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Original Research Article

A Comparative Analysis of Treatment Modalities for Mucormycosis

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ABSTRACT

Introduction

Mucormycosis is an angioinvasive fungal infection due to fungi of the order Mucorales it can lead to rhinocerebral, pulmonary, cutaneous and other forms of mucormycosis. In months of May – August 2021 unprecedented number of mucormycosis cases were seen across India where in patients were recovering from second wave of COVID 19. Treatment modalities both Conservative and surgical like Functional Endoscopic sinus surgery with debridement and Palatomaxillectomy were performed. The present study is intended to find the best treatment modality for patients based on extension of disease.

Materials and Methods

A total of 120 patients who were diagnosed with mucormycosis underwent Conservative management, FESS with Debridement or Palatomaxillectomy surgical procedure were followed by intravenous amphotericine B.

Results

Out of 120 patients involved in the study slight male predilection was noted with maximum number of cases among 51-60 years of age. Co-morbidities like Diabetes mellitus and hypertension was seen in almost all the cases.

Conclusion

FESS with debridement worked best when diagnosed earlier, Palatomaxillectomy was performed on extended disease and gave considerably good results, Post operative intravenous Amphotericine B gave best results and only12 cases which had to go through multi disciplinary approach for intracranial or intraorbital extension.

Keywords: Mucormycosis, Amphotericine B, Angioinvasive fungal infection, Palatomaxillectomy.

INTRODUCTION

Mucormycosis is an angioinvasive fungal infection due to fungi of the order Mucorales. Depending on the clinical presentation it is classified as rhinocerebral, pulmonary, cutaneous, gastrointestinal, disseminated or other rare forms, such as endocarditis, osteomyelitis, peritonitis, acute renal failure, etc. The disease was first described in 1876 by Fürbinger in Germany [1]. In 1885, Arnold Paltauf published the first case of disseminated mucormycosis, which he named “Mycosis mucorina” [2] The pathogen usually affects immunocompromised patient primarily patients having malignancies or has undergone transplantation and now the

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incidence of mucormycosis has also increased significantly in patients with diabetes [3], which is the commonest underlying risk factor globally.

In months of May – August 2021 an unprecedented number of mucormycosis cases were seen across India where in patients were recovering from second wave of COVID 19. At our institution we came across more than 120 cases of fungal rhinosinusitis with various degree of severity. These patients were promptly diagnosed and treated by various treatment modality at our centre based on extension of disease.

The aim of our study is to know the effectiveness of various treatment modalities like,

A) Conservative management

B) Functional endoscopic sinus surgery (FESS) with debridement

C) Palatomaxillectomy with FESS.

METHODS

This is an Observational analytical(Retrospective + prospective) study including all the patients of Mucormycosis diagnosed by KOH Swab. Extension of disease has been staged based on CT-Scan of nose and PNS. The patients involved in the study were those who comply with both inclusion and exclusion criteria admitted between May 2022 to August 2022.

Inclusion criteria:

1. Patients aged between 18-80 years of both genders.
2. Patient Positive for KOH swab for Mucormycosis later confirmed by Histopathology.
3. Patients with Mucormycosis involving nose and PNS extending to hard palate.

Exclusion criteria:

1) Patient less than 18 or more than 80 years of age

2) Patients with Immunocompromised status like HIV, Recent organ transplant with corticosteroid therapy, Chronic Renal Failure or cardiac illness

3) Patients with loss of vision and orbital involvement and intracranial extension

A total of 120 patients were involved in the study and written/informed consent was taken from the patient for use of their data for academic purpose and publication.

Three treatment modalities were implied for management of mucormycosis and has been classified based on KOH Swab result and CT SCAN Findings of Nose and PNS

Table 01 – Treatment Modalities with Plan of Management.

	KOH Swab	**CT- Scan Nose and Para Nasal Sinuses**	**Treatment Modality**
CONSERVATIVE MANAGEMENT	Nasal Swab Positive	No Positive CT Scan Findings	• Intravenous – Amphotericin B 3mg/kg//day for 14 days with Intranasal L-Amphotericin B Gauze packing.

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			• Followed by – Oral Tablet Posoconazole 600mg/day for 2 months. • Repeated DNE & Nasal Swab for KOH Mount Weekly.
Functional Endoscopic Sinus Surgery with debridement	Nasal Swab Positive	CT Scan involving all four Paranasal sinuses	• Functional Endoscopic Sinus Surgery with debridement • Intravenous – Amphotericin B 3mg/kg//day for 14 days with Intranasal L-Amphotericin B Gauze packing. • Followed by – Oral Tablet Posoconazole 600mg/day for 2 months. • Repeated DNE & Nasal Swab for KOH Mount Weekly
Palatomaxillectomy with FESS	Nasal Swab Positive	CT Scan involving Paranasal Sinuses and Hard Palate.	• Functional Endoscopic Sinus Surgery with Palatomaxillectomy. • Intravenous – Amphotericin B 3mg/kg//day for 14 days with Intranasal L-Amphotericin B Gauze packing. • Followed by – Oral Tablet Posoconazole 600mg/day for 2 months. • Nasal Swab for KOH Mount Weekly

All the patient undergoing treatment were regularly followed up for renal function test and general wellbeing considering high exposure to nephrotoxic drugs

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RESULTS

A total of 120 cases of mucormycosis were treated at our center with 52.5% (63) male and 47.5 (57) female patients giving a marginally high male predilection to the disease. Most patients were in age group of 51-60 33.3% followed by 61-70 29.1% the age wise distribution is shown in Table No 1.

Table No 02 – Age wise distribution of patients.

SL.NO	AGE GROUP	NO. of Patients	Percentage
1	18-30	02	1.6
2	31-40	07	5.8
3	41-50	27	22.5
4	51-60	40	33.3
5	61-70	35	29.1
6	71-80	09	7.5

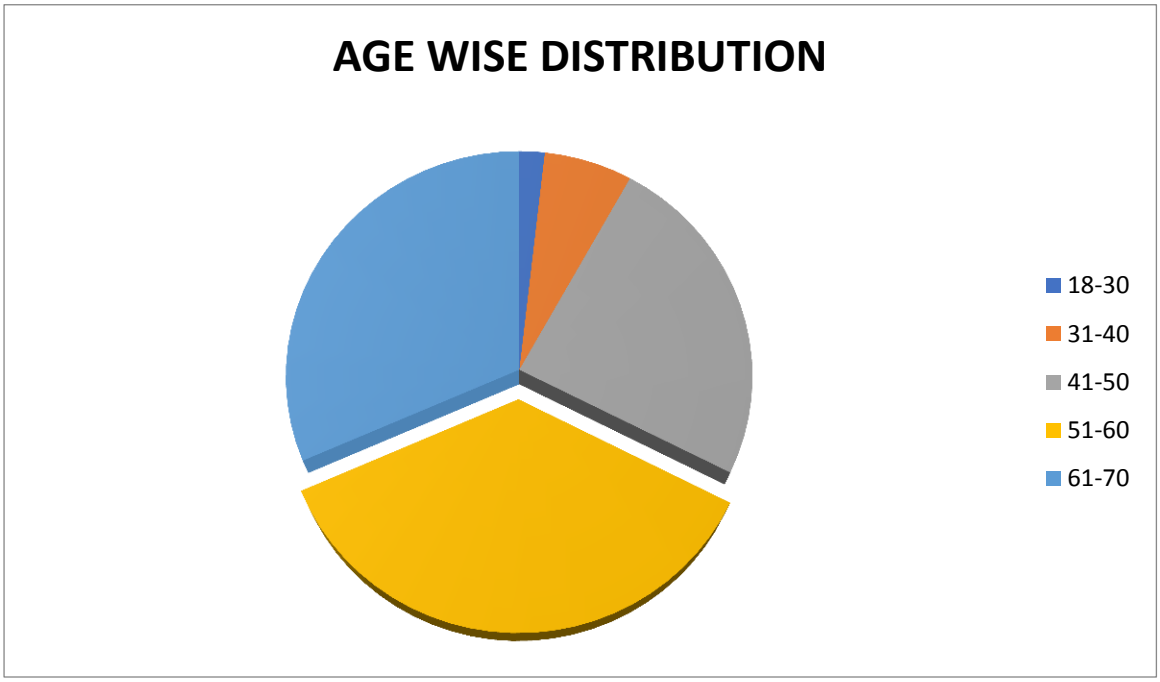

Chart 01 Age wise distribution of patients.

Many patients had co morbidities of Hypertension, Diabetes Mellitus. Table no 2 shows the number of co morbidities with patients.

Table No. 03 – Number of Co Morbidities.

SL.NO	Co morbidities	NO. of Patients
1	Diabetes Mellitus	97
2	Hypertension	68

Diabetes Mellitus was seen in most number of cases followed by Hypertension. Most patients had unilateral presentation up to 78.3%. most common clinical presentation was Facial pain and Headache, cheek swelling, Nasal bleeding patient coming at much later as complaint of eye swelling, loss of vision, giddiness and even altered sensorium.

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All the patients under went thorough evaluation and based on severity of disease were treated like wise. Patients with ocular and intracranial involvement were treated with multidisciplinary approach.

Table no 3 shows the number of patients with the treatment modality given any recurrence or unresponsive patient to treatment modality was promptly engaged with further investigation and treatment.

Table No 04 – Treatment Modalities with Patient Response.

SL.NO	TREATMENT MODALITY	Number of cases	Patients with full recovery	Recurrence/unresponsive
1	Conservative management	23	12	11
2	FESS with debridement	54	46	8
3	Palatomaxillectomy with FESS	43	33	10

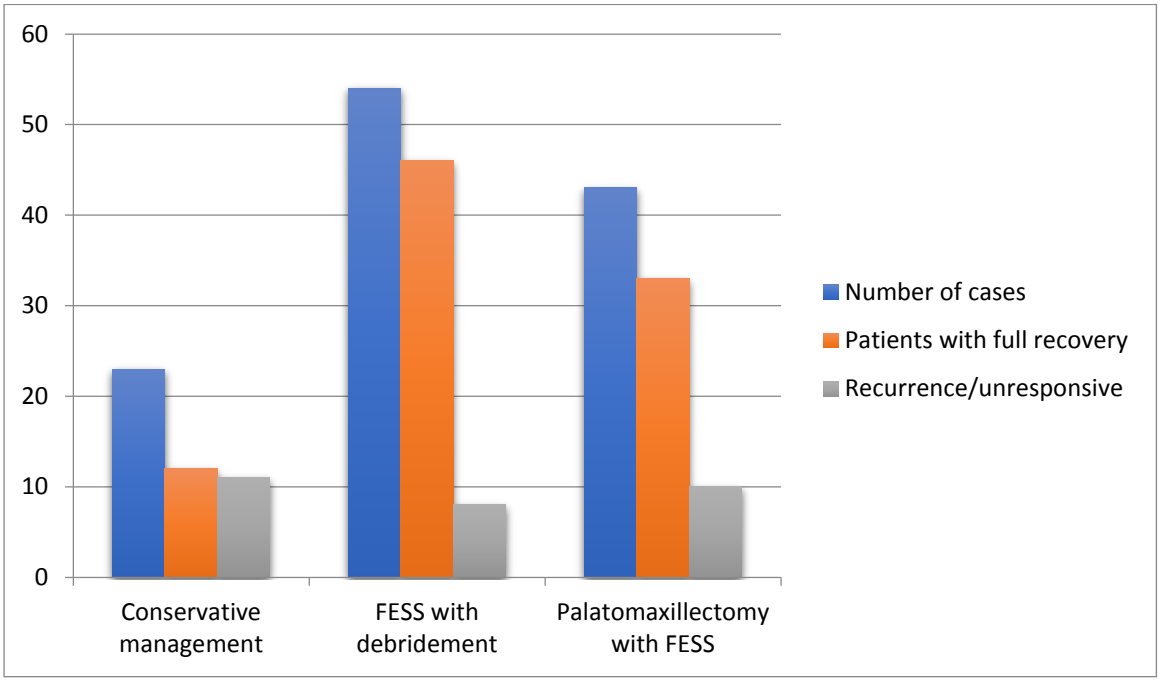

Chart 02 The number of patients with different treatment modality with number of recovery and any recurrence or unresponsive patient.

The 11 patients with no improvement on conservative management were treated with FESS and responded well. eight patient treated with fess had recurrence and extension of disease out of this six underwent Palatomaxillectomy and responded well, two patient had intracranial involvement. Forty three patients had to undergo Palatomaxillectomy with FESS out of which 33 had recovery. A total of 12 cases had to be managed with multidisciplinary approach due to Orbital and intracranial involvement.

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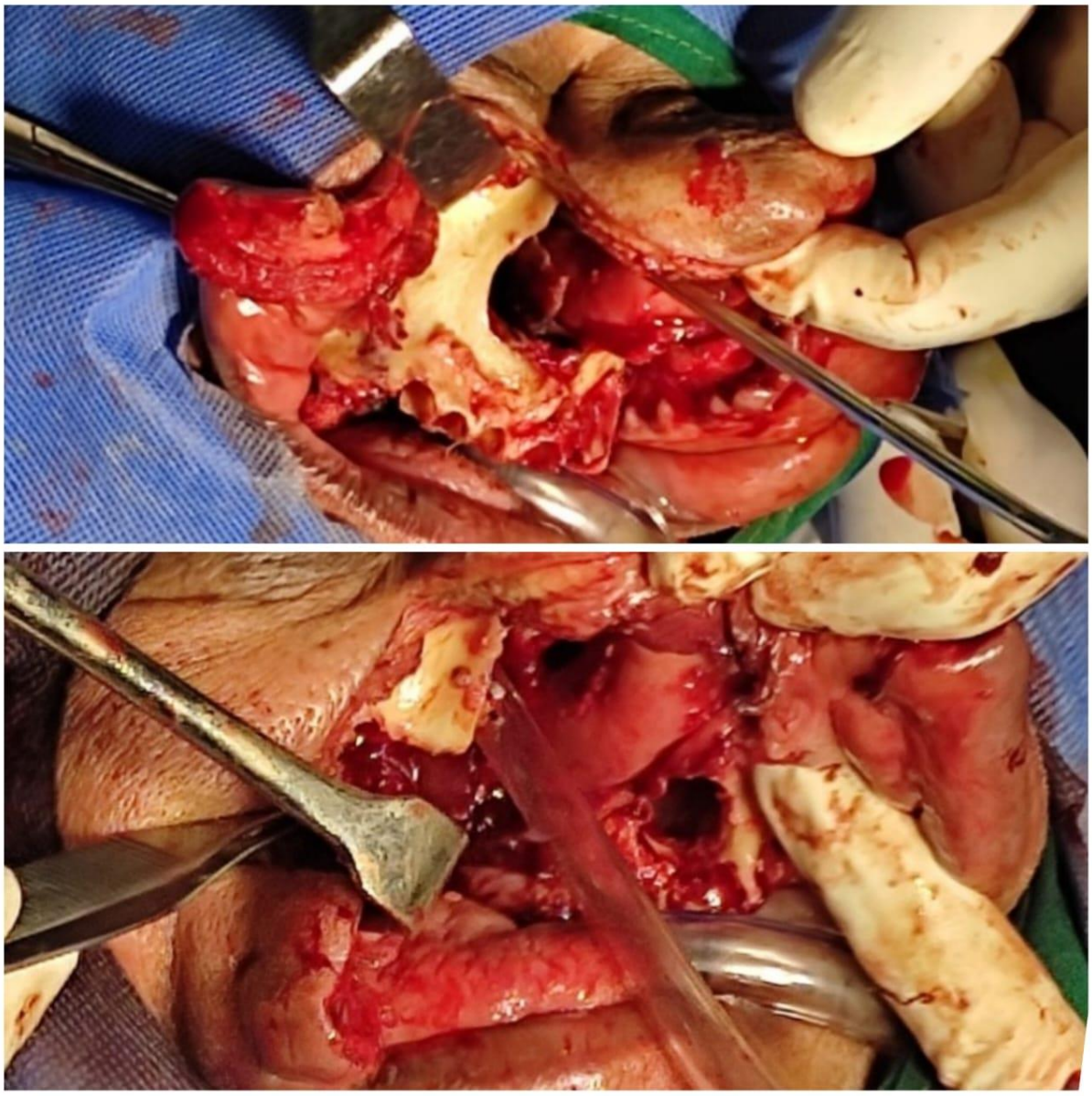

Image 01 – Palatomaxillectomy.

DISCUSSION

In the study only 2 patients below the age of 30 years developed mucormycosis post Covid-19 infection. It can be attributed to their immunity and less incidence of comorbidity at young age. Most of the patients belonged to 51-60 years of age group and were diagnosed with associated co morbidity like diabetes mellitus and hypertension. Mean age was 57 years. 52.5% patients were male giving a slight male predilection of disease. Similar results were reported by White et al. [4] in his study of 135 adults with median age 57 years and male to female ratio 2.2/1.

Diabetes mellitus type II is most common predisposing factor accounting for 97 cases. Similarly Yohai et al. [5] and Ferry et al. [6] have found diabetes mellitus type II to be the most common predisposing factor. Rhinocerebral mucormycosis This is the most common

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form, usually seen in patients with diabetes mellitus.[9,10] Hypertension was seen in 68 patients respectively.

A total of 23 patients underwent conservative management of which 12 responded well and were declared cured after three consecutive negative swabs for fungal culture most of the patients were diagnosed at very early age and were comparatively young and with few co morbidities. 11 patients did not respond satisfactorily and had increase in symptoms and clinical signs. these patients were promptly taken for FESS or FESS with Palatomaxillectomy 9 out of 11 patients recovered with FESS where as 2 underwent FESS with Palatomaxillectomy. These 11 patients had uncontrolled diabetes mellitus and had to be put on strict diet and blood sugar monitoring with timely insulin infusion.

FESS with debridement was performed for 54 patients of whom 46 patients responded well to the treatment and were discharged after complete treatment. Extensive debridement had to be performed as the mucociliary clearance function in mucormycosis is primarily effected wide open middle meatal antrostomy and opening of both anterior and posterior ethmoids with frontal sinus was performed comparatively few cases had sphenoid sinus involvement and were promptly treated. Surgery was followed by regular saline nasal douching and Intravenous – Amphotericin B infusion and nasal pack followed by oral Posoconazole 600mg/day for 2 months. Strict control of blood sugar level is necessary for desired results. All the patients were followed up regularly for any recurrence or post operative complications. A total of 8 patients did not respond for FESS with debridement of which 6 patients had developed intracranial complications and 2 with intraorbital complications which were treated with the multidisciplinary approach.

FESS with Palatomaxillectomy was performed on 43 patients these patients usually had a late presentation with complains of loose teeth, headache, tingling sensation of upper lip and halitosis. Primary involvement of maxillary sinus was seen in all the cases and FESS was performed for clearance of ethmoid and sphenoid sinus. A total of 30 patients under went Palatomaxillectomy and 13 had total bilateral Palatomaxillectomy. 10 patients had recurrence. Mortality was seen in 4 cases primarily due to impaired renal function. All the patients were rehabilitated after 4-5 months with necessary dental obturator and denture.

Debridement of necrotic tissue and removal of fungal debris is crucial in the treatment of mucormycosis. Surgery alone is not curative, but an aggressive surgical approach has shown a higher survival rate [7]. Most of the patients who under went FESS required medial maxilectomy via modified denker approach for complete endoscopic removal of the disease. Due to the aggressive and more fulminating nature of the disease. 19% Patients were managed by more conservative approached and only 10% responded well, as surgical debridement reduces the fungal load and increases survival chances by better drug delivery.

Amphotericin Bis the gold standard in the treatment of mucormycosis. The survival rate of patients increased to the 60% after the introduction of Amphotericin B[8]. Liposomal Amphotericin Bis the first choice of treatment in patients with intracranial extension as it crosses the blood–brain barrier more effectively. Most of the patients respond well with Amphotericin Beither conventional or liposomal, depending upon the renal status of the patient. Only 5% patients required Amphotericin B for more than 12 days who had presented with more advanced disease.Oral Posaconazole was given as antifungal therapy after completion of Amphotericin B treatment.

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Conclusion

Patients with early presentation have shown better results in terms of survival. Surgery like FESS and Palatomaxillectomy based on extension of disease with Injectable Amphotericin B can significantly improve prognosis. Strict control of underlying disease like Hypertension and diabetes mellitus, systemic antifungal medication and surgical debridement proved to be the mainstay of mucormycosis treatment. Regular monitoring of progress and good nutrition post operatively provided better results and patient satisfaction.

DECLARATIONS

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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