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Beyond the Survival: A Retrospective analysis of Clinical course and Outcomes of Post-COVID associated Rhino-Maxillary Mucormycosis

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ABSTARCT

Aim: To retrospectively analyze the clinical presentation, risk factors, radiological findings and management strategies in patients diagnosed with rhinomaxillary and mandibular mucormycosis.

Methods: This retrospective study included 16 patients with a documented history of COVID-19 infection and histopathologically confirmed rhinomaxillary or mandibular mucormycosis who presented to our institute between June 2021 and May 2023. Clinical features, comorbidities, radiological findings, treatment modalities, and follow-up outcomes were recorded and analyzed.

Results: The study population comprised 11 males and 5 females, with a mean age of 49.7 years. Diabetes mellitus was the most common comorbidity (69%), followed by hypertension and hypothyroidism. Ten patients required hospitalization during COVID-19 illness, and corticosteroids were administered in eight cases. Common clinical features included facial swelling, infraorbital paresthesia, visual disturbances, and intraoral findings such as tooth mobility and pus-discharging sinuses. Radiological evaluation demonstrated maxillary bone erosion and paranasal sinus involvement in all patients, with one case showing mandibular involvement. All patients underwent aggressive surgical debridement followed by systemic antifungal therapy. Postoperative complications included oroantral fistula formation in six patients, one mortality, and one recurrence.

Conclusion: Rhinomaxillary mucormycosis is an important post–COVID-19 complication, particularly in patients with diabetes mellitus and a history of corticosteroid use. Early diagnosis, aggressive surgical intervention, and appropriate antifungal therapy are essential for improving clinical outcomes and reducing disease-related morbidity.

Keywords: COVID-19, Mucormycosis, Rhinomaxillary, Amphotericin B, Corticosteroids

INTRODUCTION

Mucormycosis is an aggressive, angioinvasive opportunistic fungal infection caused by saprophytic fungi belonging to the order Mucorales, most commonly Rhizopus species. These organisms are ubiquitously present in soil, decaying organic matter, animal manure, and bread moulds. The disease predominantly affects immunocompromised individuals, particularly those with poorly controlled diabetes mellitus, and is associated with a high rate of morbidity and mortality if not diagnosed and treated promptly. Other recognized predisposing factors include hematological malignancies, solid organ transplantation, chronic renal or hepatic disease, prolonged corticosteroid therapy, and acquired immunodeficiency states.

Before the COVID-19 pandemic, mucormycosis was considered a rare entity globally, with an estimated prevalence of 0.005–1.7 cases per million population. In contrast, India has historically reported a much higher prevalence, approximately 0.14 per 1,000 population, largely attributed to the high burden of diabetes mellitus. During the second wave of the COVID-19 pandemic, a sudden and unprecedented rise in cases of rhino-cerebral and rhinomaxillary mucormycosis was observed across the country, prompting several Indian states to declare mucormycosis a notifiable disease in May 2021 in accordance with Government of India directives.

The surge in mucormycosis cases following COVID-19 has been attributed to a multifactorial interplay of host and disease-related factors. SARS-CoV-2 infection is known to cause immune dysregulation, endothelial dysfunction, and a hyperinflammatory state, which together facilitate fungal invasion. The widespread use of systemic corticosteroids during the management of moderate to severe COVID-19 further compounds this risk by inducing immunosuppression and worsening glycaemic control. Additionally, COVID-19–associated alterations in iron metabolism and microvascular thrombosis create a favourable environment for the proliferation of Mucorales species.

Clinically, rhino-cerebral and rhinomaxillary mucormycosis often presents with nonspecific symptoms resembling complicated sinusitis, including nasal obstruction, facial pain or swelling, orbital involvement, cranial neuropathies, and palatal or alveolar bone necrosis. Maxillary involvement is commonly reported due to its rich vascular supply and proximity to the paranasal sinuses, whereas mandibular involvement is exceedingly rare and sparsely documented in the literature. Given the dramatic rise in post-COVID-19–associated mucormycosis and the potential for rapid disease progression, early recognition and aggressive management are essential. The present study aims to describe the clinical profile, risk factors, radiological findings, management strategies, and outcomes of patients diagnosed

with rhinomaxillary mucormycosis in the post-COVID-19 period, with particular emphasis on a rare case of mandibular involvement managed at a tertiary care center.

MATERIALS AND METHODS

Study Design and Setting

This retrospective study was conducted at a tertiary care institute between June 2021 and May 2023. Medical records of patients diagnosed with mucormycosis during the post–COVID-19 period were reviewed. The study population included patients managed by a multidisciplinary team involving the Departments of Oral and Maxillofacial Surgery and Otolaryngology–Head and Neck Surgery.

Patient Selection

A total of 16 patients with a documented history of COVID-19 infection and histopathologically confirmed rhinomaxillary or mandibular mucormycosis were included in the study. A prior history of COVID-19 infection was confirmed through documented reverse transcription–polymerase chain reaction (RT-PCR) reports or hospital discharge summaries. Patients with a history of irradiation to the head and neck region and those receiving anti-resorptive therapy were excluded from the study.

Data Collection

Patient data were retrieved from hospital medical records and included demographic details, COVID-19–related history, comorbidities (with particular emphasis on diabetes mellitus), clinical presentation, radiological findings, microbiological and histopathological results, treatment modalities, and clinical outcomes.

Clinical features assessed included nasal obstruction, crusting, facial pain and edema, proptosis, ptosis, chemosis, ophthalmoplegia, headache, fever, neurological symptoms, black eschar in the nasal cavity or over the hard palate, and intraoral findings such as tooth mobility and pus-discharging sinuses.

Radiological and Diagnostic Evaluation

All patients underwent contrast-enhanced computed tomography (CECT) of the paranasal sinuses and maxillofacial region to evaluate the extent of bony destruction and soft tissue involvement. The diagnosis of mucormycosis was established through microbiological examination using potassium hydroxide (KOH) mount and fungal culture, and was definitively confirmed by histopathological identification of broad, non-septate hyphae with right-angle branching.

Management Protocol

All patients were managed using a standardized treatment protocol that included prompt initiation of systemic antifungal therapy and aggressive surgical debridement. Intravenous liposomal amphotericin B was administered at a dose of 8 mg/kg body weight for a duration of four weeks, followed by oral posaconazole (300 mg once daily) for three months.

Surgical intervention was tailored according to the extent of disease and included functional endoscopic sinus surgery, curettage and debridement of necrotic maxillary bone, extraction of mobile teeth, and partial or total maxillectomy when indicated. One patient required additional mandibular debridement due to mandibular involvement, and orbital exenteration was performed in one case with extensive orbital disease.

Glycaemic control and management of associated comorbidities were optimized in coordination with the respective medical specialties.

Follow-up

All patients were followed up clinically and radiologically to assess disease resolution, postoperative complications, recurrence, and healing status. A minimum follow-up period of one year was maintained for all surviving patients.

RESULTS

A total of 16 patients were included in the study, comprising 11 males and 5 females, with an age range of 35 to 75 years (mean age: 49.7 years). The relevant demographic and clinical data are summarized in Table 1. Type 2 diabetes mellitus was the most common comorbidity, present in 11 patients, followed by hypertension in two patients and hypothyroidism with hypotension in one patient. Ten patients required hospitalization during their COVID-19 illness, and corticosteroid therapy was administered in eight cases. Among these, six patients received intravenous dexamethasone for 3–5 days, while two patients received corticosteroids for a prolonged duration of up to 20 days.

Table 1: Overview of Clinical Data and Outcomes

SR. NO.	**Age/Sex**	**Established diagnosis of Diabetes mellitus**	**Covid Testing Result**	**Presentation**	**HPE and fungal smear (broad aseptate hyphae/angioinvasion)**	**Radiological evidence**	**Surgical Treatment given**	**Post-surgery complications**	Rehab and quality of life
1.	48/M	Yes	Positive	Left side facial swelling 12 days Tooth pain and mobility 4 days	Yes	Yes	Debridement and curettage wrt left maxilla. FESS	Oro-antral communication left buccal region	

2.	52/M	No	Positive	Right side infraorbital paresthesia, facial swelling 1week, mobile teeth right side, mid palatal discoloration, vision loss	Yes	Yes	Debridement and curettage wrt left maxilla. FESS. Exenteration right eye	Oro-antral communication mid palatal region	
3.	60/F	No	Positive	Leftt side infraorbital paresthesia, facial swelling, mobile teeth b/l, Multiple draining sinuses left side mandible region	Yes	Yes	Debridement and curettage wrt B/L maxilla. FESS.	Oro-antral communication mid palatal region Recurrence in mandible after 2month of surgery	
4.	35/M	Yes	Positive	B/l side facial swelling, mobile teeth and multiple draining sinuses	Yes	Yes	Debridement and curettage wrt B/L maxilla. FESS.	none	
5.	40/M	Yes	Positive	Left side facial swelling, mobile teeth	Yes	Yes	Debridement and curettage wrt Left maxilla. FESS.	none	

6.	52/M	Yes	Negative	Left side infraorbital paresthesia, facial swelling, mobile teeth	Yes	Yes	Debridement and curettage wrt B/L maxilla. FESS.	Oro-antral communication wrt left buccal region	
7.	43/M	No	Positive	Left side facial swelling, mobile teeth	Yes	Yes	Debridement and curettage wrt Left maxilla. FESS.	none	
8.	52/M	Yes	Positive	Left side infraorbital paresthesia, facial swelling, mobile teeth	Yes	Yes	Debridement and curettage wrt B/L maxilla. FESS.	Oro-antral communication wrt left buccal region	
9.	75/M	Yes	Negative	Left side infraorbital paresthesia, facial swelling	Yes	Yes	Debridement and curettage wrt B/L maxilla. FESS.	none	
10	52/F	Yes	Positive	Right side facial swelling, paresthesia, b/l upper mobile teeth	Yes	Yes	Debridement and curettage b/l maxiila with I and D right buccal space, FESS	Death 2 days after surgery due to cardiopulmonary arrest	
11.	50/F	Yes	Positive	Pain and swelling in maxillary	Yes	Yes	Debridement and curettage	none	

				anteriors and posterior region, palatal swelling also present.			wrt B/L maxilla. FESS.		
12.	39/M	No	Positive	Paresthesia on left side of mandible body region. Pus discharge left 3rd molar region	Yes	Yes	Debridement and curettage wrt left mandible	none	
13.	65/F	YES	Positive	Swelling and pus discharge wrt maxillary anteriors and posteriors region, palatal swelling also present	Yes	Yes	Debridement and curettage wrt B/L maxilla. FESS.	none	
14.	57/F	No	Positive	Right infraorbital paresthesia. Mobile right upper posterior teeth	Yes	Yes	Debridement and curettage wrt right maxilla. FESS.	Oro- antral communication right buccal region	
15.	36/M	Yes	Positive	b/l infraorbital paresthesia and	Yes	Yes	Debridement and curettage	none	

				Multiple mobile right upper teeth			wrt b/l maxilla. FESS.		
16.	40/M	Yes	Positive	Right side facial swelling, mobile right upper teeth	Yes	Yes	Debridement and curettage wrt b/l maxilla. FESS.	none	

Clinical Presentation

The most common presenting symptoms included facial swelling, infraorbital paresthesia, eye pain, and visual disturbances. Intraoral examination revealed pus-discharging sinuses in four patients, tooth mobility in twelve patients, and palatal discoloration in one patient (Figure 1). One patient presented with an atypical manifestation characterized by swelling and paresthesia involving the body of the mandible, along with pus discharge from the third molar region, in association with concurrent maxillary involvement.

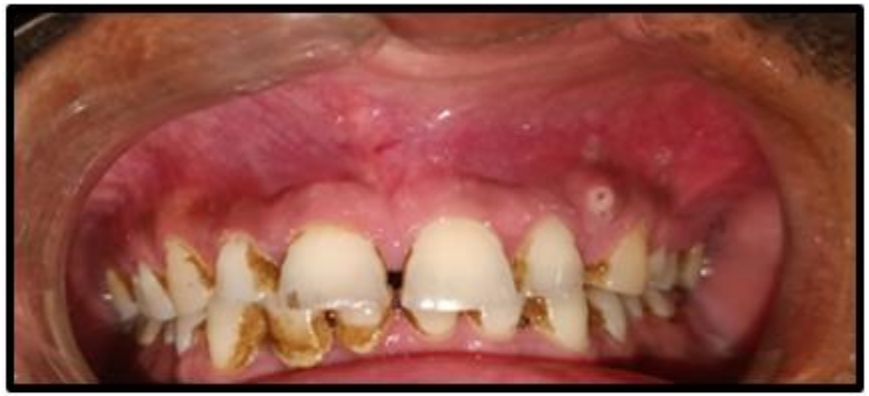

Figure 1: Intraoral view of draining sinus in left canine region

Radiological Findings

All patients underwent contrast-enhanced computed tomography (CECT) to assess the extent of disease. Imaging demonstrated lytic erosion of the alveolar process of the maxilla and hard palate, along with mucosal hypertrophy and paranasal sinus opacification in all patients (Figure 2). Destruction of the mandibular body was observed in the patient diagnosed with mandibular mucormycosis.

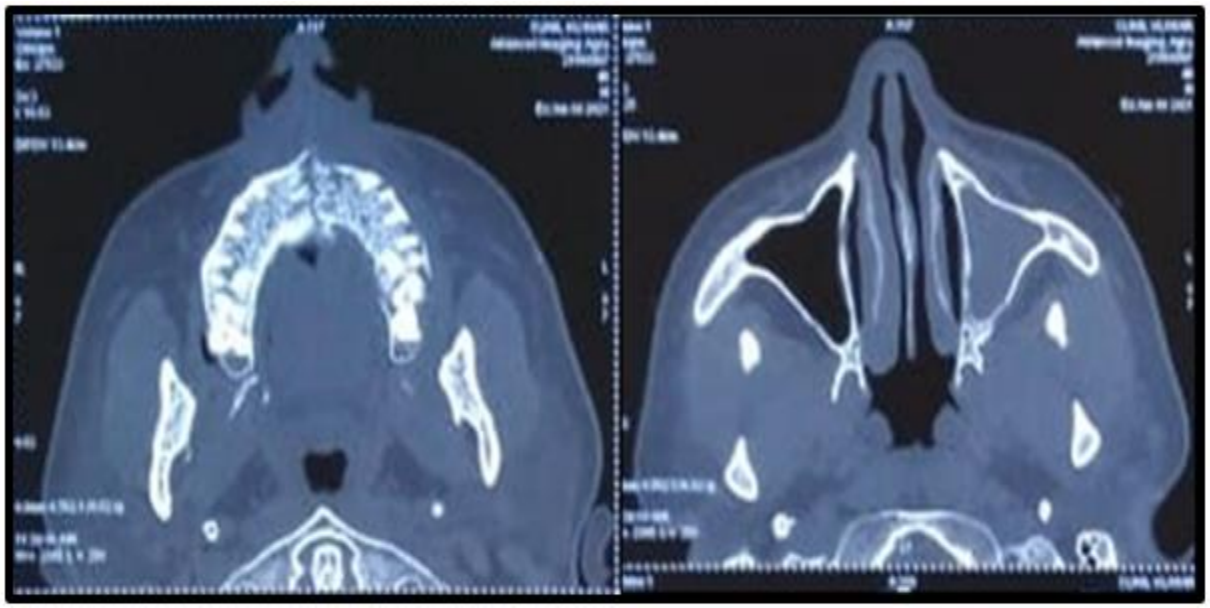

Figure 2: CECT face axial section showing lytic erosion of alveolar process of maxilla and hard palate with mucosal hypertrophy and sinus filling.

Management

Surgical intervention consisted of aggressive debridement and curettage of necrotic tissue, along with extraction of mobile teeth at the affected sites (Figure 3). Functional endoscopic sinus surgery (FESS) was performed in all cases except the patient with mandibular involvement. One patient with extensive orbital disease required orbital exenteration. Histopathological examination of surgical specimens confirmed mucormycosis in all cases, with identification of Rhizopus species (Figure 4).

All patients received intravenous liposomal amphotericin B at a dose of 8 mg/kg body weight for four weeks, followed by oral posaconazole at a dose of 300 mg once daily for three months.

Follow-up and Outcomes

During the follow-up period, six patients developed postoperative oroantral fistulae (Figure 5), which were managed using obturators. One patient succumbed to cardiopulmonary arrest in the immediate postoperative period, and one patient experienced disease recurrence involving the mandibular region. The remaining patients demonstrated satisfactory healing at the surgical sites and are currently undergoing various stages of reconstructive rehabilitation.

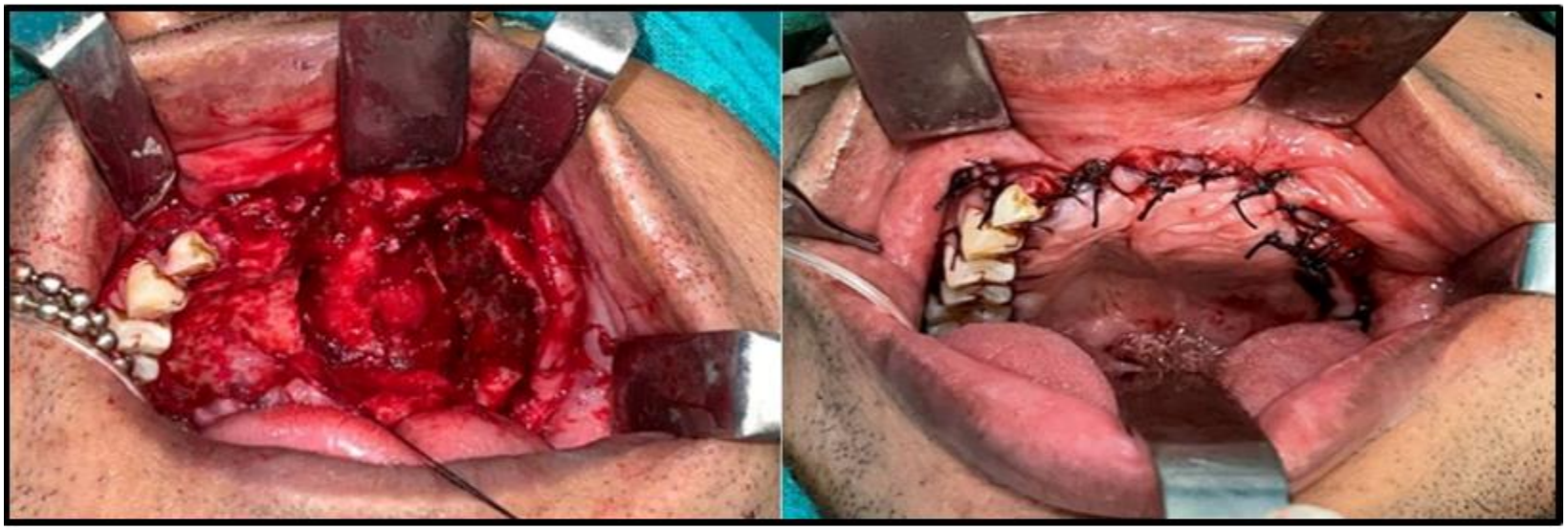

Figure 3: Intra-op picture after complete sequestrectomy, debridement and curettage and final closure.

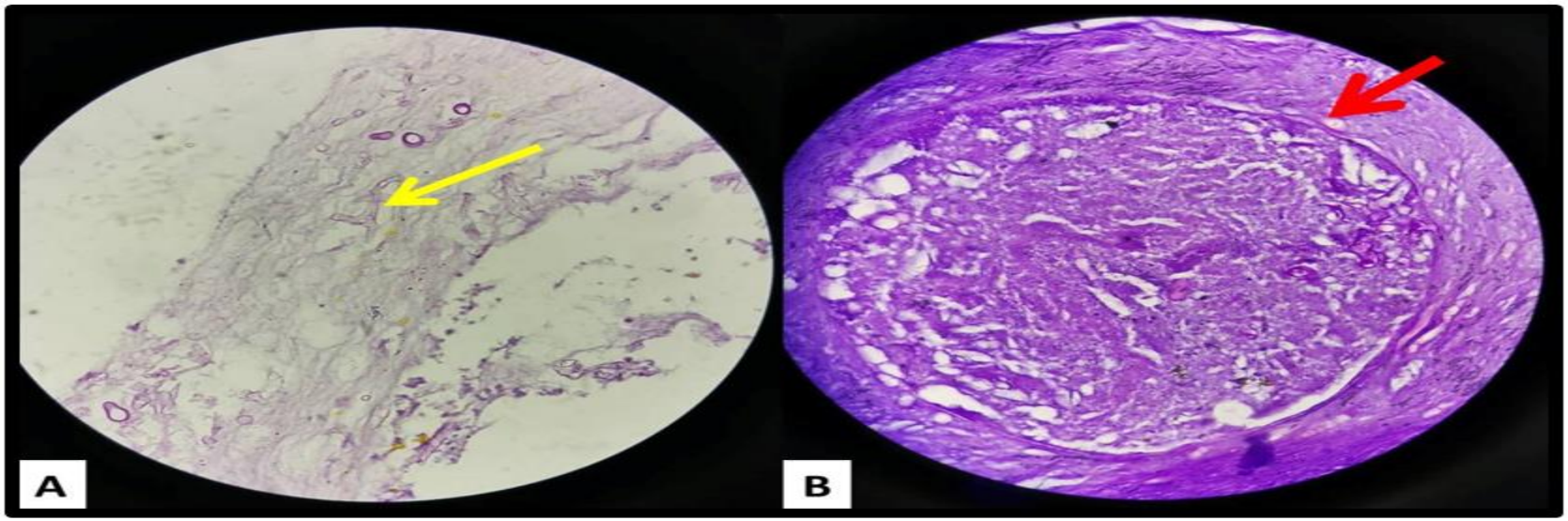

Figure 4: Final HPE showing

A. Broad branched asptate fungal hyphae (10X100 micrometer)
B. Fungal invasion of blood vessel wall (40X20 micrometer)

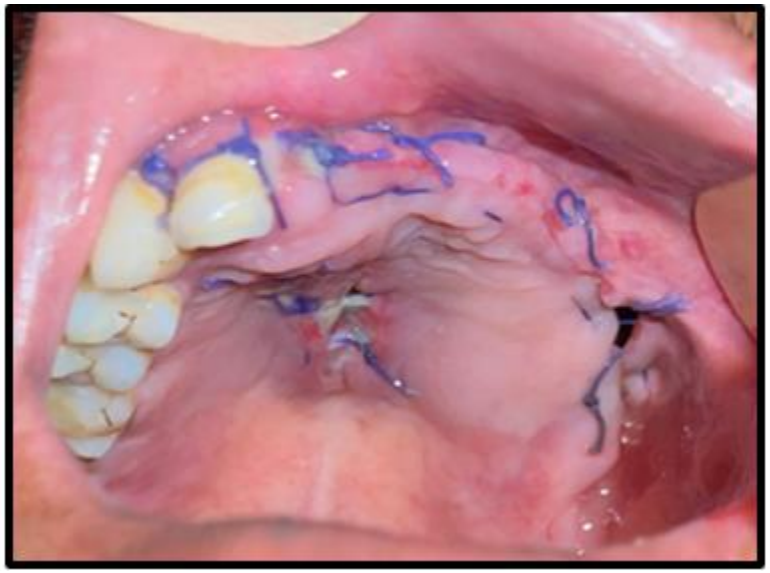

Figure 5: Intraoral view of oroantral fistula formation

DISCUSSION

Prevalence, Risk Factors, and Clinical Presentation

The second wave of the COVID-19 pandemic was associated with a marked surge in cases of mucormycosis in India [1–12]. While the global prevalence of mucormycosis ranges from 0.005 to 1.7 cases per million population, India reports a substantially higher prevalence of approximately 0.14 per 1,000 population, a difference largely attributed to the high burden of diabetes mellitus [6]. The temporal association between COVID-19 and mucormycosis is further supported by the observation of 16 cases managed at our institute over a two-year post–COVID-19 period, compared with only sporadic cases encountered prior to the pandemic. Similar trends have been reported by several authors, reinforcing the association between SARS-CoV-2 infection and secondary fungal infections [4,5].

In addition to COVID-19, mucormycosis is well recognized to occur more frequently in individuals with underlying risk factors such as diabetes mellitus, hematological malignancies, immunodeficiency states, chronic renal or hepatic disease, and prolonged corticosteroid therapy. In the Indian context, the widespread prevalence of diabetes, coupled with corticosteroid use during COVID-19 management, appears to have played a pivotal role in the increased incidence of rhinomaxillary mucormycosis.

Clinically, rhino-cerebral and rhinomaxillary mucormycosis often presents with features resembling complicated sinusitis, including facial pain and swelling, nasal obstruction, orbital symptoms, and cranial nerve involvement. Intraoral findings such as tooth mobility, pus discharge, and palatal discoloration are suggestive of maxillary bone involvement. In the present study, facial swelling, infraorbital paresthesia, eye pain, and visual disturbances were the most common presenting symptoms, with tooth mobility observed in the majority of patients. Notably, one patient presented with mandibular involvement in association with maxillary disease, an exceedingly rare presentation that has been infrequently reported in the literature.

Pathophysiological Basis of Post–COVID-19 Mucormycosis

SARS-CoV-2 infection results in significant immune dysregulation characterized by altered $CD4^+$ and $CD8^+$ T-cell responses, cytokine storm, endothelial dysfunction, and a prothrombotic state. Severe COVID-19 is also associated with profound alterations in iron metabolism, contributing to multisystem involvement [13-15]. These changes collectively create a favorable environment for the proliferation and angioinvasion of Mucorales species.

Iron plays a central role in the pathogenesis of mucormycosis. During systemic inflammation, increased ferritin release and dysregulated iron homeostasis lead to elevated levels of free serum iron, which is exploited by Mucorales for growth and tissue invasion [16]. The SARS-CoV-2 spike protein has been shown to mimic hepcidin, further disrupting iron regulation and contributing to hyperferritinemia and ferroptosis [17]. These mechanisms may explain the increased susceptibility to mucormycosis observed in patients recovering from COVID-19.

Diabetes mellitus further amplifies this risk by impairing neutrophil function, chemotaxis, and phagocytosis, while diabetic ketoacidosis creates an acidic milieu that enhances free iron availability [15]. Even in the absence of overt ketoacidosis, upregulation of endothelial glucose-regulated protein 78 (GRP78) and the fungal ligand CotH3 facilitates fungal adhesion and invasion [20]. COVID-19–related pancreatic β-cell dysfunction may also contribute to acute metabolic derangements, increasing susceptibility to opportunistic infections [19].

Role of Diabetes, Steroids, and Gender Predilection

A male predominance has been consistently reported in mucormycosis, a finding that was also observed in the present study, where male patients constituted nearly two-thirds of cases [21,22]. Diabetes mellitus was identified as the most common comorbidity, present in 69% of patients, underscoring its central role in disease pathogenesis. Comparable findings have been reported by Moorthy et al., who documented diabetes in 89% of affected patients [11].

Corticosteroid therapy, although lifesaving in severe COVID-19, is a well-established risk factor for secondary fungal infections due to its immunosuppressive effects and impact on glycaemic control. In the present study, corticosteroids were administered in half of the patients, a proportion lower than that reported by

A.K. Singh et al. [6], yet sufficient to highlight their contributory role when combined with diabetes and COVID-19–induced immune dysregulation. These observations reinforce the concept that COVID-19–associated mucormycosis results from a synergistic interaction between viral infection, metabolic dysregulation, and immunosuppression rather than a single causative factor.

Outcomes and Clinical Implications

Early diagnosis and aggressive surgical management, combined with systemic antifungal therapy, remain the cornerstone of treatment for mucormycosis. In the present study, postoperative complications included oroantral fistula formation in six patients, one mortality, and one recurrence involving the mandible. The observed mortality rate was lower than that reported in several large series, including the 44% mortality documented by Neha Mishra et al. [25], which may be attributed to early intervention and prompt surgical debridement. The recurrence rate observed in our study was comparable to previously published data [26].

Impaired mucociliary clearance following COVID-19, along with hyperglycaemia, increased free iron availability, and defective innate immune responses, may explain the predominance of rhino-cerebral and rhinomaxillary involvement observed in most patients [27,28]. The rare occurrence of mandibular mucormycosis highlights the need for heightened clinical suspicion, particularly in patients presenting with atypical odontogenic symptoms in the post–COVID-19 setting.

Limitations and Strengths

This study represents an institutional experience of post–COVID-19–associated mucormycosis managed at a tertiary care center, providing real-world insight into clinical presentation, management, and outcomes. Diagnostic accuracy was ensured through histopathological and microbiological confirmation in all cases. A standardized multidisciplinary treatment approach was consistently followed, and a minimum follow-up period of one year allowed assessment of complications and disease recurrence. The documentation of a rare case of mandibular mucormycosis adds clinical relevance to the existing literature.

However, the retrospective design and small sample size (n = 16) limit statistical power and generalizability. The single-center nature of the study introduces potential selection bias, and the absence of a non–COVID-19 control group restricts comparative analysis. Additionally, long-term functional and quality-of-life outcomes were not systematically evaluated.

CONCLUSION

Based on the findings of the present study, it can be concluded that the incidence of mucormycosis is significantly increased in patients infected with SARS-CoV-2, particularly in the presence of diabetes mellitus. The rhino-cerebral and rhinomaxillary forms were the most common clinical presentations observed. Clinicians should maintain a high index of suspicion for mucormycosis in post-COVID-19 patients, especially those with underlying comorbidities and a history of corticosteroid use. Early diagnosis, prompt initiation of antifungal therapy, and aggressive surgical debridement play a crucial role in reducing disease-related morbidity and mortality. A multidisciplinary approach and timely intervention remain key factors in improving patient outcomes in COVID-19–associated mucormycosis.

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