

## A Comparative Study of Radiological and Surgical Findings of Mucormycosis in Post-COVID Patients

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### Abstract:

Mucormycosis is the most invasive form of paranasal fungal infection caused by Mucor which is an ordinarily saprophytic, but can become an aggressive pathogen under the conditions appropriate for it.

**Methods:** In this study of Mucormycosis of Nose and PNS, 97 cases were studied at Tertiary care hospital over period of 6 months. Patients were assessed for age, gender, predisposing factors, symptoms and signs, site of extension with help of CT scan and MRI and nasal endoscopy, site of surgical debridement and prognosis.

**Results:** The commonest predisposing condition for the disease is extensive use of steroids followed by diabetes mellitus. Mucopurulent discharge was found in 71 cases. On Endoscopic examination, majority patients showed Black crust in 41 cases, 69 cases out of 97 showed KOH positivity and 77 cases out of 97 showed Histopathological positivity. Maxillary sinuses were involved in 97 cases, Ethmoid sinuses in 97 cases and Sphenoid sinuses in 97 cases as per radiological investigations but on surgical exploration 76 patients had maxillary sinuses, 62 patients had ethmoid sinuses and 57 patients had sphenoid sinuses diseased.

**Conclusions:** With increasing rate of mucormycosis in post covid patients it is utmost important to diagnose and treat this deadly disease early. The recent technology of radiological investigations is boon for the earliest diagnosis and proper planning for surgical intervention.

**Keywords:** Mucormycosis, Post Covid Patients, Radiological and Clinical Correlation, Extra Sinus Mucormycosis.

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### Introduction

Mycology is study of fungi, a diverse group that comprises of molds, yeasts mushrooms and related organisms. Over 100000 species are recognized as of which 100 are identified as pathogenic for humans and animals. Fungi are eukaryotic organisms which differ from bacteria and other prokaryotic organisms in many ways. Mycosis is an infection caused by fungi, generally depends on the state of the host defense system, the route of exposure and virulence of the fungus. Amongst mycosis, Mucormycosis is the most invasive form leading to higher morbidity and mortality. [1]

Fungal Rhinosinusitis (FRS) can be categorized into two broad groups invasive and non-invasive

based on presence or absence of fungus in the tissue (mucosa, blood vessel or bone) respectively. Most fungal sinus infections are benign or non-invasive, except when they occur in individuals who are immunocompromised, such as patients with diabetes mellitus, leukaemia, AIDS, or other conditions that impair the immune system. [2]

Mucormycosis can manifest itself in five distinct syndromes as Rhino-orbito-cerebral, pulmonary, cutaneous, gastrointestinal disseminated and miscellaneous. Rhino-cerebral mucormycosis is the commonest type seen. [3]

The underlying principle of the management for this disease remains rapid diagnosis, reversal of

underlying predisposing factors and urgent surgical debridement along with systemic broad spectrum antifungal such as Amphotericin.

Mucor is an ordinarily saprophytic but can become an aggressive pathogen under the conditions appropriate for it. Following inhalation of spores, the fungi grows in paranasal sinuses and invades neural and vascular structures, leading to vessel thrombosis and resultant mucosal necrosis. The fungi then extend beyond the affected sinus through a combination of bony destruction, perineural and perivascular spread. Mucor is almost seen in the patients with immuno-deficient status. The most common risk factor in these patients is Diabetes Mellitus.

Patients with diabetic ketoacidosis are at higher risk of developing rhino cerebral mucormycosis as they have elevated levels of available serum iron due to release of iron from binding proteins in the presence of acidosis. This medium promotes the growth of rhizopus species. Other predisposing conditions are patient on prolonged steroid therapy, Chronic renal failure, immune-suppressive agents, desferoxamine or other chelating agent. Coronavirus disease infection may be associated with a wide range of bacterial and fungal co-infection. Extensive use of steroids/monoclonal antibodies / broad-spectrum antibiotics may lead to development or exacerbation of a pre-existing fungal disease [4].

#### Aims and Objectives:

1. To assess the patient for age, gender, predisposing factors, symptoms and signs, site of extension with help of radiological tests such as CT scan and MRI of patients presenting the symptoms suggesting mucormycosis infection.
2. To compare the radiological and surgical findings in the patients undergoing surgical intervention for mucormycosis.

#### Methods

In this study of Mucormycosis of nose and paranasal sinuses, 97 cases were studied at Sheth LG Hospital, Maninagar, Ahmedabad, a tertiary referral centre over period of 6 months. Proper history and detailed clinical evaluation was done. Patients were assessed for age, gender, predisposing factors, symptoms and signs, site of extension with help of radiological tests such as CT scan and MRI, site of surgical debridement and prognosis.

#### Inclusion criteria

- Patients with diagnosis confirmed of Mucormycosis of PNS/nose in post covid patients.
- Patient giving consent for admission and study.

#### Exclusion criteria

- Those patients having nasal mass with sinusitis like antrochoanal polyp, ethmoidal polyp and nasal mass with suspected malignancy (other than mucormycosis)
- Those patients who were not giving consent.

The following investigations were done in all cases.

1. Routine Haematological and Serological and Radiological investigations.
2. Special investigation like HBA1c, CT PNS, MRI with Gadolinium contrast.
3. In all patients diagnostic nasal endoscopy with biopsy was carried out using 0 degree nasal endoscope under local anaesthesia. The biopsy material obtained was sent for histopathological examination for Haematoxylin and Eosin staining, KOH staining and fungal culture and sensitivity. The gold standard of diagnosis is pathological examination of permanent section, prepared in potassium hydroxide [5].
4. Those planned for surgical debridement were assessed preoperatively for anaesthetic fitness.

#### Results

This study was carried out in the department of otorhinolaryngology at Sheth LG Hospital, Maninagar, and Ahmedabad. The study materials comprised of 97 cases, all the patients having nasal blockage, nasal discharge, facial pain, numbness and swelling, nasal bleeding, visual impairment, oral ulcer, eye discharge were admitted to Mucor ward of the hospital.

In all patients' diagnostic nasal endoscopy and biopsy was taken under local anaesthesia. The biopsy material obtained was sent for histopathological examination for H&E staining, fungus culture and sensitivity and KOH staining.

Change in mucosal appearance is typical on endoscopic examination. In the early stages, the mucosa may appear pale, Necrosis resulting from angioinvasion results in black crusts known as eschar (i.e. Pathognomic of Mucormycosis) and sloughing of the mucosal surface of nose and septum.

**Table 1: Gender distribution**

Sex	No. of Cases	Percentage
Male	42	43.30
Female	55	56.70

**Table 2: Etiological predisposing conditions**

Mucormycosis		Present study (*n=97)	Sharma S et al[6] 2021 (n=47)	Joshi et al[7] 2021 (n=25)
Diabetes mellitus	Newly diagnosed	8(8.24%)	36(76.6%)	-
	Uncontrolled	52 (53.6%)		13(52%)
	Controlled	25 (25.77%)		9(48%)
O2 support		30(30.92%)	38 (80.9%)	6(24%)
Ventilator support		43 (44.32%)	20 (42.6%)	
Corticosteroid treatment	Intravenous Route	39 (40.2%)	29 (61.7%)	2(8%)
	Oral route	51 (52.57%)	45 (95.7%)	

**Table 3: Age distribution**

Age group (in years)	No. of cases	Percentage (%)
0-15	1	1.03
16-30	7	7.22
31-45	23	23.71
46-60	31	31.96
61-75	31	31.96
76-90	4	4.12

**Table 4: Symptoms distribution**

Symptoms	No. of cases	Percentage (%)
Nasal discharge	71	73.34
Facial pain and swelling	65	67.01
Facial numbness	56	57.73
Headache	52	53.21
Loss of sense of smell	45	46.33
Nasal blockage	32	32.98
Visual impairment	14	14.43
Nasal pain	4	4.12
Nasal bleeding	3	3.09
Discharge from eye	3	3.09

**Table 5: Distribution of Endoscopic findings**

	Present study (n=97)	Arun kumar et al[8] 2020 (n=100)#	Suresh S et al[41] 2016 (n=30)###	Ravi Meher et al[10] 2021 (n=131)####
Mucopurulent Discharge	81 (83.5%)	11%	30%	65.2%
Mucoid Discharge	9 (9.28%)	9%	-	-
Polyp	8 (8.25%)	-	43%	-
Edematous Mucosa	7 (7.22%)	-	-	20.81%
Inspissated Secretion	9 (9.28%)	-	-	-
Black crust	41 (42.6%)	-	13.3%	91%
Clear mucosa	65 (67.01%)	72%	-	-

**Table 6: Distribution of modalities of management**

Endoscopic	Conventional ESS	31 (31.96%)
	Modified Denker	83 (85.57%)
Combined (endoscopic included)	Intra-oral	14 (14.43%)
	Caldwell luc	1 (1.03%)
External	Weber Ferguson	2 (2.06%)
Orbital Exenteration		8 (8.24%)
Craniotomy		1(1.03%)

**Table 7: Surgical procedures adopted in patients with mucormycosis and extra sinus diseases.**

Surgical procedures		No. Of Surgeries
Limited maxillectomy	Modified denker	83
	Infrastructure Maxillectomy	3
	Anterior partial Maxillectomy	48
	Partial palate removal	1
	Alveolectomy	1
Subtotal Maxillectomy		2
Total Maxillectomy		59
Infratemporal fossa debridement		2
Tarsorrhaphy		4
Orbital exenteration		8
Craniotomy & Drainage		1

**Table 8: Distribution of sites of sinus and extra sinus involvement on basis of radiology findings(CT/MRI)**

Involvement in Radiology	Present study	Arun kumar et al[8]; 2002 (n=100)#	Suresh S et al [9] 2016 (n=30) ##	Bhansali et al [11] 2004 (n=35) ###
Maxillary sinus	97 (100%)	29 (29%)	14 (46.6%)	80%
Ethmoid sinus	97 (100%)	27 (27%)	12 (40%)	86%
Sphenoid sinus	97 (100%)	5 (5%)	11 (36.6%)	17%
Frontal sinus	95 (97.94%)	8 (8%)	-	17%
Pansinusitis	95 (97.94%)	-	-	14%
Orbit	19 (19.59%)	-	-	=
Palate	13 (13.4%)	-	-	80%
Brain	16(16.49%)	-	-	11%
Others	23(23.71%)	-	-	20%

**Table 9: Comparison of Radiological (CT/MRI) findings and operative findings of sites of sinuses and extra-sinus sites of involvement**

Site of Involvement	Ct/Mri Involvement	Involvement In Surgery
Maxillary Sinus	97	76
Ethmoid Sinus	97	62
Sphenoid Sinus	97	57
Frontal Sinus	95	41
Pansinusitis	95	40
Orbit	19	46
Palate	13	52
Pterygo-Palatine Fossa	13	18
Infra-Temporal Fossa	10	8
Cerebral Lobes	10	3

In Table 1: In the present study 42(57%) males and 55(43%) females were observed.

In Table 2: The commonest predisposing condition for the disease is extensive use of Corticosteroids (by intravenous and oral route) followed by Diabetes Mellitus, Ventilatory support and Oxygen support.

Mucor spores are found commonly in the environment and are usually non-pathogenic fungi which are likely to inhale daily. Mucormycosis occur as a systemic infection following dissemination from a primary focus in the upper respiratory tract or nasal cavity, where the spores germinate and mycelia invade the adjacent tissues-the paranasal sinuses, orbit and brain. The Rhino-cerebral form, in which the nose, paranasal sinuses

and orbit are involved, is well recognised and is usually a fatal complication of diabetes mellitus. Hyperglycaemia common feature in Mucormycosis patients can cause excessive glycosylation of proteins such as ferritin and transferrin. This in addition to low pH strongly impairs their ability to chelate iron. Low serum pH affects both the phagocytic effect of macrophages and the chemotactic and oxidative burst of neutrophils. Thus it diminishes the main host defences against the invasion of mucormycetes. Other reasons may be poor recognition, reduced uptake and a low cytokine response to fungi in diabetic patients. Patients with history of diabetes and on prolong steroid treatment are more prone to Mucormycosis as a result of immune suppression. The pathology in all these sites are same with blood vessel

invasion and tissue necrosis as hallmark and specific organ dysfunction depending on the location of the infection [12].

In Table 3: In present study youngest patient was 24 years old and oldest patient was 76 years old. The most common affected age group was more than 40 years with increased incidence of diabetics detected in same group. Mean age is 54.58 years.

In Table 4: In present study nasal discharge (73.34%), facial pain and swelling (67.01%), facial numbness (57.73%) was main symptoms and least common was visual impairment. Patients with rhino cerebral Mucormycosis may present with symptoms typical of sinusitis.

However, progression of symptoms over several days indicates a more serious process than the most common bacterial or viral sinusitis. As the infection spreads, hypoesthesia or numbness of face overlying the infection may develop. Concomitant symptoms include headache, bloody nasal discharge and change in mental status. The black eschar of the palate is widely described as a hallmark of rhino cerebral Mucormycosis.

These subtler lesions, which may consist of discoloured, often hyperaemic areas on the palate will, if untreated, progress rapidly to the commonly recognized black eschar, which indicates angioinvasion and tissue necrosis. Involvement of the orbit compromises proper ocular muscle function and normal movement of the eye within the orbit, resulting in diplopia.

If the blood supply to the eye is affected by invasion of the retinal artery, blindness develops, often quite rapidly. Proptosis and ptosis are late findings reflecting a mass lesion within the orbit and cranial nerve involvement, respectively.

Progression of the infection into the brain results in the formation of brain abscess; symptoms and sign depend on the location of these lesions [13].

In Table 5: Mucopurulent discharge was found in 81 cases (i.e. 83.5%), majority patients showed Black crust in 41 cases (i.e. 42.6%) 69 cases out of 97 showed KOH positivity and 77 cases out of 97 showed Histopathological positivity.

In Table 6: In endoscopic approach majority of patients were managed by Modified Denker's approach with Intra Oral exploration of involved maxilla. Only 2 patients were managed by Weber Ferguson approach. Orbital exenteration was done in 8 patients.

In Table 7: In extra sinus Mucormycosis, 83 Modified Denker's surgeries were done followed by 59 Total Maxillectomy, 2 partial Maxillectomy, 3 Infrastructure Maxillectomy, 1 Alveolctomy, 8 orbital exenteration and other surgeries. Plan for

management was done on the basis of radiological correlation and the surgical findings were confirmed according to the correlations.

Like in one the patient's mucosal thickening was found in Left side paranasal sinuses and altered marrow signal density was present in left side alveolar process of maxilla in MRI PNS. Likewise, surgery was planned, intraoperatively black crusting was found in maxillary sinus which extended towards the floor of Left maxillary which was removed by Modified Denker's approach and palatal flap was raised and evaluated for bony involvement but significant involvement was not found so only palatal debridement was done. In some studies, orbital and other sinus areas were irrigated and packed with Amphotericin B for direct action as vaso-occlusive property of Mucormycosis diminishes the effective delivery of intravenous Amphotericin B.

In Table 8: In all the patients i.e. 97 patients Maxillary, Ethmoid and Sphenoid sinuses were involved as per radiological investigations. In 19 patients orbit was involved, ---- patients palate was involved, 16 patients brain was involved, 23 patients other areas like infra-temporal fossa and pterygopalatine fossa was involved.

In Table 9: 97 patients showed involvement of maxillary sinus in CT/MRI from which 76 showed surgical involvement. 97 patients showed ethmoid sinus involvement in CT/MRI from which 62 patients showed surgical involvement. Sometimes mucosal thickening and oedema or secondary infection/collection were considered involvement on Radiology, but was found normal tissue during surgery.

## Discussion

In the present study we evaluated the Radiological and surgical correlation of patient with rhino cerebral mucormycosis The incidence was found to be male 43.3% with female 56.7% in ratio of 0.76:1 in study. Nasal symptoms such as nasal obstruction with facial pain, nasal discharge, headache, facial numbness and unilateral facial swelling are more common symptoms present in all cases. Radiological findings such as mucosal thickening and clouding of sinuses and bone erosion were seen in all cases and intracranial extension seen in 16.5% cases.

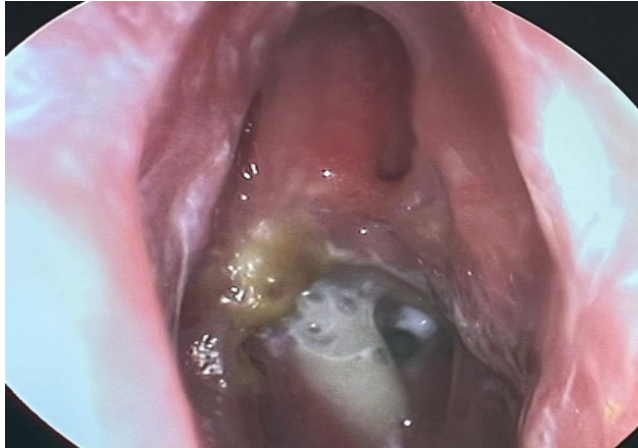
Three factors are key to a successful outcome of the therapy for mucormycosis [1] Reversal of the underlying predisposition; [2] Aggressive surgical debridement; and [3] Aggressive antifungal therapy, with early initiation and high drug doses. Failure to undertake all three of these interventions simultaneously has a significant and negative impact on outcome. As we have seen in our study we found though we evaluate every patient with

radiological investigation which are utmost necessary to plan for surgical management but actual plan is always decided on the basis of the surgical findings intraoperatively. According to

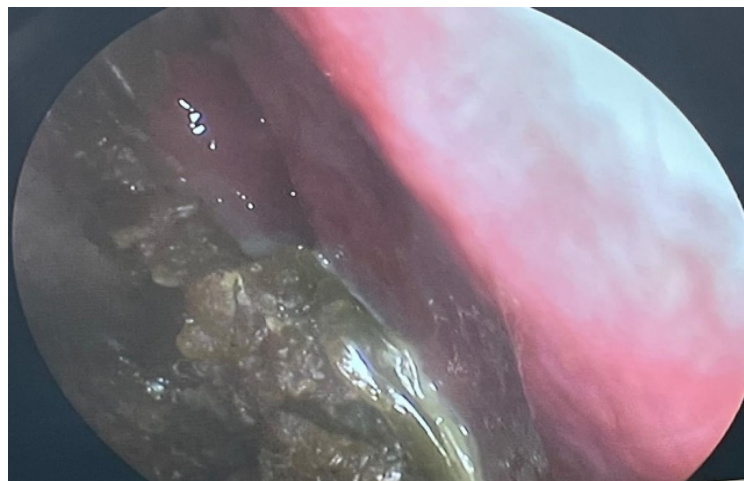
study surgical findings have more specificity than radiological findings in diagnosis and management of mucormycosis in covid 19 patients.



**Figure 1: Black eschar Image**



**Figure 2: Pre-operative nasal endoscopic seen over hard palate, Findings of patient**



**Figure 3: Post operative nasal endoscopic findings of patient**

Aggressive surgical debridement requires removal of all dead tissue and of tissue that appears to be so severely compromised that its continued viability is in questioned. Reconstruction of defect may be required once the infection has been cured.

The optimal duration of therapy for mucormycosis is not known precisely. If possible, antifungal administration should be continued for at least 3 months after [1] All clinical abnormalities resolve or stabilize, leaving no clinical evidence of infection at the involved sites; and [2] Scans, x-rays

and laboratory studies yield normal or stable results. Careful follow up should continue for at least 1 year to confirm that there is no evidence of recurrent infection. With this approach, recurrence should be rare [5].

Mucormycosis, formerly thought to be always community acquired, is now recognized as also being a nosocomial infection associated with various procedures or devices used in hospitals, including antifungal prophylaxis, bandages or medication patches, intravenous catheters and even tongue depressors.

### Conclusion

With increasing rate of mucormycosis in post covid era it is utmost important to diagnose and treat the deadly disease of mucormycosis as soon as possible.

The recent technology of radiological investigations is boon for the earliest diagnosis and proper planning for management forehead surgical intervention.

Radiological investigation serves as road map for the management and also helps in locating the disease in hidden space like infratemporal fossa. At the same time clinical assessment during surgery is also important as vital tissue and necrosed tissue can be distinguished on surgical findings.

In few cases there was dispute in correlation of radiological and surgical findings while in most of the cases both correlated.

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