

MAXILLECTOMIES AND ORBITAL EXENTERATIONS IN COVID-19 PATIENTS WITH MUCORMYCOSIS – OUR EXPERIENCE WITH RESECTIONS, RECONSTRUCTION AND THEIR OUTCOMES

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Abstract

Background: Infection causes reduced immunity and increased susceptibility to Mucormycosis. Mucorales invade blood vessels, resulting in hemorrhage and thrombosis of blood vessels and tissue necrosis. Rhino-orbito-cerebral form is the frequent type with necrosis of tissues in nasal mucosa, nasal septum, the maxilla, the ethmoids, the orbit and contents, sphenoid sinuses, and Intracerebral extension through cavernous sinuses with thrombosis. The current study aimed to determine the pattern of Mucor infections, the type and extent of maxillary and other resections, and the role of primary flap cover in patients with rhino-orbital Mucormycosis.

Methodology: The study was done from May to August 2021 at Gandhi Hospital and 250 patients with a rhino-orbito-cerebral form of Mucormycosis were included.

Results: Age-wise distribution 52.40% were in the age group of 45-65 years with males at 67.20%. More than 80% were COVID-affected. Diabetes was the major risk factor along with steroid use. 63% of admissions were for Rhino-Orbito cerebral form. Type IIB and IIIB were the common maxillectomy done. Eleven primary flaps were done with four developing complications. 16.80% of deaths were seen.

Conclusions: Rhino-orbit cerebral Mucormycosis was the common form, the majority were diabetic on steroid usage having got COVID-19. Pedicled flaps were the flaps of choice for primary cover after resection. Type IIB and III Maxillectomy were needed in the majority of cases.

Keywords: Mucormycosis, COVID, Maxillectomy, Reconstruction, Flap.

Introduction

The global health crisis of coronavirus disease 2019 (COVID-19), stemming from the novel Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), persists as a considerable concern worldwide. The efficacy of systemic glucocorticoids in enhancing survival rates among individuals with moderate to severe COVID-19 infections is widely acknowledged. However, their extensive utilization poses a serious threat of secondary bacterial or fungal infections. [1, 2] While the susceptibility to fungal infections such as *candida*, *aspergillus*, and *pneumocystis jiroveci* in the context of COVID-19 is well-documented. [2-5] The sudden and unprecedented rise in reported cases of Mucor infection within these specific groups presents a novel and emerging challenge. The second wave of COVID-19 was accompanied by a new epidemic of Mucormycosis in India. Patient risk factors for Mucormycosis are poorly controlled diabetes mellitus, metabolic acidosis, high-dose glucocorticoid therapy, penetrating trauma or burns, persistent neutropenia, and chelation therapy with deferoxamine. Mucorales have an exceptional capacity to invade blood vessels, resulting in hemorrhage and thrombosis of blood vessels and tissue necrosis. [6] Cytokine storm in COVID patients, along with risk factors like Diabetes mellitus, steroid use, hypoxia, and prolonged hospitalization with oxygenation facilitated mucormycosis. The rhino-orbito-cerebral form has been the common presenting type in COVID-19 patients. In this form, avascularity and necrosis of tissues in the nasal mucosa and nasal septum are seen along with maxilla, ethmoids, eye with orbit, sphenoid sinuses, and Intracerebral extension. Mucormycosis is caused by a fungus mucormycetes which destroys tissue and necrosis due to its capacity to invade blood vessels to cause thrombosis. [7] Therefore, maintaining a heightened level of clinical suspicion with the goal of prompt diagnosis and vigorous treatment is crucial for achieving a favorable outcome in these patients. Recent entries in the medical literature have highlighted several reports detailing the manifestation of mucormycosis in COVID-19 patients across diverse presentations. To study the pattern of Mucor infections, the type and extent of maxillary and other resections, and the role of primary flap cover in patients with rhino orbital Mucormycosis.

Material and Methods

The study was done at Gandhi Hospital and Medical College, Secunderabad, Telangana, from May to August 2021. A total of 250 patients with the rhino-orbito-cerebral form of Mucormycosis were included in the study after obtaining the necessary consent to include the photographs. A clearance from the Institutional Ethical Committee was taken for conducting the study.

Inclusion criteria

- ✧ Patients admitted with Mucormycosis requiring maxillary resections with or without orbital exenteration irrespective of COVID-19 status
- ✧ Post FESS (functional endoscopic sinus surgery) patients presenting again with disease

Exclusion criteria

- ✧ Patients of Mucormycosis infection with indications for maxillectomy but terminally ill.
- ✧ Patients who did not consent to surgery.

A total of 1017 patients were admitted with Mucormycosis till the end of August 2021. All clinical forms of Mucor mycosis were encountered. The patients were screened with either a CT of the paranasal sinuses or an MRI of the sinuses and orbit with the brain before undertaking surgical procedures to know the extent of the Mucormycotic disease. In almost all the patients the Maxillary sinuses were involved. Anterior Ethmoids and posterior ethmoid sinuses were the next frequently involved. The less involved were the sphenoid sinuses. Most of the patients had a disease involving all the sinuses. In 21 patients, the MRI findings were suggestive of intracranial extension in the form of cavernous sinus thrombosis and abscesses.

Preoperative dental impressions were taken of the patients who were planned for bony resections. Later after discharge, the patients were provided with temporary obturators.

Operative procedure in these patients was planned based on both the clinical and CT or MRI findings of the paranasal sinuses. Debridement and Resection of the diseased bone were done either through a Weber Ferguson incision or an intra-oral incision. The extent of resection of the maxilla was decided based on the intraoperative finding of the necrosed bone.

Statistical analysis: All the available data was uploaded to an MS Excel spreadsheet and analyzed by SPSS version 21 in Windows format. The continuous variables were represented as mean, standard deviation, and percentages, and the categorical variables were represented as p values, and values (<0.05) were considered significant.

Results

All the Mucormycosis patients were admitted during the months of May to July 2021 to this hospital. A total of two hundred and fifty (250) patients presenting with symptoms of rino-orbital Mucormycosis have been included in this study. We have observed a spectrum of clinical presentations in these patients with symptoms of sinusitis, nasal blockage, nasal discharge of brown-colored fluid, oral cavity involvement in the form of loose tooth and gingival sinuses, necrosis of gingival and/or palatal mucosa, orbital involvement presenting with loss of vision. Skin involvement was seen in a few with multiple sinuses or necrosis of skin overlying the bony maxilla. work.

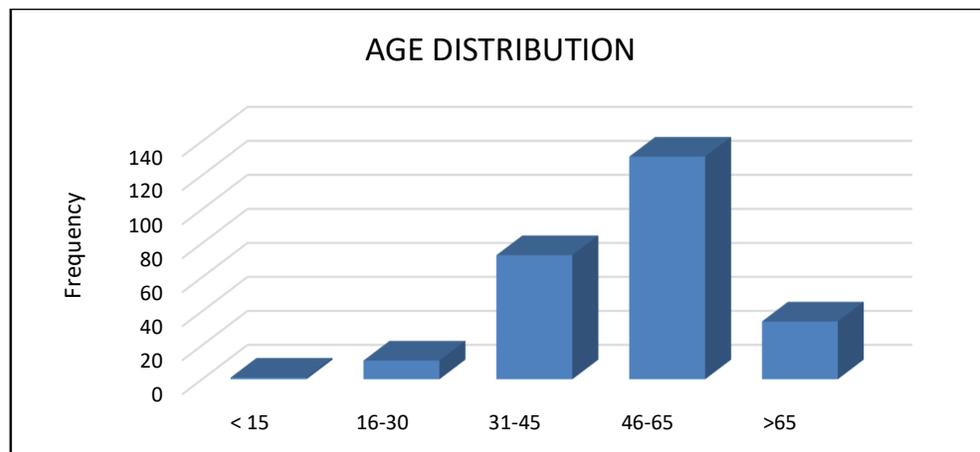


Figure 1: Age-wise distribution of cases of mucormycosis included in the study.

In this study most common involvement was the age group of 46 – 65 years 131/250 (52.4%) followed by 31 – 45 years 73/250 (29.2%) depicted in Figure 1. The number of males in this study was 168/250 (67.2%) and the number of females in the study was 82/250 (32.8%).

The COVID-19 infections in this epidemic were during the months of April to June 2021. 86.80% were infected. (Figure 2) Almost 76.80% were hospitalized for COVID-19 infection, 23.20% were not hospitalized and were in home isolation. Nearly 79.60% were oxygen-dependent during COVID-19 infection. About 77.20% were treated with steroids during COVID-19 infection and few who were in home isolation also were prescribed steroids leaving only 22.80% in whom steroids were not used. Remdesivir and Tocilizumab were also used in treatment for COVID-19 infection which are immunomodulating drugs increasing the risk for Mucor infections. 94.40% of the patients were not vaccinated for COVID-19 infection. 5.6% had the first dose of vaccination.

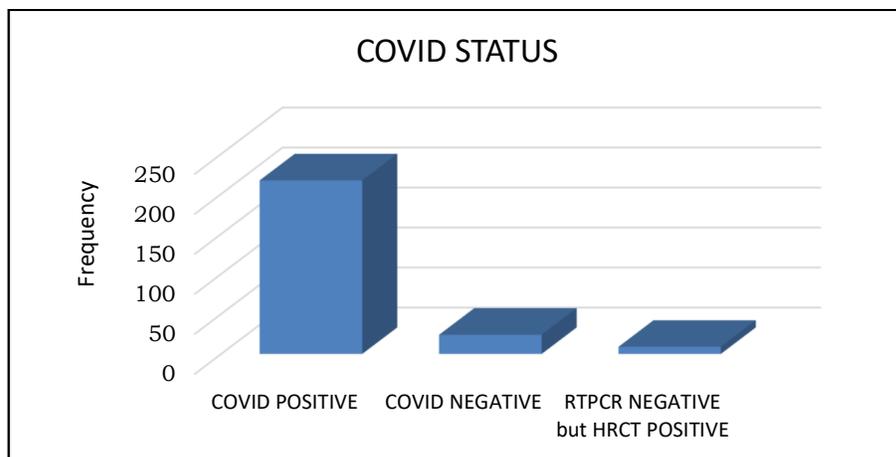


Figure 2: Covid status of the patients with mucormycosis included in the study

Co-morbidities: Diabetes mellitus either Denovo or of long duration was the major comorbid condition. Other associated co-morbidities have been Hypertension in 61.2%, hypothyroidism in 9.2%, cardiovascular disease in 8.4%, 27(10.80%) patients had acute kidney injury at the time of admission, chronic kidney disease in 16, one patient had Hemophilia.

Clinical presentation: 63.81% of the 1017 patients presented with a Rhino-orbital form of infection.

Rhino orbito cerebral type: We observed three clinical patterns and spread In the Rhino-orbito cerebral type. (Table 1) Type I: The disease starts in the nasal mucosa and spreads to the sinuses in the order of maxillary, ethmoids, lamina papyracea, eye, frontal and sphenoid. In some, this spread reaches the cavernous sinus causing thrombosis (51.9%). Type II: Here, the disease starts in the nasal mucosa spreading laterally to the maxillary sinuses, causing skin and subcutaneous tissue necrosis of the cheek (16.8%). Type III: in this type, the disease starts in the nasal mucosa or tooth, and spreads to involve the alveolus of the tooth causing loosening of the tooth, gingival and palatal abscess, and infratemporal fossa abscess (31.3%). We have encountered 42 patients who had involvement of the skin overlying the bony maxilla. At admission, 21(8.4%) had cavernous sinus thrombosis, 9 (3.6%) had a frontal abscess, and 4 (1.6%) had a frontal abscess.

Table 1: Clinical pattern of disease spread in the cases of the study

Pattern of Disease Spread	Number of Patients
TYPE I	158 (63.2%)
TYPE II	49 (19.6%)
TYPE III	43 (17.2%)

Operative treatment: Standard classification of maxillectomy described in NELLIGAN textbook of plastic and reconstructive surgery.

Type I: Limited Maxillectomy: Palate intact, Orbital floor intact

TYPE II: Subtotal Maxillectomy:

IIA Palatal defect <50%, Orbital floor intact

IIB Palatal defect >50%, Or Anterior arch defect. Orbital floor intact

TYPE II: Subtotal Maxillectomy:

IIA Palatal defect <50%, Orbital floor intact

IIB Palatal defect >50%, Or Anterior arch defect. Orbital floor intact

TYPE IV: Orbitomaxillectomy: Palate intact. Orbital exenteration

In most patients, the resection involved the palate, the tooth-bearing segment of the maxilla, and the anterior wall of the antrum. We have tried to segregate our resection into the proposed standard classification. The majority of the resections fell into TYPE IIB, and TYPE IIIB followed by IIA, I, and IIIA (Table 2). The approach was intraoral in 88.2% and Weber Ferguson incision in 10.8%.

Table 2: Type of Maxillary Resection

<i>Type of Resection</i>	<i>Number of Patients</i>
TYPE IA	25 (10.0%)
TYPE IB	17 (6.8%)
TYPE IIA	36 (14.4%)
TYPE IIB	77 (30.8%)
TYPE IIIA	31 (12.4%)
TYPE IIIB	64 (25.6%)
TYPE IV	0(0.00%)
TOTAL	250(100%)

In standard TYPE I, there is resection of the bony maxilla keeping the palate intact. During this study, we have observed that in some the anterior wall of the maxilla was viable but the mucosa lining the cavity was necrosed. In these patients, we undertook two types of procedures keeping the bony maxilla intact and hence we came up with this proposal of subclassifying TYPE I into two.

TYPE IA: Resection of the alveolar segment only. The palate and the maxillary antrum are intact. Access to the sinus cavity can be gained from the resected alveolus for the clearance of the necrotic tissue in the antrum. (Figure 3) and (Table 2)



Figure 3: showing the Type IA: Resection of the alveolar segment

TYPE IB: Removal of the alveolar segment and anterior wall of the antrum keeping the palate intact. (Figure 4) and (Table 2)

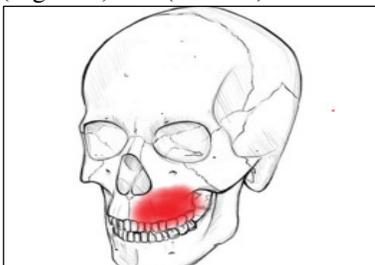


Figure 4: Type IIB Removal of the alveolar segment and anterior wall of the antrum

Orbital exenterations: Simultaneous orbital Exenterations were done by the team of Ophthalmologists and Plastic surgeons in 81(32.0%) patients of which 70 were done along with maxillectomies and 11 were only orbital exenterations.

Reconstructive procedures: A total of eleven (11) primary reconstructive procedures in the form of skin flaps were done to cover the compound defect after bone resection. In one patient, a Cervico facial advancement flap was done to cover the compound defect of the face a week after the primary surgery. (Table 3) In a few patients who were presented with necrosis and or abscess of palate and mucosa, we faced difficulty in closure on the intra-oral side after resecting the palate, and the patients were left with an oroantral fistula. We have provided obturators for temporary support till the patient's nutritional status improves and the treatment for Mucormycosis is completed. We intend to take up these patients for further reconstructive surgeries.



Figure 5: Showing the reconstruction flap designs and complications

Table 3: Primary Reconstruction (N=11)

<i>Primary Reconstruction with Flaps</i>	<i>Number of Patients</i>
Cervico Facial Advancement Flap	4
Extended Forehead Flap	1
Buccal Mucosal Flap	3
Cheek Advancement Flap	2
Scalping Flap	1
Total	11

Post-operative care: During the postoperative stay of these patients, we have seen a wide range of presentations like acute kidney injury, hypokalemia, and hyponatremia. Other complications Table 4. Oro-antral fistula was a major concern noted in seven of Weber Fergusons and 27 intra-oral approach patients. All these patients were managed by antibiotics, wound debridement, and regular dressings. Few have been discharged and those with compound defects are waiting for reconstruction. Few patients needed a second surgery. Out of the fourteen (14) intracranial abscesses, five patients had frontal abscesses, and eight developed temporal abscesses which were operated by neurosurgeons.

Post-operative complications of flaps: A persistent complication had been repeated wound dehiscence even after flap division inset was done in the patients where the forehead and scalp flaps were used. But surprisingly there was no loss of flap even after division (Figure 5). In one of these patients, we had to take a cervicofacial flap to prevent further marginal dehiscence. Mucormycosis is not only a disfiguring and morbid disease but is also a cause of significant mortality (16.80%).

Table 4: Postoperative complication in the cases of the study

<i>Post Operative Complications</i>	<i>Number of Patients</i>
Contralateral Hemiparesis	11
Ipsilateral Hemiparesis	8
Suture Infection	9
Wound Infection	11
Wound Dehiscence	6
Marginal Skin Necrosis	7
Flap Necrosis	5
Intracranial Abscess	14

Discussion

Mucormycosis is a life-threatening infection mostly observed in immunocompromised patients. The major risk factors for mucormycosis include uncontrolled diabetes mellitus in ketoacidosis, other forms of metabolic acidosis, treatment with corticosteroids, organ or bone marrow transplantation, neutropenia, trauma and burns, malignant hematologic disorders, and deferoxamine therapy in patients undergoing hemodialysis [8, 9]. Although Mucormycosis infections have surfaced, we have faced an epidemic of the disease in India. The incidence of mucormycosis has increased more rapidly during the second wave than during the first wave of COVID-19 in India [10]. Mucors involving the nose and sinuses followed by the rhino orbital were the common types of presentation here [11, 12]. COVID-19-positive immunocompromised status with newly surfacing hidden diabetes, steroid use for durations exceeding that recommended by WHO, and prolonged stay in intensive care units were predisposing factors for the rapid surge in mucorepidemic [13]. In this study, only the rhino orbito cerebral form was observed, where the maximum number of patients were diabetics [11]. Although Mucormycosis has been reported in a few non-diabetics, for some unknown reasons, our hospital received patients who were diagnosed with diabetes during the study period. The epidemic is fading and there are occasional admissions. Mucormycosis infections in association with COVID-19 have been a big challenge for medical professionals in this part of the country over the past few months. Despite aggressive treatment, either in the form of surgical debridement or antifungal medications, the mortality rate was around 16.80% as compared to other studies where it was higher [8].

All patients with mucormycosis included in this study were admitted between May and August 2021. All patients who were infected with coronavirus were infected between April and July 2021. There were no cases of mucormycosis in patients infected with COVID-19 during the first wave. An important observation in this study was that mucormycosis was mostly observed in men [2]. Agricultural or construction workers with poorly controlled diabetes are mostly at risk. The common age group at presentation is 45-65 years [9]. Mucormycosis is a devastating and highly morbid disease. This can to some extent be prevented with awareness among the population regarding diabetes, its early detection, proper treatment, and keeping the blood sugars in the normal range. Mucormycosis treatment

is a multispecialty treatment and needs thorough surgical debridement [14]. In all patients, necrosed skin, mucosa, and bone were debrided [15]. Treating patients with mucormycosis has been very challenging for surgeons because the extent of disfigurement to the patients in some cases had been very extensive to the extent of involving the entire half of the face, including the bone framework. Oroantral and Oronasal fistulas and loss of the palate incapacitate the patient, causing regurgitation and difficult deglutition. Reconstructive procedures must be performed early to prevent malnutrition and disability. Similar studies on primary reconstruction have been published, in which free flaps were used for reconstruction [16]. In this study, only primary locoregional flaps were used to reconstruct the defect. In one patient, there was a need for recurrent surgery and multiple flaps [17]. Treatment for mucormycosis in COVID-recovering patients is a different scenario from that in the pre-pandemic disease. The extent of the spread of the fungal infection in this epidemic with COVID-19 infections was fast and extensive. The surgical resection in this setup needed to be determined based on the extent of bone or tissue necrosis on the operating table. The lack of high-end investigations, such as bone scintigraphy, to determine the extent of necrosis and the need to make early and fast decisions for patients in this government hospital has helped us develop an algorithm for maxillectomy in this epidemic. Nearly all patients with mucormycosis were COVID-positive; 98% of them were diabetic and were hospitalized, requiring steroids and oxygen. Most of them were agricultural or construction workers. Poor oral hygiene with recent tooth extractions and uncontrolled diabetes have been noted as risk factors. Wearing the same mask repeatedly without proper washing, drying, or disposal may also be a trigger for the epidemic. Reconstruction of the compound defects by a plastic surgery team was performed in a few patients and was confined to only pedicled flaps, and the flaps survived well. There were a few complications, such as flap necrosis, but there was no complete loss of flaps.

Conclusion

Rhino-orbito cerebral Mucormycosis was the common form, majority were diabetic on steroid usage having got COVID infected. Pedicled flaps were the flaps of choice for primary cover after resection. Type IIB and III Maxillectomy were needed in the majority of cases. While there were some complications, including flap necrosis, complete loss of flap did not occur. We believe that pedicled flaps remain a viable option following meticulous primary mucor resection.

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