ORIGINAL ARTICLE

Clinical Features and Outcome of Mucormycosis Cases in A Tertiary Care Hospital: A 10-year Experience

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ABSTRACT

Objective: The study aimed to describe the clinical features and outcomes of mucormycosis and identify variables associated with in-hospital mortality.

Study Design: Retrospective observational study.

Place and Duration of Study: Rehman Medical Institute, Peshawar between 1st January 2015 and 31st December 2024.

Materials and Methods: The study included all histopathological confirmed cases of mucormycosis diagnosed during the study period. Demographic data, clinical and radiological features, treatment, and outcomes at discharge were retrieved from patient hospital records. Data were summarized as frequencies and percentages for categorical variables and as median (interquartile range) for continuous variables. Mann–Whitney U test and Fisher's exact test were applied to do mortality analysis between two groups.

Results: Of 35 study participants, the median (IQR) age was 55(21) years, 68.6% (n=24) were male. Rhino-orbito-cerebral mucormycosis (ROCM) was the most common presentation in 94.2% (n=33). About 77.1% (n=27) of patients had diabetes mellitus (DM), 85.7% (n=23) had poor glycemic control. Surgical intervention was performed in 97.1% (n=34). About 20% (n=7) of patients required ICU care. The in-hospital mortality was 17.1% excluding patients who left against medical advice. ICU admission, intracranial extension, and septic shock were strongly associated with mortality ($p < 0.001$ each). Higher C -reactive protein (CRP) (49.26 vs 7.75 mg/L, $p= 0.007$), neutrophilia (87.8 vs 73.3%, $p = 0.005$) and HbA1c (13.9% Vs 11.4%. $P= 0.03$) were associated with high mortality.

Conclusion: Mucormycosis mostly affected middle aged adults with poorly controlled DM. ROCM was common with worse outcomes. Extensive organ involvement at presentation, high CRP, HbA1c levels, and neutrophil counts were associated with mortality.

Key Words: *Mucormycosis, Diabetes Mellitus, Mortality.*

Introduction

Mucormycosis is a rare, opportunistic, life-threatening fungal infection. The causative organisms belong to the Rhizopus genus. Rapid tissue invasion and necrosis are the hallmark of this disorder from its ability to invade blood vessels. Rhino-orbito-cerebral mucormycosis (ROCM) is the most common form worldwide, followed by pulmonary, cutaneous, gastrointestinal, and disseminated forms.[1]

Immunocompromised individuals are most prone to developing the disease.[1,2] Uncontrolled diabetes mellitus, absolute neutropenia, organ transplantation and/or immunosuppressant drug use, hematological malignancies, and steroid use are major risk factors in this patient cohort. A significant surge in mucormycosis was reported during the COVID-19 pandemic as well. The use of steroids, presence of hypoxemia and poor glycemic control in patients with diabetes, was deemed to be responsible for this surge during COVID-19.[2] Indian researchers reported, around 40,000 cases during the COVID-19 pandemic, further reiterating the statistics reported worldwide.[3]

Prevalence of mucormycosis is significantly higher in underdeveloped countries (140 vs 1.7 cases per million population) compared to the developed world.[4] Globally, the prevalence of mucormycosis has been estimated as 0.005 to 1.7 per million people for the year 2019-2020, with the incidence in India

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about 80 times greater than in industrialized nations.[5,6] A significant burden on healthcare systems has been reported in the underdeveloped countries in mucormycosis infections. Tens of thousands of US dollars are often needed for effectively treating a single episode of the disease due to the need for prolonged hospitalization, unavailability and costly antifungal medications (e.g., liposomal amphotericin B), multiple surgeries, and post-recovery rehabilitation.[7]

Mucormycosis carries a high mortality rate of 25-87%, despite the advancements in diagnosis and treatment.[8] Prognosis, including mortality rates, is influenced by several variables. Disseminated disease, brain involvement, radiological bone erosions, diagnostic delays, underlying medical conditions like uncontrolled diabetes and presence of hematological malignancies etc., and inadequate surgical resection were associated with increased mortality rates. Reports of improvement in the disease outcome have been associated with the early introduction of antifungal therapy and aggressive surgical debridement if warranted.[8]

To date, studies highlighting the clinical and radiological presentations, and outcomes of mucormycosis in Pakistan are limited. Data from our region is important as patients frequently present in advanced stages of disease due to delayed access to healthcare centers. Moreover, limited availability of anti-fungal drugs and advance surgical procedures also effect disease outcome. The scarcity of data in Pakistan, underscores the need for research to understand the epidemiology, risk factors, outcomes and management challenges within this region. This study aims to help identify trends in the clinical features and outcomes of this rare but fatal disease. The aim of the study is to evaluate the demographic, clinical, and radiological characteristics, clinical course, and discharge outcomes of mucormycosis and to identify factors associated with poor outcomes.

Materials and Methods

This retrospective observational study was conducted at Rehman Medical Institute, Peshawar, and included all histopathological confirmed cases of mucormycosis diagnosed and managed between 1st January 2015 and 31st December 2024. Ethical approval was obtained from the institutional review board and ethics committee of Rehman Medical Institute before data collection under reference number RMI/IRB-EC/approval/259 dated June 18th,2025. Patient consent for the use of their data was routinely taken at the time of admission. Only cases with complete medical records were included, while cases with incomplete data or those diagnosed outside the institution were excluded.

Data were collected from the hospital medical records, laboratory databases, radiology reports, and surgical records. The variables retrieved included demographic information, clinical presentation (symptoms and site of involvement), underlying risk factors such as diabetes, Hypertension (HTN), history of COVID-19 infection. Diagnostics such as CT or MRI scans and histopathological characteristics were also recorded. Data regarding treatment modalities, including medical and surgical management, and clinical outcomes such as recovery, complications, or death at the time of discharge were also retrieved. All data was anonymized and handled with strict confidentiality.

Statistical analysis was performed using SPSS 27. Normality of continuous variables was assessed using the Shapiro–Wilk test. As data was non-normally distributed hence whole cohort or subgroup continuous data were presented as median (IQR) or Median (range) where IQR was unstable. Categorical variables were expressed as frequencies and percentages. Comparative analyses between groups (survivors vs. non-survivors) at discharge (after excluding patients who left against medical advice) were conducted using Fisher's exact test and Mann-Whitney U test due to unequal group size. Mortality association analysis was performed after excluding patients who left against medical advice. A p-value of less than 0.05 was considered statistically significant.

Results

During the study period, a total of 35 patients with confirmed mucormycosis were identified from the hospital records. Of these, 68.6% (n=24) were males and 31.4% (n=11) were females. The median (IQR) age of patients was 55 (21) years. In terms of nationality, 80% (n=28) were Pakistani, while 20% (n=7) were Afghan citizens.

The predominant clinical presentation was Rhino-

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orbito-Cerebral mucormycosis in 94.2% (n=33), whereas 2.8% (n=1) each had pulmonary and isolated orbital involvement. Patients were mainly admitted under the care of ENT division 65.7% (n=23), followed by Maxillofacial Surgery 22.9% (n=8), Neurology 5.7% (n=2), Cardiothoracic surgeon or physicians 2.9% (n=1), and Pediatrics 2.9% (n=1).

Radiological evaluation included CT sinuses and brain in 48.6% (n=17), MRI brain in 25.7% (n=9), while the remaining patients underwent alternative or combined imaging modalities.

The most common underlying risk factor was diabetes mellitus in 77.1% (n=27). Among patients with diabetes, 85.7% (n=23) had poorly controlled diabetes (HbA1c > 9%), 9.5% (n=3) had inadequately controlled diabetes (HbA1c 7–9%), and 4.7% (n=1) had well-controlled diabetes (HbA1c < 7%). Regarding hypoglycemic therapy, 28.6% (n=10) were on oral hypoglycemic agents, 34.3% (n=12) were on insulin, and 11.4% (n=4) were on dual therapy with insulin and oral agents. Other comorbidities included hypertension in 37.1% (n=13), ischemic heart disease in 14.3% (n=5), and a history of COVID-19 in 34.3% (n=12) patients.

Surgical intervention was performed in 97.1% (n=34) of patients. FESS being the most performed procedure i.e. 71.4%(n=25). All the patients were treated with amphotericin B. ICU care was required in 20% (n=7) patients.

Mortality association was performed on 31 patients with known discharge outcomes (25 survivors, 6 non-survivors); 4 patients discharged against medical advice hence excluded from mortality associated analysis.

Overall, complications were observed in 37.1% (n=13) patients, including drug-induced acute kidney injury in 11.4% (n=4). All patients who developed AKI received conventional amphotericin B. (p value 0.11 yielded by Fisher's exact test)

The in-hospital mortality rate was 17.1% (6/35), while the outcome of 11.4% (n=4) patients could not be ascertained as they took early discharge against medical advice (DAMA). These DAMA cases were excluded from further analysis between survivor and non-survivor groups. Further details of demographic, clinical and radiological features, management, and clinical outcomes are provided in Table 1 and 2.

Multiple factors were assessed for their association with mortality. ICU admission was significantly associated with mortality in our cohort. This association likely reflects underlying disease severity among critically ill patients rather than a causal relationship between ICU admission and adverse outcome. Out of 7 patients admitted to ICU 5 (71.4%) died, compared to 1 of 24 non-ICU patients (4.2%) ($p < 0.001$). Similarly, presence of complications such as shock or brain extension was significantly linked to

Table I: Demographic, Clinical, laboratory and radiological features of the patients with mucormycosis (n=35)

Demographic features	**n (%) or median (IQR)**
Age (years), mean ± SD	55(21)
Gender	
Male	24 (68.6)
Female	11 (31.4)
Comorbidities	**n (%)**
Diabetes mellitus	27 (77.1)
Hypertension	13 (37.1)
Ischemic heart disease	5 (14.3)
Clinical features	**n (%)**
Visual loss	12 (34.3)
Epistaxis (nosebleed)	2 (5.7)
Sinusitis	22 (62.9)
Oral involvement	9 (25.7)
Eye swelling	14 (40.0)
Facial pain	16 (45.7)
Focal neurological deficit	5 (14.3)
Third nerve palsy	4 (11.4)
Central retinal artery occlusion	2 (5.7)
Drooping of eyelid (ptosis)	6 (17.1)
Laboratory features	**Median (IQR)**
Total leukocyte count ($\times 10^9$/L)	14.06(8.82)
Neutrophils (%)	79.2(16.1)
C-reactive protein (mg/L)	25(39.48)
HbA1c (%)	11.50(2.40)
Radiological Features	**n (%)**
Sinus involvement	34(97.1)
Maxillary sinus	32(91.4)
Ethmoid sinus	22(62.9)
Frontal sinus	9(25.7)
Sphenoid sinus	13(37.1)
Cavernous sinus	5(14.3)
Bone erosion	17(48.6)
Orbit involvement	17(48.6)
Brain involvement	9(25.7)

mortality (p < 0.001). Among laboratory markers, CRP was substantially elevated in non-survivors (median ≈ 49.26 mg/L) versus survivors (median ≈ 7.75 mg/L), with a highly significant difference (p= 0.007). Neutrophilia was also significantly higher in those who died (median ≈ 87.8%) than in survivors (median ≈ 73.3%; p = 0.005). HbA1c was significantly higher in non-survivor group (median ≈ 13.9% vs 11.4%, P = 0.03). No significant differences were noted in gender, age, comorbidities, or total leukocyte count by outcome. Details are described in Table III.

Table II: Management strategies and in-hospital outcomes of patients with mucormycosis (n = 35).

Factors		n (%)
Management		
Medical Treatment		
Conventional amphotericin B		20(57.1)
Liposomal amphotericin B		15(42.9)
Surgical treatment*		
FESS		25(71.4)
Orbital exenteration		3(8.6)
Maxillectomy		6(17.1)
Debridement		3(8.6)
Pneumonectomy		1(2.9)
Clinical outcome		
Mean Duration of stay in hospital (median (IQR))		3(2.50)
Complications	Acute kidney injury	4(11.4)
	Extension to brain	8(22.9)
	Septic shock	2(5.7)
Death		6(17.1)

* Some patients underwent more than one surgical intervention (e.g., FESS with maxillectomy and debridement); hence, the total percentage exceeds 100%.

Discussion

We identified 35 confirmed cases over a 10 year period, which is comparable to reports from the various regions i.e., 33 cases in 11 years reported by Abanamy et al, from 3 tertiary care hospitals of the Kingdom of Saudi Arabia (KSA)[9] and 43 cases over a 14 year period by Allaw et al, from a tertiary care hospital, Lebanon.[10] These findings may reflect a similar disease burden across the Middle Eastern and

Table III: Comparison Of Clinical and Laboratory Variables Between Survivors and Non-Survivors with Known Outcomes (n=31) (4 DAMA cases excluded)

Categoric variables		Survivors (25/31) n%	Non-survivors (6/31) n%	P value (Fisher's exact test
Gender	Male	20 (80%)	5 (83.3%)	0.20
	Female	5 (20%)	1 (16.7%)	
Diabetes Mellitus		21 (84%)	5 (83.3%)	0.85
Hypertension		10 (40%)	2 (33.3%)	0.76
COVID positive		10 (40%)	1 (16.7%)	0.28
ICU admission		2(8%)	5 (83.3%)	<0.001
Complications	AKI	3(12%)	1 (16.7%)	0.75
	Brain extension	4(16%)	4(66.7%)	0.002
	Septic Shock	0(0%)	2(33.3%)	<0.001
continuous variables		Median(min-max) *	Median(min-max) *	P value (Mann Whiteny U test)
Age (years)		60 (33-67)	40 (31-50)	0.12
Duration of admission (days)		2.5(2-6)	3.5(3-4)	0.27
TLC($(\times 10^9/L)$)		14.02(7.16-16.3)	14(4.63-23.5)	0.13
Neutrophilia (%)		73.3(56-81.3)	87.8(83.2-92.4)	0.005
CRP (mg/L)		7.75 (0.8-29.7)	49.26(42-58)	0.007
HbA1c (%)		11.4(9.5-12.8)	13.9(13-14.8)	0.03

*Due to small sample in non-survival group, IQR was unstable so median (min-max) is used

South Asian cohorts. However, Priya et al[11] from India, reported a disproportionately higher incidence of mucormycosis compared to the rest of the regional statistics i.e. 38 cases in 4years. In a review on epidemiology of mucormycosis in India, has reported the rising incidence of the disease in India, exceptionally higher than regional and international statistics.[12] The relatively high prevalence of poorly controlled diabetes in India, may be one of the reasons for this statistical deviation compared to reports from the rest of the region. Additionally, the widespread use of glucocorticoids, especially during COVID-19, and environmental factors favoring disease transmission may have played a role as well.

The middle-aged adults and male predominance of our patient cohort align with the international data[9,11-15] suggesting a comparable, predominant disease trend among middle-aged adults worldwide. The gender predominance may be attributed to both a higher diabetes burden and increased

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environmental exposure to fungal spores among men.

In our study, Rhino-orbito-cerebral mucormycosis constituted 94.2% of cases, which is substantially higher than reported globally. Rhino-orbito-cerebral mucormycosis is widely recognized as the most common type of mucormycosis due to the site of entry of the organism. However, the number of cases seen in our cohort is still higher than reported elsewhere in literature. International data show lower frequencies. Allaw et[10] al. reported 74.4% of Rhino-orbito-cerebral mucormycosis in their patient cohort, while a meta-analysis of 66 studies over a period of 62 years has reported Rhino-orbito-cerebral mucormycosis in 75.2% of cases.[16] Some other studies have reported even lower rates of Rhino-orbito-cerebral mucormycosis. For example, 67.1% reported by A. Petal and colleagues in a multicenter study from India 2019[17] and 58.2% by Petal et al in 2021.[15] Pulmonary mucormycosis has been reported as a predominant form (~22%), followed by Rhino-orbito-cerebral mucormycosis (~20%) in a review by Alqahiri et al. [18] Data from Middle East reflects a different distribution, with cutaneous mucormycosis being most prevalent (27.2%), followed by localized sinusitis (21.21%), while pulmonary and Rhino-orbito-cerebral mucormycosis each accounted for 18.1% of cases[9]. These findings accentuate a distinctly skewed clinical distribution of Rhino-orbito-cerebral mucormycosis in this study, in comparison to the studies from neighboring regions and global cohorts. Several factors may explain this divergence, including a very high burden of poorly controlled diabetes in our region, differences in the patterns of healthcare access and a patient referral bias. Our tertiary level center frequently receives cases of mucormycosis with disseminated ENT, orbital, and cranial involvement. Environmental exposure and post-COVID susceptibility may have additionally predisposed patients in our study population to Sino-nasal inoculation and subsequent rhino-orbito-cerebral mucormycosis.

Diabetes mellitus emerged as the predominant comorbid condition in this study's cohort, aligning with the trends reported worldwide. However, the magnitude of contribution of diabetes to the disease burden varied for different regions. In our population, nearly all diabetic patients had poor glycemic control, affirming it as the leading predisposing factor for mucormycosis as documented in literature.[19] Comparable studies from Ghavami et al. reported diabetes in 76.5% of cases[13], Mishra et al, from India reported 87% of the study participants with mucormycosis, had poorly controlled diabetes.[20] A meta-analysis by Osaigboro et al, reported diabetes in 49.8%[16] and Abanamy et al, reported diabetes in 48% of the cases of mucormycosis in a multicenter study from KSA.[9] These regional differences, are likely influenced by disparities in metabolic health and healthcare availability . In contrast, studies from the western regions revealed results that are significantly different to our study cohort. In Europe, hematological malignancies are the most common risk factor for mucormycosis.[21] Hariprasath et al, described hematological malignancy as the most common risk factor for mucormycosis in Europe and the United States, ranging from 38% to 62%.[6] In another review, hematological malignancy has been recorded as a leading predisposing factor for mucormycosis in Europe i.e. 50% in France and 62% in Italy.[5] A French cross sectional prospective surveillance program on 550 patients reported hematological malignancies as the primary risk factor (65.1%), and diabetes only contributed to 7.5% of their patient population, [14] emphasizing that mucormycosis epidemiology mirrors local health burdens. Reports from Australia show 49% of the cases are in patients with hematological malignancies.[5]

Mortality in mucormycosis remains high globally and is strongly influenced by comorbidity profiles, diagnostic timelines, as well as sites of organ involvement. Mortality rates ranging from 25% to 87% have been reported with a clear predilection for higher mortality rates in disseminated disease involving the respiratory system.[8] Burak et al, documented a 48.4% one-year mortality and 46% overall mortality,[22] whereas a meta-analysis by Osaigboro et al, recorded 49.9% mortality associated with mucormycosis.[16] In a systematic review by L. Shamithra M. Sigera et al, mortality in untreated patients was 100%, whilst those treated with antifungal medications and having undergone surgical intervention, the mortality rates decreased

by 25.7% and 21.8% respectively.[23] These findings indicate that despite advances in antifungal therapy and surgical debridement techniques, outcomes still remain poor, particularly in settings with delayed presentation or advanced underlying illness. The high burden of poorly controlled diabetes in our study population likely contributes significantly to both disease susceptibility and adverse outcomes. A broad spectrum of clinical, laboratory, and host-related predictors of mortality has been consistently recognized in the literature, thus reflecting the diverse nature of disease presentation in mucormycosis. Phenotypes with disseminated infection at presentation, renal impairment, central nervous system involvement, and poor response to antifungal therapy are major determinants of mortality.[8] Abdulkadir et al. demonstrated that involvement of the orbit (HR 2.0), intracranial extension (HR 2.6), ICU admission (HR 6.4), poor glycemic control (HR 2.3), and multiple comorbidities (HR 1.6) independently predicted fatal outcome,[24] underscoring the combined influence of disease burden and host physiology. Burak et al. further highlights the prognostic value of immune-inflammatory markers, with non-survivors exhibiting significantly lower lymphocyte counts, markedly elevated neutrophil–lymphocyte ratios, and substantially higher rates of ICU admission and the need for mechanical ventilation. COVID-19–associated mucormycosis also showed disproportionate mortality rates, attributed to profound immune dysregulation.[22]A study by Amina Al-Jardani et al, reported a statistically significant association between COVID-19 status and patient survival (p = 0.024), and no correlation with age or diabetes control.[25]

Ghavami et al described rising age (P-value= 0.037), platelet count (P-value=0.006), C-reactive protein (CRP) levels (P-value= 0.001), and treatment duration (P-value= < 0.001) were significantly associated with higher mortality rates while the association of diabetes control with mortality in their study population remained insignificant. [13] Our findings align closely with the evidence reported in the studies mentioned above. Laboratory markers, such as CRP and neutrophil levels, were markedly higher in our study cohort supporting prior studies by Ghavami et al[13] and Mishra et al, [20] highlighting the prognostic relevance of inflammatory markers.

To conclude, both the published literature and findings from our cohort demonstrate that mortality in mucormycosis is driven predominantly by markers of severe disease, systemic complications, immune-inflammatory dysregulation, and the severity of the disease, which necessitates intensive care. These findings reinforce the importance of early recognition, aggressive and timely management of high-risk patients with clinical features suggesting aggressive disease, to improve survival rates. It is also vital to recognize the fact that prognostic predictors such as demographic and metabolic variables have a diverse influence worldwide, especially diabetes control which has been found to be a main player as a risk factor in Southeast Asia and showed strong impact on prognosis.

There are certain limitations to our study**.** Being a single center study, findings may not be observable or generalizable to other regions of Pakistan, where referral patterns, microbiological profiles, or healthcare infrastructure may be dissimilar to this center. Although consistent with the rarity of the disease, the small sample size limits statistical power, particularly in subgroup analyses. Reliance on documentation may have resulted in incomplete symptom reporting and limited assessment of certain clinical variables. Outcomes were recorded only at discharge; hence, recurrence, delayed complications, and long-term mortality could not be assessed.

Conclusion

This 10-year review highlights that mucormycosis in our region predominantly affects middle-aged individuals with poorly controlled diabetes and predominantly presented as rhino-cerebral disease. Despite surgical intervention, mortality remained substantially high and was strongly associated with markers of severe disease, particularly ICU admission, intracranial extension, septic shock, and elevated inflammatory markers. These findings emphasize the urgent need for early and accurate diagnosis. Furthermore, aggressive glycemic control, timely surgical debridement, and escalation of care for high-risk patients should be included in the management guidelines for mucormycosis, to help reduce preventable mortality.

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Declarations

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Conflict of Interest / Competing Interests
The authors declare no competing interests.

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CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

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DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon request.