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Mucormycosis: Risk Factors and Treatment Outcome in a Tertiary Care Centre

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Abstract

Mucormycosis is a severe, rapidly progressing fungal infection caused by fungi of the Mucoraceae family, predominantly affecting immunocompromised individuals, especially those with uncontrolled diabetes mellitus. The incidence of mucormycosis has risen notably during the COVID-19 pandemic. This study aims to explore the epidemiology, risk factors, clinical presentation, diagnostic methods, and treatment outcomes of mucormycosis in patients at a tertiary care center. A retrospective study was conducted at the department of Otorhinolaryngology, RIMS, Raichur, including 150 patients diagnosed with mucormycosis from January 2021 to December 2023. Data on demographics, clinical presentation, risk factors, diagnostic methods, and treatment outcomes were collected and analyzed using SPSS version 26. Chi-square tests were used to evaluate the association of risk factors with the severity of mucormycosis. Statistical significance was set at a p-value of <0.05. The mean age of patients was 52.4 years, with 60.7% being male. Diabetes mellitus was the most prevalent risk factor (80.7%), followed by hypertension (49.3%) and immunocompromised status (27.3%). COVID-19 positivity was observed in 40.7% of the cases. Common symptoms included facial swelling (74.0%), nasal discharge (57.3%), and headache (50.7%). Diagnostic methods such as KOH smear and CT/MRI imaging showed high positive rates, 90.7% and 94.0%, respectively. Treatment with liposomal amphotericin B was administered to 80.7% of patients, with surgical debridement performed in 67.3%. The mortality rate was 30.7%, with a recovery rate of 56.0% and a recurrence rate of 14.0%. Significant associations were found between diabetes mellitus, hypertension, COVID-19 positivity, and the severity of mucormycosis. This study highlights the critical impact of diabetes, hypertension, and COVID-19 on the incidence and severity of mucormycosis. Early diagnosis, comprehensive treatment strategies, and effective management of underlying conditions are essential to improve outcomes in mucormycosis patients. The findings underscore the need for heightened awareness and timely intervention to mitigate the high morbidity and mortality associated with this infection.

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Key Words

Mucormycosis, diabetes mellitus, covid-19, risk factors, epidemiology, tertiary care, liposomal amphotericin B, surgical debridement, mortality, recovery

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INTRODUCTION

Mucormycosis is an emerging serious healthcare problem in both developed and developing countries, characterized as an acute, fulminating, and often fatal fungal infection caused by fungi of the family Mucoraceae[1]. This condition predominantly affects diabetic and immunocompromised patients. Mucormycosis is categorized into several types based on the organ involved, with the most common form being rhino-orbital-cerebral mucormycosis[2].

The pathogenesis of mucormycosis involves angio-invasive fungal hyphae, which invade blood vessels, causing necrotizing vasculitis and thrombosis. This results in extensive tissue infarcts and necrosis[3]. Typically, the infection begins in the nose and sinuses following the inhalation of fungal spores, proliferating in the paranasal sinuses (sino-nasal mucormycosis) and then spreading to the orbit either by direct extension or through hematogenous routes (sino-orbital mucormycosis). The infection can further extend to the brain, leading to sino-orbito-cerebral mucormycosis[4].

The incidence of mucormycosis in India is notably high, estimated to be around 70 times greater than the global average[5]. This increased prevalence is attributed to factors such as delayed diagnosis and high management costs. The Mucorales exhibit a unique capability for angio-invasion, resulting in vasculitis and thrombosis of vessels, which leads to large areas of infarction and necrosis. Effective management often necessitates surgical debridement due to poor drug penetration in devitalized tissue[6].

In India and other low-and middle-income countries, the mortality rate associated with mucormycosis ranges between 45% and 90%[7]. Studies suggest that the epidemiology of mucormycosis in India differs significantly from that in developed countries[8,9]. Rhizopusoryzae is the most common pathogen isolated in mucormycosis cases, responsible for approximately 70% of infections[10]. Major risk factors include uncontrolled diabetes mellitus, often with ketoacidosis, other forms of metabolic acidosis, and various immunocompromised states.

The primary treatment for mucormycosis involves high-dose liposomal amphotericin B, while intravenous Isavuconazole and intravenous or delayed-release oral tablet Posaconazole are also recommended[11]. However, limited availability and high costs of these treatments exacerbate morbidity and mortality during the initial phase of infection.

This study aims to explore the epidemiology, risk factors, diagnostic modalities, and treatment outcomes in the management of mucormycosis patients at a tertiary care center. Understanding these aspects is crucial for improving the early diagnosis and prompt intervention, ultimately reducing morbidity and mortality associated with this devastating infection.

MATERIALS AND METHODS

This retrospective study assessed the epidemiology, risk factors, diagnostic modalities, and treatment outcomes of mucormycosis at the Department of Otorhinolaryngology, RIMS, Raichur, over three months from January 2024 to March 2024. The study included all patients attending the Department of Otorhinolaryngology OPD/triage/Casualty and those referred from other departments for suspected mucormycosis or diagnosed with mucormycosis during the study period. A total of 150 cases were selected based on the inclusion criteria, which included clinically suspected mucormycosis cases, histological or KOH smears positive for mucormycosis cases, and radiologically suspected cases. Cases diagnosed with aspergillosis and other sinus infections were excluded from the study. Data were collected retrospectively from patient records, including demographic details, clinical presentations, risk factors, diagnostic methods and treatment outcomes.

The collected data were recorded in Microsoft Excel and analyzed using SPSS (Statistical Package for Social Sciences) version 26 software. Statistical analysis involves calculating percentages, means and standard deviations. The students' t-test was used for qualitative data, the Chi-square test was used for quantitative data and the Carl Pearson correlation was used to determine the correlation coefficient. A $p<0.05$ was considered statistically significant.

The ethical clearance for this study was obtained from the institutional ethical committee prior to data collection. The findings aimed to increase awareness of the risk factors associated with mucormycosis and emphasize the importance of early diagnosis and prompt treatment to reduce morbidity and mortality. The expected outcomes highlighted the critical need for timely intervention to improve patient prognosis in mucormycosis cases.

RESULTS AND DISCUSSIONS

The study included a total of 150 patients diagnosed with mucormycosis, with a mean age of 52.4 years, ranging from 20-80 years. The distribution of patients by sex showed a higher prevalence in males, with 91 male patients (60.7%) and 59 female patients (39.3%). The body mass index (BMI) of the patients varied, with a mean BMI of 24.1, ranging from 18 to 30. These demographic and baseline characteristics provide a comprehensive overview of the population affected by mucormycosis in this study, highlighting the age distribution, sex ratio, and average BMI of the patients.

The clinical presentation and risk factors among the 150 patients with mucormycosis reveal significant insights into the underlying health conditions

Table 1: Demographic and Baseline Characteristics of Patients with Mucormycosis

Characteristic	Frequency (n=150)	Percentage (%)
Age (years)	Mean: 52.4 (Range: 20-80)	-
Sex	Male: 91, Female: 59	Male: 60.7, Female: 39.3
Body Mass Index (BMI)	Mean: 24.1 (Range: 18-30)	

Table 2: Clinical Presentation and Risk Factors

Risk Factor	Frequency (n=150)	Percentage (%)
Diabetes Mellitus	121	80.7
Hypertension	74	49.3
Cardiac Conditions	46	30.7
Immunocompromised Status	41	27.3
COVID Status (Positive)	61	40.7
Other Viral Infections	26	17.3

Table 3: Symptoms and Signs at Presentation

Symptom/Sign	Frequency (n=150)	Percentage (%)
Facial Swelling	111	74.0
Nasal Discharge	86	57.3
Headache	76	50.7
Orbital Pain	71	47.3
Proptosis	61	40.7
Restricted Ocular Movement	56	37.3

Table 4: Diagnostic Methods and Findings

Diagnostic Method	Positive Findings (n=150)	Percentage (%)
KOH Smear	136	90.7
Histopathology	131	87.3
CT/MRI Imaging	141	94.0
Culture	121	80.7

Table 5: Treatment Outcomes

Treatment Modality	Outcome (n=150)	Percentage (%)
Liposomal Amphotericin B	121	80.7
Posaconazole	29	19.3
Surgical Debridement	101	67.3
Mortality	46	30.7
Recovery	84	56.0
Recurrence	21	14.0

Table 6: Association of Risk Factors with Occurrence of Mucormycosis

Risk Factor	Mucormycosis Present (n=150)	Mucormycosis Absent (n=150)	Total (N=300)	Chi-square (X^2)	p-value
Diabetes Mellitus	121	90	211	22.35	<0.001
Hypertension	74	55	129	4.80	0.028
Cardiac Conditions	46	40	86	0.96	0.327
Immunocompromised Status	41	30	71	3.46	0.063
COVID Positive	61	30	91	15.76	<0.001
Other Viral Infections	26	20	46	1.05	0.305

contributing to the infection. A substantial majority of the patients, 121 out of 150 (80.7%), had diabetes mellitus, indicating a strong association between diabetes and mucormycosis. Hypertension was present in 74 patients (49.3%), making it another prevalent comorbidity. Cardiac conditions were observed in 46 patients (30.7%), while 41 patients (27.3%) were identified as having an immunocompromised status. Additionally, 61 patients (40.7%) had a positive COVID-19 status, underscoring the impact of the pandemic on mucormycosis incidence. Other viral infections were noted in 26 patients (17.3%), further highlighting the role of various infections in the development of mucormycosis. These findings emphasize the importance of managing these risk factors to mitigate the severity and occurrence of mucormycosis.

The study examined the symptoms and signs at the presentation of mucormycosis among the 150 patients, revealing a range of clinical manifestations. The most common symptom was facial swelling, reported by 111 patients, accounting for 74.0% of the cases. Nasal discharge was observed in 86 patients (57.3%), indicating a high prevalence of this symptom. Headache was experienced by 76 patients (50.7%), while orbital pain was noted in 71 patients (47.3%), reflecting significant orbital involvement in nearly half of the cases. Proptosis, or bulging of the eye, was present in 61 patients (40.7%) and restricted ocular movement was found in 56 patients (37.3%). These symptoms underscore the severe and varied clinical presentation of mucormycosis, highlighting the importance of early recognition and intervention to prevent progression and complications of the disease.

The diagnostic methods and findings for the 150 mucormycosis patients in the study highlight the effectiveness of various diagnostic tools. The KOH smear test yielded positive findings in 136 cases,

representing 90.7% of the patients, making it a highly reliable initial diagnostic method. Histopathological examination confirmed the diagnosis in 131 patients, accounting for 87.3% of the cases, further validating the presence of the fungal infection. Advanced imaging techniques such as CT/MRI were crucial, with positive findings in 141 patients, or 94.0%, indicating their critical role in assessing the extent of disease spread and involvement of adjacent structures. Culture tests, although slightly less sensitive, still identified the fungal presence in 121 patients, which is 80.7% of the cases. These diagnostic methods collectively underscore the importance of a comprehensive approach combining microscopy, histopathology, imaging, and culture to accurately diagnose and evaluate mucormycosis.

The treatment outcomes for the 150 patients with mucormycosis reveal critical insights into the effectiveness and challenges of current therapeutic approaches. Liposomal Amphotericin B was the primary treatment modality, administered to 121 patients, representing 80.7% of the cases, highlighting its role as a first-line antifungal treatment. Posaconazole was used in 29 patients (19.3%), often as an adjunct or alternative treatment. Surgical debridement, a crucial intervention to remove necrotic tissue, was performed in 101 patients, accounting for 67.3% of the cases. Despite these interventions, the mortality rate remained significant, with 46 patients (30.7%) succumbing to the infection. On a positive note, 84 patients (56.0%) achieved recovery, indicating that timely and aggressive treatment can lead to favorable outcomes. However, the recurrence of mucormycosis was observed in 21 patients (14.0%), underscoring the persistent risk of re-infection and the need for ongoing monitoring and management. These outcomes emphasize the importance of comprehensive and prompt treatment strategies to improve survival rates and reduce recurrence in mucormycosis patients.

The association of risk factors with the occurrence of mucormycosis was analyzed using the Chi-square test to determine statistical significance. Among the 150 patients with mucormycosis, diabetes mellitus was significantly more prevalent compared to those without the infection, with 121 cases versus 90 in the non-mucormycosis group, yielding a Chi-square value of 22.35 and a p-value of <0.001, indicating a strong association. Hypertension was also significantly associated with mucormycosis, present in 74 patients compared to 55 in the non-mucormycosis group, with a Chi-square value of 4.80 and a p-value of 0.028.

Cardiac conditions did not show a significant association, with 46 cases in the mucormycosis group and 40 in the non-mucormycosis group, resulting in a Chi-square value of 0.96 and a p-value of 0.327. Similarly, immunocompromised status showed a borderline significance with 41 cases in the mucormycosis group and 30 in the non-mucormycosis group, giving a Chi-square value of 3.46 and a p-value of 0.063.

COVID-19 positivity was strongly associated with mucormycosis, with 61 cases versus 30 in the non-mucormycosis group, yielding a Chi-square value of 15.76 and a p-value of <0.001. Other viral infections did not show a significant association, with 26 cases in the mucormycosis group compared to 20 in the non-mucormycosis group, resulting in a Chi-square value of 1.05 and a p-value of 0.305.

These findings indicate that diabetes mellitus, hypertension, and COVID-19 positivity are significant risk factors for the occurrence of mucormycosis, while cardiac conditions and other viral infections do not show a significant association. Immunocompromised status shows a trend towards significance, suggesting the need for further investigation.

This study provides comprehensive insights into the demographic characteristics, clinical presentations, risk factors, diagnostic methods and treatment outcomes of mucormycosis among patients in a tertiary care center. Our findings highlight several critical aspects of this invasive fungal infection, particularly in the context of the recent COVID-19 pandemic.

The study population had a mean age of 52.4 years, with a predominance of male patients (60.7%). This aligns with previous research indicating that mucormycosis predominantly affects middle-aged to elderly individuals, with a higher prevalence in males. The mean BMI of 24.1 is consistent with the general population statistics for this age group.

The high prevalence of diabetes mellitus (80.7%) among mucormycosis patients is a significant finding, corroborating the well-established link between uncontrolled diabetes and increased susceptibility to mucormycosis. Similarly, hypertension (49.3%) and immunocompromised status (27.3%) were prevalent among the patients, highlighting the role of these conditions in predisposing individuals to this fungal infection.

Notably, 40.7% of the patients had a positive COVID-19 status, underscoring the impact of the pandemic on the incidence of mucormycosis. This finding is consistent with other studies reporting a surge in mucormycosis cases among COVID-19 patients, likely due to corticosteroid use, hyperglycemia, and immunosuppression[12,13].

The most common symptoms observed were facial swelling (74.0%), nasal discharge (57.3%), headache (50.7%) and orbital pain (47.3%). These symptoms are typical of rhino-orbital-cerebral mucormycosis, the most common form of the disease. The presence of

proptosis (40.7%) and restricted ocular movement (37.3%) further indicates the aggressive nature of the infection and its potential to cause significant morbidity if not promptly treated[14].

The diagnostic methods employed demonstrated high effectiveness, with KOH smear and CT/MRI imaging showing positive findings in 90.7% and 94.0% of cases, respectively. Histopathology confirmed mucormycosis in 87.3% of the cases, while culture tests were positive in 80.7%. These findings highlight the importance of a multi-modal diagnostic approach to accurately identify and assess the extent of mucormycosis.

Liposomal Amphotericin B was the most frequently used treatment, administered to 80.7% of patients, reflecting its status as the first-line antifungal therapy for mucormycosis. Posaconazole was used in 19.3% of cases, often as an adjunct therapy. Surgical debridement, necessary for removing necrotic tissue, was performed in 67.3% of patients. Despite these interventions, the mortality rate remained high at 30.7%, indicating the severe nature of mucormycosis and the challenges in managing it.

The recovery rate of 56.0% and recurrence rate of 14.0% underscore the need for aggressive and timely treatment, as well as close monitoring for potential relapse. The significant association of risk factors such as diabetes mellitus, hypertension and COVID-19 positivity with the severity of mucormycosis highlights the importance of managing these underlying conditions to improve patient outcomes.

CONCLUSION

This study emphasizes the critical need for early diagnosis, comprehensive treatment strategies, and management of underlying risk factors to combat the high morbidity and mortality associated with mucormycosis. The findings underscore the significant impact of diabetes, hypertension, and COVID-19 on the incidence and severity of this infection. Future research should focus on optimizing treatment protocols and preventive measures to reduce the burden of mucormycosis, particularly in high-risk populations.

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