

Original Article

Study of Management of Mucormycosis in COVID and Post-COVID Patients with Liposomal Amphotericin B its Outcome and Complications in a dedicated COVID Hospital from Eastern India

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Abstract

Background: Mucormycosis, an invasive fungal infection caused by Mucorales, has emerged as a significant concern in COVID-19 patients, particularly in regions heavily affected by the pandemic. Liposomal Amphotericin B is the primary treatment modality for mucormycosis; however, data on its efficacy and safety in COVID-19-associated mucormycosis are limited. This prospective observational study aimed to evaluate the management of mucormycosis in COVID-19 and post-COVID patients treated with Liposomal Amphotericin B at a dedicated COVID-19 hospital in IGIMS, Patna from Eastern India. Primary objectives were the study of liposomal amphotericin for the initial treatment of mucormycosis and treatment outcomes. The secondary objective was to study various complications of Liposomal Amphotericin B therapy.

Methodology: In total, 121 adult patients diagnosed with mucormycosis and either active COVID-19 infection or in the post-COVID recovery phase were included in the study. The treatment outcomes, complications, and factors influencing patient prognosis were assessed. Data analysis was performed using SPSS statistical software, including logistic regression and Cox Proportional Hazards modelling.

Results: Most patients achieved resolution of mucormycosis infection (70.2%), but the mortality rate was notable at 24.8%. Adverse events including nephrotoxicity (20.7%), infusion-related reactions (12.4%), and electrolyte imbalances (33.1%) were prevalent. Logistic regression analysis identified that older age ($p = 0.002$), diabetes ($p = 0.01$), delayed treatment initiation ($p = 0.001$), higher doses of Amphotericin B ($p = 0.04$), and pre-existing renal impairment ($p = 0.01$) were significant predictors of treatment outcomes. Cox Proportional Hazards modelling showed a trend towards improved outcomes with longer treatment duration ($p = 0.06$).

Conclusion: This study provides added information into the management of mucormycosis in COVID-19 patients treated with Liposomal Amphotericin B. Despite achieving a relatively high-resolution rate, the significant mortality and complication rates underscore the challenges in managing this fungal infection.

Keywords: Mucormycosis; COVID-19; Liposomal Amphotericin B; Treatment Outcomes; Complications.

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How to cite: Dinkar JK, Ranjan R, Priyanka, Kumar S, Kumar N. Study of Management of Mucormycosis in COVID and Post-COVID Patients with Liposomal Amphotericin B its Outcome and Complications in a dedicated COVID Hospital from Eastern India. Niger Med J 2025;66 (2):746-753. <https://doi.org/10.71480/nmj.v66i2.666>.

Quick Response Code:



Introduction

The COVID-19 pandemic caused by the novel coronavirus SARS-CoV-2 has led to a global health crisis, overwhelming healthcare systems worldwide and posing unprecedented challenges to public health [1][2][3]. In addition to the direct impact of COVID-19, there has been growing recognition of secondary infections and complications associated with the disease, including opportunistic fungal infections such as mucormycosis [4][5][6]. Mucormycosis, also known as zygomycosis, is an invasive fungal infection caused by members of the order Mucorales, primarily affecting immunocompromised individuals and those with underlying medical conditions [7][8]. India has witnessed a surge in mucormycosis cases among COVID-19 patients, leading to significant morbidity and mortality [9][10][11].

The convergence of factors such as diabetes mellitus, immunosuppression, and widespread use of corticosteroids and broad-spectrum antibiotics in COVID-19 management has contributed to the heightened risk of mucormycosis in this population [12][13][14]. Moreover, challenges in early diagnosis, limited access to antifungal medications, and delays in initiating appropriate treatment have further compounded the burden of mucormycosis in COVID-19 patients [15][16]. In this context, there is an urgent need for robust clinical evidence to guide the management of mucormycosis in COVID-19 patients. Liposomal Amphotericin B, a broad-spectrum antifungal agent, has emerged as the primary treatment modality for mucormycosis because of its efficacy and favourable safety profile [17][18][19]. However, data on the optimal dosing, duration, and outcomes of Liposomal Amphotericin B therapy in COVID-19-associated mucormycosis is limited, particularly in resource-constrained settings, such as Eastern India [20][21].

Therefore, this prospective observational study was conducted at a dedicated COVID-19 hospital in Eastern India to evaluate the management of mucormycosis in COVID-19 and post-COVID patients treated with Liposomal Amphotericin B. This study aimed to assess the treatment outcomes, complications, and factors influencing patient prognosis. By elucidating the clinical course and therapeutic response to mucormycosis in the context of COVID-19, this study seeks to inform evidence-based guidelines and optimize patient care strategies in similar settings.

The rationale for this study stems from the pressing need to address the escalating burden of mucormycosis in COVID-19 patients, particularly in regions experiencing high disease prevalence and limited healthcare resources. The objectives of this study were to evaluate the efficacy of Liposomal Amphotericin B in resolving mucormycosis infection in COVID-19 and post-COVID patients and to assess the mortality and relapse rates among patients treated with Liposomal Amphotericin B.

Furthermore, the study aimed to characterize the complications and adverse effects associated with Liposomal Amphotericin B therapy, including nephrotoxicity, infusion-related reactions, and electrolyte imbalances. Another objective was to identify factors influencing treatment outcomes, such as age, comorbidities, treatment duration, and liposomal amphotericin B. Finally, the study sought to explore the time to clinical resolution of mucormycosis and the factors affecting this outcome using Cox Proportional Hazards modelling.

Methodology

Study Design/Study Area

This prospective observational study was conducted at a dedicated COVID-19 hospital in IGIMS, Patna from Eastern India.

Study Population

The study included 121 adult patients (≥ 18 years) who were diagnosed with mucormycosis and had either active COVID-19 infection or were in the post-COVID recovery phase.

Exclusion Criteria

Patients were excluded from the study if they had known hypersensitivity to Liposomal Amphotericin B. Those with known cases of any hematological malignancies, or solid organ/hematopoietic stem cell transplant recipients. Those Patients who had received alternative antifungal treatments before the initiation of Liposomal Amphotericin B were also excluded to ensure the consistency of treatment regimens across the study population. Furthermore, pregnant or lactating women were excluded from the study owing to potential risks to the fetus or infant and the lack of comprehensive safety data for this population.

Data Collection

Data for the study were gathered from patients' medical records to ensure comprehensive analysis and accurate outcomes. The collected data encompassed a wide range of parameters that were carefully categorized to capture all relevant aspects of the patients' medical profiles and treatment experiences.

Demography

This study collected detailed demographic data, including patient age, sex, and comorbidities like diabetes and hypertension, to assess their impact on mucormycosis outcomes. COVID-19 status was classified as active or post-recovery within 12 weeks of diagnosis to explore timing effects on disease progression. The infection sites were categorized as rhino-orbital-cerebral, pulmonary, gastrointestinal, or others, with symptoms such as facial swelling, nasal congestion, headache, and fever documented to correlate presentation with severity.

Treatment

Treatment with Liposomal Amphotericin B (5 mg/kg/day) was tracked, noting dosage adjustments, treatment duration (4-6 weeks), and concurrent medications like corticosteroids and immunomodulators to evaluate therapeutic variations and outcomes.

Outcomes

Primary outcomes focused on infection resolution based on clinical improvement and radiological clearance. Mortality, time to death, and relapse rates were recorded for comprehensive treatment evaluation.

Complications

Complications, including nephrotoxicity (monitored by serum creatinine and GFR), infusion-related reactions, and electrolyte imbalances, were carefully documented to assess safety.

Laboratory and Imaging

Routine blood tests (renal/liver function, complete blood count) and periodic imaging (CT/MRI) were used to monitor health status and infection progression.

Outcome Measures

The primary measure was treatment efficacy, marked by symptom relief and radiological improvement. Secondary outcomes included mortality rates, safety profiles (complication rates), and the influence of underlying conditions on treatment success, aiming to refine future protocols.

Statistical Analysis

Data analysis was performed using statistical software. Descriptive statistics were used to summarize demographic and baseline characteristics and adverse events. Logistic regression analysis was conducted to identify the factors associated with treatment outcomes and complications. The Cox Proportional

Hazards Model was used to evaluate the factors influencing the time to clinical resolution in patients treated with Liposomal Amphotericin B for mucormycosis.

Results

The study cohort comprised 121 patients with mucormycosis in the context of COVID-19 or post-COVID recovery. The mean age of the patients was 55.3 years (SD \pm 14.7), with a predominantly male sex distribution (80 males and 41 females). Most patients had comorbidities, with diabetes being the most prevalent (70.2%), followed by hypertension (53.7%). Most patients were in the post-COVID recovery phase (58.7%), and the most common site of mucormycosis infection was the rhino-orbital-cerebral (57.9%). See Table 1.

Table 1: Demographic and Baseline Characteristics

Characteristic	Value
Age(mean \pm SD)	55.3 \pm 14.7years
Gender (Male/Female)	80/41
Comorbidities	Number (%)
Diabetes	85(70.2%)
Hypertension	65(53.7%)
other comorbidities	30(24.8%)
COVID-19 Status	Number (%)
Active Infection	50(41.3%)
Post-COVID Recovery	71(58.7%)
Site of Mucormycosis	Number (%)
Rhino-Orbital-Cerebral	70(57.9%)
Pulmonary	30(24.8%)
Gastrointestinal	15(12.4%)
Other	6 (5.0%)

Clinical outcomes revealed that 70.2% of the patient's achieved resolution of mucormycosis infection. However, the mortality rate was notable at 24.8%, and 5.0% of the patients experienced disease relapse. The mean time to clinical resolution was 28 days, indicating a relatively prompt response to treatment in most cases. See Table 2.

The study identified several complications and adverse effects associated with the treatment regimen. Nephrotoxicity was observed in 1 participant (0.8%), while infusion-related reactions were reported in 15 participants (12.4%). Electrolyte imbalances were notably frequent, affecting 40 participants (33.1%), with hypokalemia observed in 30 participants (24.8%) and hypomagnesemia in 20 participants (16.5%). These findings highlight the high incidence of electrolyte imbalances compared to other complications, underscoring the need for careful monitoring and management of electrolyte levels during treatment to mitigate these common adverse effects. See Table 3.

Table 2: Clinical Outcome of patients

Outcome Variable	Value n(%)
Resolution of Infection	85(70.2%)
Mortality Rate	30(24.8%)
Relapse	6(5.0%)
Time to Clinical Resolution (mean)	28days

Table 3: Complications and Adverse Effects

Complication/Adverse Effect	Number of Participants	Percentage (%)
Nephrotoxicity	1	0.8
Infusion-Related Reactions	15	12.4
Electrolyte Imbalances	40	33.1
Hypokalemia	30	24.8
Hypomagnesemia	20	16.5

Logistic regression analysis identified several factors that were significantly associated with the treatment outcomes. Older age was inversely associated with treatment success (OR = 0.95, 95% CI: 0.92 - 0.98, $p = 0.002$), whereas diabetes was associated with a lower likelihood of successful treatment (OR = 0.40, 95% CI: 0.20 - 0.80, $p = 0.01$). Early treatment initiation significantly increased the odds of treatment success (OR = 3.50, 95% CI: 1.80 - 6.80, $p = 0.001$). Additionally, higher doses of liposomal Amphotericin B and pre-existing renal impairment were associated with poorer treatment outcomes ($p < 0.05$).

Table 4: Logistic Regression Analysis for Factors Associated with Treatment Outcomes

Variable	Odds Ratio (OR)	95% Confidence Interval (CI)	P-Value
Age	0.95	0.92-0.98	0.002
Diabetes	0.40	0.20-0.80	0.01*
Early Treatment Initiation	3.50	1.80-6.80	0.001*
Dose of Amphotericin B	1.20	1.05-1.35	0.04
Pre-existing Renal Impairment	2.50	1.30-4.80	0.01*

The Cox Proportional Hazards Model was used to analyse factors influencing the time to clinical resolution. Age, diabetes, site of infection (pulmonary), and treatment duration were also examined. While none of the variables reached statistical significance ($p > 0.05$), longer treatment duration showed a trend towards improved outcomes (HR = 0.92, 95% CI: 0.85 - 1.00, $p = 0.06$). See Table 5.

Table 5: Cox Proportional Hazards Model for Time to Clinical Resolution

Variable	Hazard Ratio (HR)	95% Confidence Interval (CI)	P-Value
Age	0.98	0.95-1.02	0.32
Diabetes	0.70	0.42-1.16	0.17
Site of Infection (Pulmonary)	1.25	0.75-2.10	0.39
Treatment Duration	0.92	0.85-1.00	0.06

Discussion

Mucormycosis, a severe opportunistic fungal infection, posed significant challenges during the COVID-19 pandemic, particularly in patients with underlying conditions. This study, conducted at a dedicated COVID-19 hospital, provides critical insights into its management using Liposomal Amphotericin B. The patient profile indicates that middle-aged to older adults, especially those with diabetes, were more susceptible. This aligns with the established link between diabetes and increased fungal infection risk due to impaired immune function and elevated blood sugar levels [22].

Treatment outcomes were promising, with most patients achieving resolution. However, the substantial mortality rate highlights the aggressive nature of mucormycosis and the urgent need for early and effective treatment. The low recurrence rate observed suggests that Liposomal Amphotericin B was effective in suppressing the infection when administered adequately. Nonetheless, the high mortality emphasizes that treatment must be initiated promptly and tailored to individual patient needs to enhance survival. Adverse effects were notable, particularly nephrotoxicity and electrolyte imbalances. Nephrotoxicity, a known risk with Amphotericin B, requires careful monitoring of kidney function to prevent long-term damage. The frequent occurrence of hypokalemia and hypomagnesemia reflects the drug's impact on the renal handling of electrolytes, underscoring the need for regular laboratory evaluations and corrective measures to maintain stability.

Statistical analysis confirmed that early treatment initiation significantly improves outcomes, while older age and diabetes are strong negative predictors of recovery. These findings emphasize the importance of timely antifungal intervention and tailored approaches for high-risk groups. Higher doses and renal impairment were also linked to poorer outcomes, suggesting that dosage adjustments and kidney function monitoring are critical components of management. While longer treatment duration appeared beneficial in improving recovery, further studies are needed to determine the optimal length of therapy. This observation reinforces the need for flexible treatment protocols that adapt to patient progress rather than rigid timelines.

This study highlights the multifactorial challenges in managing COVID-19-associated mucormycosis. A proactive approach focusing on early diagnosis, individualized treatment strategies, and close monitoring of adverse effects is crucial for improving outcomes. A multidisciplinary team, including specialists in infectious diseases and critical care, is essential to address this life-threatening condition effectively. Future research should explore strategies to minimize complications and optimize therapy duration to enhance patient survival.

Conclusion

This study provides valuable insights into the management of mucormycosis in COVID-19 patients treated with Liposomal Amphotericin B. Despite achieving a relatively high-resolution rate, the significant mortality and complication rates underscore the challenges in managing this complex fungal infection. Further research is needed to explore novel treatment strategies, improve risk stratification, and enhance patient outcomes in this vulnerable population.

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