

MUCORMYCOSIS OUTCOMES IN THE COVID 19 ERA: A RETROSPECTIVE COHORT STUDY

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ABSTRACT

BACKGROUND: COVID-19 and the extensive use of glucocorticosteroids triggered a surge in mucormycosis, a rapidly progressive angioinvasive fungal infection. This study investigates the major factors influencing mucormycosis outcomes during the COVID-19 pandemic.

OBJECTIVE: To evaluate the survival outcomes and potential prognostic factors of patients with mucormycosis during the COVID-19 pandemic and assess treatment strategies.

METHODOLOGY: This retrospective cohort study included 30 patients diagnosed with mucormycosis between January 2020 to December 2023. Clinical, radiological, and surgical data was collected. All patients underwent functional endoscopic sinus surgery (FESS) and surgical debridement. Data were analyzed using SPSS.

RESULTS: The mean age was 50.31 ± 1.91 years. There were 21 (70%) males, and 12 (40%) patients were COVID-19 positive. Disease extent included paranasal sinus (PNS) involvement in 9 (30%), PNS + orbital (OR) in 9 (30%), and PNS + OR + intracranial (IC) in 11 (37%). Mortality was higher in patients with extensive disease (PNS + OR + IC) at 6 (54.5%) ($p=0.018$). COVID-positive patients had a mortality rate of 6 (50%). FESS alone was performed in 18 (60%) of patients, while 12 (40%) required more extensive surgeries such as exenteration or external approaches and were linked to worse outcomes ($p=0.025$).

CONCLUSION; Advanced age, COVID-19 positivity, and extensive disease involving the paranasal sinuses, orbit, and intracranial regions were associated with higher mortality. Patients treated solely with FESS demonstrated better survival outcomes compared with those requiring more invasive procedures. Early diagnosis, timely surgical intervention, and appropriate antifungal therapy are essential for improving survival in mucormycosis cases.

KEYWORDS: Mucormycosis, COVID-19, mortality, immunocompromised.

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INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a deadly viral infection caused by SARS-CoV-2, first reported in Wuhan, China, in 2019. Declared a pandemic by WHO in March 2020, it resulted in millions of deaths worldwide. Glucocorticosteroids have been widely used as first-line treatment due to proven efficacy, but this has contributed to increased opportunistic infections such as aspergillosis, candidiasis, and mucormycosis.¹

Before COVID-19, the global incidence of mucormycosis ranged from 0.005 to 1.7 per million.² A sharp rise in mucormycosis cases among COVID-19 patients has since been reported, particularly in South Asia. Mucormycosis is an angioinvasive fungal infection causing vascular compromise and tissue necrosis.³ Transmission occurs via inhalation of spores, making the sinonasal tract and lungs the main sites of infection.^{3,4}

India reported a dramatic increase in rhino-orbital-cerebral mucormycosis, while other countries such as Egypt, Iran, Peru,

and Turkey published smaller series.⁵ The prevalence of rhino-orbital and rhino-cerebral mucormycosis in COVID-positive patients remains uncertain.⁶⁻⁸ Clinical features include facial pain, eye swelling, numbness, and neurological deficits.^{9,10} Diagnosis relies on clinical suspicion and radiological imaging. Standard treatment involves aggressive surgical debridement with antifungals such as Amphotericin B followed by Posaconazole.^{11,12} Early detections, antifungal therapy, and timely surgery remain key to improved survival.

Despite the rising burden of covid 19 associated mucormycosis, data from Pakistan examining the disease extent remains limited. This study aims to address this gap.

METHODOLOGY:

This retrospective cohort study was conducted at Northwest General Hospital and Research Centre, Peshawar, from January 2020 to December 2023. Patients of either gender, aged ≥ 18 years, diagnosed with mucormycosis, including both COVID-

19–positive and –negative cases, were included in the study. Covid positivity was based on the PCR result of the patients. Patients who declined surgery or did not have a postoperative follow-up visit at 2 months were excluded. A total of 30 patients met the inclusion criteria during this period.

Patient information was extracted from the hospital's electronic record system. Data on demographics, comorbidities, radiological findings, surgical procedures, and outcomes were collected. Radiological assessment was performed using CT/MRI scans to evaluate disease extent. Ethical approval was obtained from the Institutional Review Board (Ref: IRB&EC/2024-GH/0184), dated 02/01/2023.

Continuous variables were assessed for normality. As age and hospital stay showed skewed distribution, they were reported as median with interquartile range. Data were analyzed using SPSS version 25. Frequencies and percentages were calculated for categorical variables. Chi-square tests or Fisher's exact tests, where appropriate, were used to assess associations between categorical variables.

RESULTS

This study included 30 patients. The median age of the patients was 52 years (IQR:44-61; Range:30-69). Median length of hospital stay was 9 days (IQR: 6-14; Range: 1-29). 19 patients (63%) were alive by the end of the study. A significant portion 12 (40%) of the patients were COVID-19 positive, and corticosteroid use was reported in 11(37%) of the patients.

Radiological findings highlighted the extent of disease involvement, with 9(30%) of the patients exhibiting only paranasal sinus (PNS) involvement, 9(30%) having both PNS and orbital (OR) involvement, and 11(37%) having the most severe form of the disease, involving PNS, OR, and intracranial (IC) regions. PNS involvement was equally divided between unilateral

and bilateral cases 15(50%) each. Surgical data revealed that 18(60%) of the patients underwent functional endoscopic sinus surgery (FESS) alone, while 12(40%) required more extensive surgeries such as exenteration or external approaches. Orbital structures were successfully preserved in 21 (70%) patients. All patients 30(100%) received antifungal therapy. At two months' follow-up, clinical residual disease was observed in 8 (27%) patients, and revision surgery was required in 7 (23%) patients (table 1).

The association between disease extension and life status revealed a significant statistical relationship ($p=0.018$), with the most extensive disease (PNS + OR + IC) being associated with a higher mortality rate 6(54.5%) table 2.

Table 3 explores the association between COVID-19 status and disease outcomes. Although bilateral disease involvement and the most extensive form of the disease (PNS + OR + IC) were more common among COVID-19 positive patients, no significant association was observed in terms of surgical procedures or revision surgeries between COVID-19 positive and negative groups. The survival rate was lower among COVID-19 positive patients 6(50% mortality), as compared to negative cases 5(28% mortality), although the results were not statistically significant.

A significant relationship was noted between surgical procedures and orbital sparing, clinical residuals, and revision surgeries. Patients who underwent FESS alone had a high rate of orbital sparing 16(89%) but were less likely to have clinical residuals or require revision surgery 2(11%). In contrast, those who required both FESS and exenteration had worse outcomes, with 3(60%) having clinical residuals and 2(40%) needing revision surgery. The most extensive surgeries, involving FESS, exenteration, and external procedures, were associated with the highest rates of residual disease and revision surgeries 2(100%) table 4.

Table 1. Radiological and Surgical Findings

CT/MRI findings/ Disease extension (n, %)	
Paranasal Sinuses (PNS)	9 (30%)
Paranasal Sinuses (PNS)+OR	9 (30%)
Paranasal Sinuses (PNS)+IC	1 (3%)
Paranasal Sinuses (PNS)+ Orbital + Intracranial	11 (37%)
PNS involvement (n, %)	
Unilateral	15 (50%)
Bilateral	15 (50%)
Surgical procedure (n, %)	
Functional endoscopic sinus surgery (FESS) alone	18 (60%)
Functional endoscopic sinus surgery (FESS) + External	5 (17%)
Functional endoscopic sinus surgery (FESS) + Exenteration	5 (17%)
Functional endoscopic sinus surgery (FESS)+External+ Exenteration	2 (6%)
Orbital sparing (n, %)	21 (70%)
Antifungal therapy (n, %)	30 (100%)
Clinical residual (2 months) (n, %)	8 (27%)
Revision surgery (n, %)	7 (23%)

Note: PNS: paranasal sinuses; OR: orbital; IC: intracranial; FESS: functional endoscopic sinus surgery

Table 2: Association between life status and disease extension

Life status	Disease extension (n, %)					P value
	PNS	PNS + OR	PNS + IC	PNS + OR + IC	Total	
Alive	8 (42.1%)	9 (47.4%)	0 (0%)	2 (10.5%)	19 (100%)	0.018
Dead	1 (9.1%)	3 (27.3%)	1 (9.1%)	6 (54.5%)	11 (100%)	

Note: PNS: paranasal sinuses; OR: orbital; IC: intracranial; FESS: functional endoscopic sinus surgery; Fisher Exact test was used to calculate p value

Table 3: COVID status and its Association with Mucormycosis outcomes

Mucormycosis outcomes	COVID Status		p value	
	Negative	Positive		
PNS involvement	Unilateral	10(56%)	5(42%)	0.355
	Bilateral	8(44%)	7(58%)	
Extent of disease	PNS	6(33%)	3(25%)	0.433
	PNS+OR	8(44%)	4(33%)	
	PNS+IC	1(6%)	0(0%)	
	PNS+OR+IC	3(17%)	5(42%)	
Surgical procedure	FESS alone	11(61%)	7(58%)	0.537
	FESS+external	2(11%)	3(25%)	
	FESS+extenteration	3(17%)	2(17%)	
	FESS+ extenteration + external	2(11%)	0(0%)	
Revision Surgery	No	14(78%)	9(75%)	0.597
	Yes	4(22%)	3(25%)	
Live Status	Dead	5(28%)	6(50%)	0.197
	Alive	13(72%)	6(50%)	

Note: PNS: paranasal sinuses; OR: orbital; IC: intracranial; Fisher Exact test was used due to small sample size

Table 4. Association between surgical procedure with orbital sparing, clinical residual and revision surgery

Surgical procedure	Orbital sparing (n,%)		Clinical residual (n, %)		Revision surgery (n.%)	
	No	Yes	No	Yes	No	Yes
FESS alone	2(11%)	16(89%)	16(89%)	2(11%)	16(89%)	2(11%)
FESS + external	0(0%)	5(100%)	4(80%)	1(20%)	4(80%)	1(20%)
FESS + extenteration	5(100%)	0(0%)	2(40%)	3(60%)	3(60%)	2(40%)
FESS+ extenteration + external	2(100%)	0(0%)	0(0%)	2(100%)	0(0%)	2(100%)
p value	<0.001		0.014		0.031	

Note: FESS: functional endoscopic sinus surgery; Fisher Exact test was used to calculate p value

DISCUSSION

Mucormycosis is a rare but lethal fungal infection caused by a group of molds called mucormycetes; most commonly the *Rhizopus*, *Mucor* and *Rhizo-mucor* species. These molds live throughout the environment. Mucormycosis mainly affects patients with co-morbidities, especially Diabetes Mellitus or those with an adversely affected immune system. It most commonly affects the paranasal sinuses and/or the lungs after inhaling fungal spores from the surrounding air. Mucormycosis has different types.

Rhino cerebral Mucormycosis is most common in people who have diabetes and are immunosuppressed e.g. Post Renal Transplant. It is an infection of the paranasal sinuses that can easily spread to the brain. Pulmonary Mucormycosis commonly affects patients presenting with cancer, organ transplant or stem cell transplant. Other types, relatively insignificant for this study include Gastrointestinal Mucormycosis, Cutaneous Mucormycosis and Disseminated Mucormycosis.

One of the most important and lethal factors for developing Rhino-orbital-cerebral Mucormycosis associated with Covid-19 virus is Diabetes Mellitus. Early diagnosis with clinical findings and imaging scans along with timely treatment, with either Amphotericin B and/or surgical debridement of the disease could result in a favorable outcome.¹³ Chein-Ming Chao states that Covid-19 associated with Mucormycosis has been reported worldwide but most commonly in countries such as India, Iran and Egypt. Poor compliance to medications leading to poor or uncontrolled diabetes and the administration of systemic corticosteroids are precipitating factors for the development of Mucormycosis in patients with the sars-cov-2 virus. Conversely, the virus itself may affect the performance of the immune system adversely leading to Mucormycosis.¹⁴

Rimesh Pal, in his systematic review, states that most cases of COVID-19-associated mucormycosis were reported from India with a heavy percentage (72%) and the risk factors included male sex and underlying diabetes mellitus. An average time of 15 days was reported between patients recovering from the sars-cov-2 virus and then going on to develop Mucormycosis. Glucocorticoid therapy was used in the majority of cases (85%) and surgical debridement was associated with better clinical outcomes.¹⁵

A national survey was done in Germany on Covid-19 associated Mucormycosis whose findings suggested that although the condition was rare in that part of the world, it still exhibited its lethal effects on the meager population that was affected. It also stated that the risk for developing covid-19 associated Mucormycosis was higher in hospitalized patients than those who weren't and even more so in those who were admitted in the intensive care units and/or on mechanical ventilation.¹⁶

A meta-analysis done by Ostovan VR (2022) concluded that Mucormycosis associated with Covid-19 is a major public health issue particularly in developing countries such as Pakistan and India and that identifying mortality-related risk factors and providing optimized treatments may lead to an overall decreased rate of mortality.^{17,18}

In our study, we have looked at the paranasal sinus involvement status and covid status. There is a huge difference between unilateral and bilateral involvement of the paranasal sinuses and their covid statistics. Those patients with bilateral involvement of the sinuses have a substantial positive covid rate (58%) as opposed to those with unilateral involvement (42%).

This is one of the few studies from Pakistan examining outcome predictors of COVID 19 associated mucormycosis. We have investigated and considered factors that could be kept in mind for future admissions. This study also paves the way for future studies aimed at intervening in the management of Covid-19 associated Mucormycosis. However, the study has some limitation including its small sample size, retrospective and single-center design and short follow-up period, which limit the statistical power and generalizability of the findings. Future prospective, multicenter studies with standardized protocols and extended follow-up are recommended to validate these findings and strengthen the evidence base.

CONCLUSION

The study on mucormycosis during the COVID-19 era highlights significant outcomes and prognostic factors influencing patient survival. Older age, COVID-19 positivity, and extensive disease (involving paranasal sinuses, orbit, and intracranial regions) showed a statistically significant association with higher mortality. Patients who underwent only functional endoscopic sinus surgery (FESS) had better outcomes compared to those

requiring more aggressive surgeries. Corticosteroid use and COVID-19 status were associated with disease severity but did not significantly impact surgical intervention outcomes. Early diagnosis, prompt surgical debridement, and antifungal therapy remain critical for improving survival in mucormycosis cases. The diagnosis is made mainly by clinical findings however, imaging such as CT/MRI scans can also be done along with histopathological examination of the biopsied tissue via surgery.

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