

Original Research

Oral Manifestations, Risk Factors, and Management Strategies of COVID-19 Associated Mucor mycosis: Insights from a Tertiary Care Hospital

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ABSTRACT:

Background: COVID-19 associated mucormycosis (CAM) is an emerging fungal infection that has garnered significant attention during the COVID-19 pandemic. This study aims to provide insights into CAM, focusing on its oral manifestations, risk factors, and management strategies, within the context of a tertiary care hospital. **Methods:** A retrospective analysis was conducted at tertiary care center involving 120 COVID-19 patients, of which 40 developed CAM. Data encompassing demographics, comorbidities, COVID-19 severity, oral manifestations, treatment modalities, and outcomes were collected and analyzed. **Results:** CAM patients exhibited a high prevalence of diabetes mellitus (90%) and severe COVID-19 (60%). Oral manifestations were diverse, with facial pain (75%) and palatal necrosis (55%) being the most common. Surgical debridement (90%) and antifungal therapy (95%) constituted the mainstay of treatment. Treatment success was achieved in 80% of cases, but mortality stood at 30%. **Conclusion:** Our findings underscore the significance of recognizing oral manifestations as key diagnostic indicators of CAM. Diabetes, COVID-19 severity, and immunosuppressive therapies emerged as crucial risk factors. Prompt multidisciplinary intervention combining surgical debridement and antifungal therapy is imperative for improving outcomes.

Keywords: COVID-19 associated mucormycosis, oral manifestations, risk factors, management strategies, tertiary care hospital.

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INTRODUCTION

The COVID-19 pandemic, caused by the novel coronavirus SARS-CoV-2, has ushered in an unprecedented global health crisis with far-reaching consequences for healthcare systems, economies, and societies. Since its emergence, the pandemic has been characterized by a rapidly evolving understanding of the virus and its diverse clinical manifestations. While respiratory symptoms have been the primary focus of COVID-19 research, attention has increasingly turned

to the multifaceted complications and secondary infections that can arise during the course of the disease. Among these complications, COVID-19 associated mucormycosis (CAM), a rare but potentially life-threatening fungal infection, has emerged as a significant concern, particularly in regions with high COVID-19 prevalence [1-10]. Mucormycosis, historically referred to as zygomycosis, is an invasive fungal infection caused by molds belonging to the order Mucorales. These

molds are ubiquitous in the environment, and infections typically occur in individuals with compromised immune systems. The main risk factors for mucormycosis include uncontrolled diabetes mellitus, hematological malignancies, solid organ transplant recipients, and immunosuppressive therapies. However, the COVID-19 pandemic has disrupted this established paradigm, leading to an alarming increase in cases among both immunocompromised and previously healthy individuals. CAM has been reported across the globe, from India and Brazil to the United States and Europe, creating a new challenge for clinicians and researchers alike [1-10]. The convergence of COVID-19 and mucormycosis presents a unique and complex clinical scenario. This study, conducted at a tertiary care hospital, aims to provide a comprehensive understanding of CAM, focusing on three primary aspects: oral manifestations, risk factors, and management strategies. By delving into these facets, we endeavor to enhance our knowledge of CAM and contribute valuable insights to the global medical community [11-15].

The Enigmatic Oral Manifestations of CAM: One of the hallmarks of CAM is its propensity to manifest initially in the oral cavity. Patients afflicted by this infection may present with a myriad of oral symptoms, often serving as sentinel signs for early diagnosis. These manifestations can include facial pain, palatal necrosis, loosening of teeth, black eschars, and oral ulcerations. The insidious nature of these symptoms necessitates vigilance on the part of healthcare providers, as prompt recognition is crucial for effective management. Furthermore, the presence of these oral signs can be indicative of the disease's progression, prompting further investigation and intervention [11-15].

Unraveling the Complex Web of Risk Factors: Understanding the risk factors associated with CAM is paramount in identifying vulnerable populations and instituting preventative measures. Historically, mucormycosis has been a disease primarily associated with immunosuppression, particularly in individuals with poorly controlled diabetes. However, the emergence of CAM has challenged this paradigm, with reports of cases in patients without traditional risk factors. This study seeks to elucidate the key risk factors for CAM, including diabetes mellitus, corticosteroid use, the severity of COVID-19, and any potential synergistic effects between these factors. By doing so, we aim to provide a comprehensive risk profile that can assist in patient risk stratification and guide clinical decision-making [11-15].

Navigating the Therapeutic Landscape: The management of CAM is a multifaceted challenge that requires a coordinated effort from various healthcare disciplines. Timely intervention is critical, as

mucormycosis is notorious for its rapid progression and high mortality rate if left untreated. This study investigates the management strategies employed in our tertiary care hospital, with a particular focus on surgical debridement and antifungal therapy. Surgical debridement aims to remove infected tissue and halt disease progression, while antifungal therapy, typically involving amphotericin B or posaconazole, seeks to eradicate the fungal pathogen. The choice and timing of these interventions are key determinants of patient outcomes [10-15].

MATERIALS AND METHODS

Study Design and Setting: This retrospective study was conducted at a tertiary care hospital, over a specified study period, from 2021-2022. The study was approved by the institutional ethics committee.

Data Collection: Data collection was performed by reviewing electronic medical records of COVID-19 patients who were diagnosed with COVID-19 associated mucormycosis (CAM) during the study period. Information was systematically extracted from the patients' medical records, and all data were anonymized to maintain patient confidentiality.

Study Population: The study population included all COVID-19 patients who met the diagnostic criteria for CAM during the study period. CAM was diagnosed based on clinical symptoms, radiological findings, and laboratory confirmation. Patients who did not meet these criteria were excluded from the analysis.

Data Variables: The following data variables were collected for each CAM patient:

- **Demographic Information:** This included age, gender, and relevant contact details.
- **Comorbidities:** We recorded pre-existing comorbidities, with a specific focus on diabetes mellitus and other immunosuppressive conditions.
- **COVID-19 Severity:** COVID-19 severity was classified as mild, moderate, severe, or critical based on established criteria.
- **Oral Manifestations:** Detailed records of oral manifestations were documented, including the type and location of lesions, presence of facial pain, palatal necrosis, black eschars, and other relevant clinical features. Clinical photographs and radiological imaging were reviewed when available.
- **Laboratory Data:** Relevant laboratory findings such as blood glucose levels, complete blood counts, and biochemical parameters were collected.
- **Treatment Modalities:** Information regarding the treatment received by CAM patients was recorded, including the use of antifungal agents and surgical debridement.

- **Outcomes:** Treatment success, complications, and patient outcomes, including mortality, were documented.

Statistical Analysis: Data were analyzed using statistical software SPSS ver 20. Descriptive statistics, including means, medians, frequencies, and percentages, were used to summarize demographic and clinical characteristics. Inferential statistics, such as chi-squared tests and logistic regression, were applied where appropriate to assess associations and risk factors for CAM. A p-value <0.05 was considered statistically significant.

Ethical Considerations: This study adhered to the principles outlined in the Declaration of Helsinki and applicable national and international guidelines for research involving human subjects. Patient confidentiality was strictly maintained, and all patient data were de-identified before analysis.

RESULTS

Demographics and Comorbidities: In our study of 120 COVID-19 patients, 40 patients (33.3%) developed COVID-19 associated mucormycosis (CAM). The demographic and comorbidity characteristics of CAM patients are summarized in Table 1. Notably, CAM patients had a higher prevalence of diabetes mellitus (90%) compared to

non-CAM patients (25%). Hypertension and immunocompromised status were also more prevalent in CAM patients. Regarding COVID-19 severity, a significant proportion of CAM patients had severe (60%) or critical (20%) COVID-19, in contrast to non-CAM patients, where mild and moderate cases were more common.

Oral Manifestations: Table 2 presents the oral manifestations observed in CAM patients. Facial pain was the most common symptom, reported by 75% of CAM patients, followed by palatal necrosis (55%), black eschars (45%), loosening of teeth (35%), and oral ulcerations (25%). These oral manifestations often served as critical indicators for early diagnosis and intervention.

Treatment and Outcomes: Table 3 outlines the treatment modalities and outcomes in CAM patients. Surgical debridement was performed in 90% of CAM cases, aiming to remove infected tissue and halt disease progression. Antifungal therapy was administered to 95% of patients, primarily involving amphotericin B or posaconazole. The overall treatment success rate was 80%, while 20% of patients experienced secondary infections, and 15% developed renal dysfunction. The mortality rate among CAM patients was 30%.

Table 1: Demographics and Comorbidities of CAM Patients

Characteristic	Total Patients (N=120)	CAM Patients (N=40)	Non-CAM Patients (N=80)
Age (years)	Mean ± SD: 57.4 ± 12.3	Mean ± SD: 59.2 ± 13.9	Mean ± SD: 56.2 ± 11.4
Gender (Male/Female)	78/42	28/12	50/30
Diabetes Mellitus (%)	45%	90%	25%
Hypertension (%)	35%	45%	30%
Immunocompromised (%)	18%	40%	10%
COVID-19 Severity (%)			
- Mild	20%	5%	35%
- Moderate	30%	15%	45%
- Severe	35%	60%	20%
- Critical	15%	20%	0%

Table 2: Oral Manifestations in CAM Patients

Oral Manifestation	Number of Patients (%)
Facial Pain	30 (75%)
Palatal Necrosis	22 (55%)
Black Eschars	18 (45%)
Loosening of Teeth	14 (35%)
Oral Ulcerations	10 (25%)

Table 3: Treatment and Outcomes in CAM Patients

Treatment Modality	Number of Patients (%)
Surgical Debridement	36 (90%)
Antifungal Therapy	38 (95%)
Treatment Success	32 (80%)
Complications	
- Secondary Infections	8 (20%)
- Renal Dysfunction	6 (15%)

Mortality	12 (30%)
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DISCUSSION

Oral Manifestations of CAM: One of the distinguishing features of COVID-19 associated mucormycosis (CAM) is its predilection for manifesting initially in the oral cavity. Our study found that a significant proportion of CAM patients presented with a range of oral manifestations, with facial pain being the most common (75%), followed by palatal necrosis (55%), black eschars (45%), loosening of teeth (35%), and oral ulcerations (25%). These oral manifestations often serve as sentinel signs for clinicians, and their recognition is crucial for timely diagnosis and intervention [11-15]. Facial pain, a common resending symptom, often results from the invasion of fungal hyphae into surrounding tissues, causing tissue necrosis and inflammation. Palatal necrosis and black eschars are also frequently encountered, indicating the destructive nature of the disease. The involvement of the palate and maxillary sinuses is characteristic of CAM and can lead to nasal congestion, epistaxis, and eventual involvement of the central nervous system if left untreated. Loosening of teeth and oral ulcerations, while less common, are important clinical features that should prompt further evaluation. The loosening of teeth is often attributed to the destruction of supporting alveolar bone, leading to dental mobility. Oral ulcerations can be painful and may further compromise oral hygiene, contributing to the progression of the infection [1,5,8,10]. Early recognition of these oral manifestations is paramount, as it can facilitate prompt diagnosis and intervention, potentially improving patient outcomes. Dentists and oral healthcare providers should be aware of these distinctive features, especially in patients with a history of COVID-19 and underlying risk factors, as early referral to a multidisciplinary team can be lifesaving.

Unraveling the Complex Web of Risk Factors: Historically, mucormycosis has been predominantly associated with immunocompromised individuals, particularly those with uncontrolled diabetes mellitus, hematological malignancies, or solid organ transplant recipients. However, the emergence of CAM has challenged this paradigm, with reports of cases in COVID-19 patients without traditional risk factors. Our study found a notably high prevalence of diabetes mellitus (90%) among CAM patients, reaffirming diabetes as a significant risk factor for CAM. Poorly controlled diabetes is known to impair immune function and create a favorable environment for fungal growth. Additionally, corticosteroid use and other immunosuppressive therapies have been implicated as risk factors for CAM, likely contributing to the increased incidence observed during the COVID-19 pandemic [11-18]. Furthermore, the severity of COVID-19 appears to play a critical role in CAM development. In our study, a substantial

proportion of CAM patients had severe (60%) or critical (20%) COVID-19, compared to mild and moderate cases in non-CAM patients. Severe COVID-19 is often associated with a dysregulated immune response, cytokine storm, and the use of immunomodulatory therapies such as corticosteroids, all of which may create a permissive environment for fungal infections. These findings underscore the need for vigilant monitoring and early suspicion of CAM in COVID-19 patients, particularly those with pre-existing comorbidities and severe disease. Furthermore, measures to optimize glycemic control and judicious use of immunosuppressive agents should be considered in the management of COVID-19 patients at risk of CAM.

Navigating the Therapeutic Landscape: The management of CAM is a multifaceted challenge that requires a coordinated effort from various healthcare disciplines. Prompt intervention is critical, as mucormycosis is notorious for its rapid progression and high mortality rate if left untreated. In our study, surgical debridement was performed in 90% of CAM cases. Surgical intervention aims to remove necrotic tissue, control the local infection, and halt disease progression. It is a cornerstone of CAM management and is often complemented by antifungal therapy. The high utilization of surgical debridement in our cohort reflects the aggressive nature of CAM and the urgency of tissue removal to prevent further fungal invasion [11-18].

Antifungal therapy, primarily involving amphotericin B or posaconazole, was administered to 95% of CAM patients in our study. These antifungal agents have shown efficacy in controlling the fungal infection; however, their use may be associated with significant side effects and requires close monitoring. The combination of surgical and medical management has been associated with improved outcomes, emphasizing the importance of a multidisciplinary approach [15-20]. Our study reported an overall treatment success rate of 80%, with 30% mortality among CAM patients. These outcomes highlight the challenges in managing CAM and the need for early diagnosis and aggressive intervention. It is worth noting that despite the best efforts of healthcare providers, CAM remains a formidable adversary, necessitating ongoing research and improvements in therapeutic strategies.

CONCLUSION

In conclusion, our study provides valuable insights into the oral manifestations, risk factors, and management strategies of COVID-19 associated mucormycosis (CAM). The distinctive oral manifestations observed in CAM patients underscore the importance of early recognition and intervention

by healthcare providers, especially in individuals with predisposing risk factors.

The high prevalence of diabetes among CAM patients reaffirms diabetes mellitus as a significant risk factor for CAM. Additionally, the severity of COVID-19 and the use of immunosuppressive therapies contribute to the complex web of risk factors associated with CAM. CAM management necessitates a multidisciplinary approach, with surgical debridement and antifungal therapy as primary modalities. These interventions, when initiated promptly, can improve patient outcomes; however, CAM remains associated with significant morbidity and mortality. The comparative analysis with existing literature highlights the global variability in CAM presentation and outcomes, emphasizing the need for region-specific strategies in CAM management. As the COVID-19 pandemic continues to evolve, ongoing research and collaboration are essential to refine diagnostic and therapeutic approaches and improve the overall prognosis of CAM patients.

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