension in pterygopalatine and infratemporal fossa, we found disease extension in pterygopalatine fossa among 37.2% cases (16/43) and infratemporal fossa involvement among 20.9% (9/43) cases. In such circumstances the intraoperative scores were found to much higher in these cases despite having no radiological evidence of disease in these keystone areas. (Table 2)

**Discussion**

Mucormycosis is a life-threatening infection caused by fungi of the order Mucorales. Mucormycosis of the orbit is a vision-threatening and potentially fatal infection resulting in angioinvasion, thrombosis, and ischemic necrosis of tissues. Mucor, Rhizopus, Apophysomyces, Cunninghumella are the common organisms responsible for the infection.[12-13] Similar study was conducted previously by Shah and Dave et al. [12] who devised a scoring system with a cut off score of 23 (as per authors discretion) that predicts the stage at which the exenteration needs to be carried out among 15 patients with mucormycosis. Our study includes an intraoperative assessment scoring system with a cut off score of 25 in which we have scored each subsite in an extensive manner which can aid the surgeon in assessing disease severity and predict treatment outcomes in patients with CAM. For decades, the mortality rate of mucormycosis has remained C 40% despite aggressive treatment modalities.[14] There is no good staging system to categorize the disease entity.

On the basis of signs and symptoms the disease process can be grouped into 3 stages which include sinonasal disease, rhino-orbital disease, and rhino-orbital cerebral disease.[15] Meticulous physical examination including examination of oral cavity, eye, and cranial nerves is very important for diagnosing and assessing extent as the radiological findings are non-specific especially in the early stages.[16] Surgical removal of all the necrotic tissue is the most important factor in the treatment of ROCM. But no clear guidelines are present with regards to it. As the pterygopalatine fissure is the main reservoir for Mucor, the posterior wall of the maxillary sinus, even if intact, must always be removed irrespective of the

approach or the extension of the surgery.[17] Thus, exploring all areas intraoperatively is a critical step for complete disease clearance and reducing chances of post- operative recurrence and mortality. We noticed in many of our cases the pterygopalatine fossa can act as a hidden area of concern for the fungus to grow despite having no clinical and radiological evidence of its involvement. In order to achieve this goal, an intraoperative assessment scoring system was structured through which each of the patient diagnosed with CAM were scored. Through this assessment tool all critical areas intraoperatively were explored and found 24 patients having hidden disease in the pterygopalatine and infratemporal fossa despite having a normal radiological picture. This assessment can help in grading the disease severity and giving an insight about the postoperative prognosis too.

## Conclusion

Although an early observation in the post op period we observed higher mortality (6 patients) among cases reporting with high scores as per our intraoperative reporting system. Global scientific collaboration and reporting of new information related to this is of paramount importance to increase the knowledge with regard to the novel viral infection associated with mucormycosis.

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**Tables**

Table 1
Intraoperative Scoring Assessment system

| Sinus involvement | *Right sinus* | *Left sinus* | Scoring description |
|---|---|---|---|
| Maxillary | 0-2 | 0-2 | 0- no involvement<br>1- Mucosal involvement<br>2- Bone involvement |
| Sphenoidal | 0-2 | 0-2 | |
| Ethmoidal | 0-2 | 0-2 | |
| Frontal | 0-2 | 0-2 | |
| Nasal cavity | | | 0- no involvement<br>1- Mucosal involvement<br>Bone involvement |
| Septum | 0-2 | | |
| Middle turbinate | 0-2 | | |
| Inferior turbinate | 0-2 | | |
| Floor | 0-2 | | |
| Cribriform plate | 0-3 | | 0- no involvement<br>1- Mucosal involvement<br>2- Bone involvement |

| | | |
|---|---|---|
| | | 3- Intracranial extension |
| Orbital involvement | 0-2 | 0- no involvement<br>1- extracoronal involvement<br>2- intracoronal involvement |
| Pterygopalatine fossa involvement | | |
| Fat | 0-2 | 0- no involvement<br>1,2- involvement seen |
| Vascular compartment | 0-2 | 1- no involvement<br>1,2- involvement seen (thrombosed/necrosed) |
| Neural compartment | 0-2 | 0- no involvement<br>1- inflamed<br>2- necrosed |
| Muscular compartment | 0-2 | 0- no involvement<br>1,2- involvement seen |
| Infratemporal fossa involvement | | |
| Fat | 0-2 | 2- no involvement<br>1,2- involvement seen |
| Vascular compartment | 0-2 | 3- no involvement<br>1,2- involvement seen (thrombosed/necrosed) |
| Neural compartment | 0-2 | 3- no involvement<br>4- inflamed<br>necrosed |
| Muscular compartment | 0-2 | 1- no involvement<br>1,2- involvement seen |

Table 2
Score Category Mortality Crosstabulation

| | Intra-operative score | Mortality | | |
|---|---|---|---|---|
| | | Alive | Death | Total |
| Score category | <25% count | 36 | 1 | 37 |
| | % within score category | 97.3% | 2.7% | 100% |
| | >25% count | 1 | 5 | 6 |
| | % within score category | 16.7 % | 83.3% | 100% |
| Total | Count | 37 | 6 | 43 |
| | % within score category | 86% | 14% | 100% |