Section: Pulmonology

Original Research Article

A COMPARATIVE ANALYSIS OF MUCORMYCOSIS VERSUS ASPERGILLOMA: BASED ON POST-VATS OUTCOMES IN THE MANAGEMENT OF RECURRENT HEMOPTYSIS ASSOCIATED WITH FUNGAL BALLS IN RESIDUAL TUBERCULOSIS CAVITIES

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Received *: 08/10/2025*
Received in revised form *: 30/11/2025*
Accepted *: 15/12/2025*

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DOI: 10.70034/ijmedph.2025.4.477

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2025; 15 (4); 2654-2659

ABSTRACT

Background: Aspergilloma develops from Aspergillus colonization within lung cavities, typically following tuberculosis. In contrast, pulmonary mucormycosis progresses rapidly in severely immunocompromised patients, often as a breakthrough infection resistant to antifungals effective against aspergillosis. It is characterized by aggressive angioinvasion, thrombosis, and tissue necrosis, with a mortality rate of 50-70% that exceeds 90% with extrathoracic spread. Accurate differentiation from aspergillosis is vital due to the ineffectiveness of treatments like voriconazole and the infrequent occurrence of classic imaging signs. Prompt diagnosis is essential for guiding effective therapy and improving patient outcomes. **Aim:** To analyze and compare post-VATS outcomes and clinical profiles of mucormycosis and aspergilloma in recurrent hemoptysis associated with fungal balls in residual tuberculosis cavities after bronchial artery embolization.

Materials and Methods: We conducted a case series at NRI Hospital, Mangalgiri, Guntur, from September 2024 to April 2025. The study included 23 cases of recurrent hemoptysis following bronchial artery embolization in residual tuberculosis cavities, which showed the air-crescent sign on CT. We evaluated clinical features, comorbidities, and histopathological characteristics of post-VATS fungal mycetomas.

Results: Among 23 cases, 17 were male (73.9%) and 6 were female (26.1%). Mucormycosis was identified in 9 cases (39.13%), aspergilloma in 12 (52.17%), both in 1 (4.32%), and 1 (4.32%) was inconclusive. Compared to aspergilloma, mucormycosis patients were more likely to be malnourished (BMI 19.11±1.55 vs. 22.19±2.64, p=0.001), experience severe/massive hemoptysis (p=0.001), have a post-COVID history (44.4% vs. 8.3%, p=0.01), and develop post-op stump leaks (44.4% vs. 8.3%, p=0.01).

Conclusion: Fungal balls with the air crescent sign on CT in post-tubercular cavities are not always aspergillomas. Differentiating them from mucormycosis requires thorough clinical, microbiological, bronchoscopic, serological, and histopathological evaluation. This distinction is crucial, as the two conditions require different treatments, and mucormycosis is associated with higher morbidity, mortality, and poor prognosis.

Keywords: Mucormycosis, Aspergilloma, Post-Tubercular cavities, Bronchial Artery Embolisation, VATS.

INTRODUCTION

Saprophytic colonization of a lung cavity by Aspergillus is known as aspergilloma, mycetoma, or a fungus ball. Cavitatory lesions are seen in tuberculosis, sarcoidosis, histoplasmosis, nocardiosis, bronchiectasis and bullous lung disease. In developing countries, tuberculosis is the main predisposing factor, responsible for over 90% of aspergilloma cases. Pulmonary mucormycosis is a rapidly advancing infection that can spread to other organs if untreated, mainly affecting severely immunocompromised patients, including those with hematologic malignancies or recent transplants.[1,2] It often occurs as a breakthrough infection in patients on antifungals effective against Aspergillus but not Mucorales, such as voriconazole. Key features include extensive angioinvasion leading to vessel thrombosis and tissue necrosis, with a mortality rate of 50-70%, exceeding 90% with spread beyond the lungs. Symptoms are similar to those of Aspergillus infections, but halo and air crescent signs are less common. Timely diagnosis is crucial, as first-line antifungals for Aspergillus are ineffective against Mucorales.[3,4]

Aim

To analyze and compare post-VATS outcomes and clinical profiles of mucormycosis and aspergilloma in recurrent hemoptysis associated with fungal balls in residual tuberculosis cavities after bronchial artery embolization.

Objectives

1. Assess the characteristics of fungal balls in residual tubercular cavities.
2. Identify risk factors associated with aspergilloma versus mucormycosis.
3. Evaluate intraoperative and postoperative complications in cases of aspergilloma versus mucormycosis.

MATERIALS AND METHODS

We conducted a case series at NRI Hospital, Mangalgiri, Guntur, from September 2024 to April 2025. The study included 23 cases of recurrent hemoptysis following bronchial artery embolization in residual tuberculosis cavities, which showed the air-crescent sign on CT. We evaluated clinical features, comorbidities, and histopathological characteristics of post-VATS fungal mycetomas.

Inclusion Criteria

- Patients who provided informed consent.
- Individuals with recurrent hemoptysis following bronchial artery embolization, presenting with residual tuberculosis cavities and an air crescent sign on ct.

Exclusion Criteria

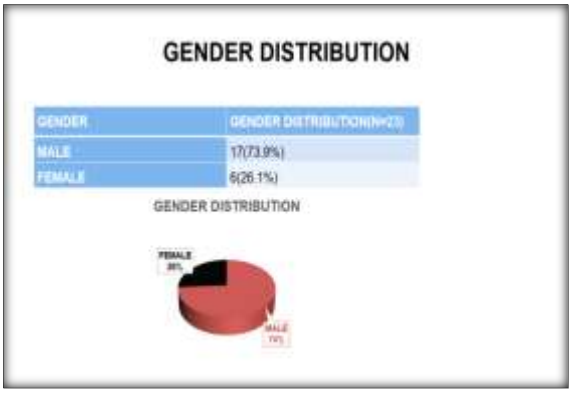
- Patients not fit for surgery

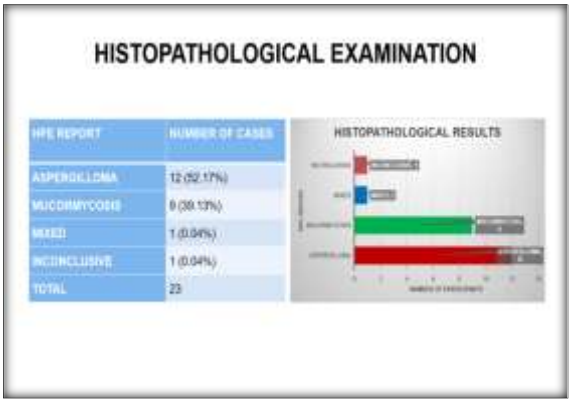
RESULTS

Table 1: Demographic and Clinical Characteristics of Study Participants

Variable		N(%)(23)
SEX	MALE	17(73.9%)
	FEMALE	6(26.1%)
BMI	Under Weight	6(26.1%)
	Normal Weight	14(60.9%
	Over Weight	3(13.0%)
Risk factor	COVID 19	5(21.7%)
	DM	10(43.5%)
	HTN	8(34.8%)
Addictions	Smoking	9(39.1%)
	Alcohol	5(21.7%)
Hemoptysis	Moderate	9(39.1%)
	Severe	13(56.5%)
	Massive	1(4.3%)
BAL		4(17.4%)
Post Operative Complications	Stump Leak	5(21.7%)
	Intra Po Bleeding	6(26.1%)

Variable	Mean±SD
Age	50.34±9.08
BMI	21.12±2.86
ANC	5190.00±1116.45
AEC	435.65±259.16



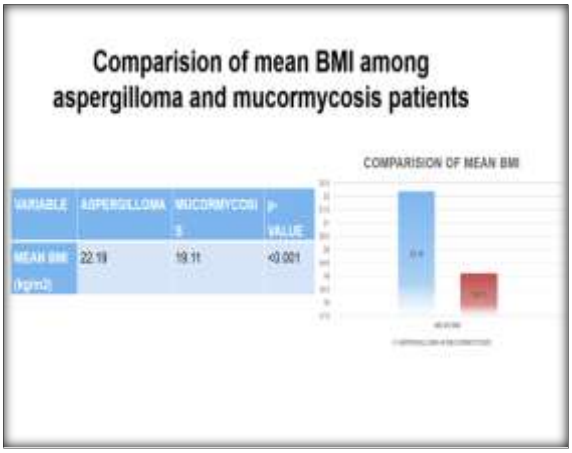


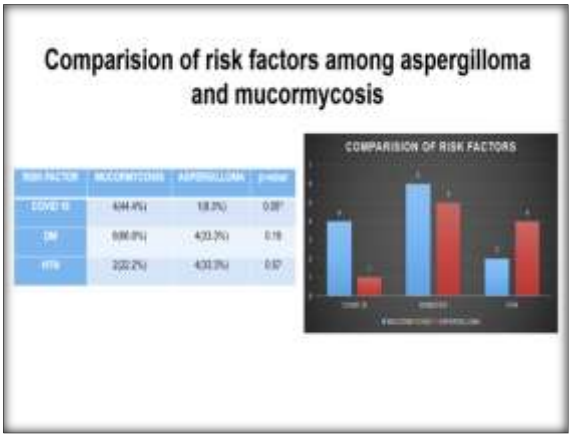
Comparision of different variables between two groups using the Chi-Square test

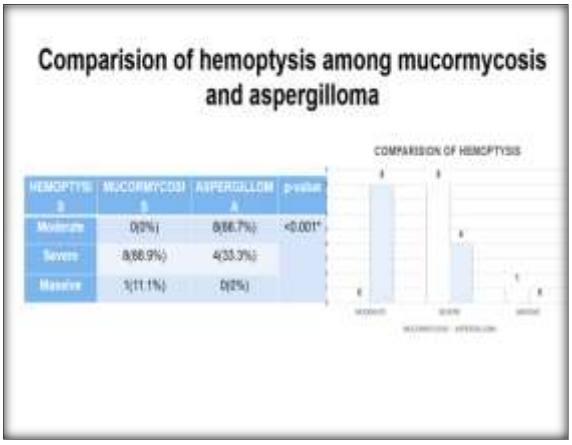
Variable		N(%)		χ^2 Value	P Value
		Mucormycosis (9)	Aspergilloma (12)		
SEX	MALE	7(77.8%)	9(75%)	0.02	0.88
	FEMALE	2(22.2%)	3(25%)		
BMI	Under Weight	4(44.4%)	2(16.7%)	2.99	0.22
	Normal Weight	5(55.6%)	8(66.7%)		
	Over Weight	0(0%)	2(16.7%)		
RISK FACTORS	COVID 19	4(44.4%)	1(8.3%)	3.69	0.05*
	DM	6(66.6%)	4(33.3%)	1.45	0.19
	HTN	2(22.2%)	4(33.3%)	0.31	0.57
Addictions	Smoking	5(55.6%)	3(25.0%)	2.03	0.15
	Alcohol	2(22.2%)	2(16.7%)	0.10	0.74
Hemoptysis	Moderate	0(0%)	8(66.7%)	10.11	<0.001*
	Severe	8(88.9%)	4(33.3%)		
	Massive	1(11.1%)	0(0%)		
BAL		2(22.2%)	2(16.7%)	0.10	0.74
Peri-Operative Complications	Stump Leak	4(44.4%)	1(8.3%)	3.69	0.05*
	Intra Po Bleeding	4(44.4%)	2(16.7%)	1.94	0.16

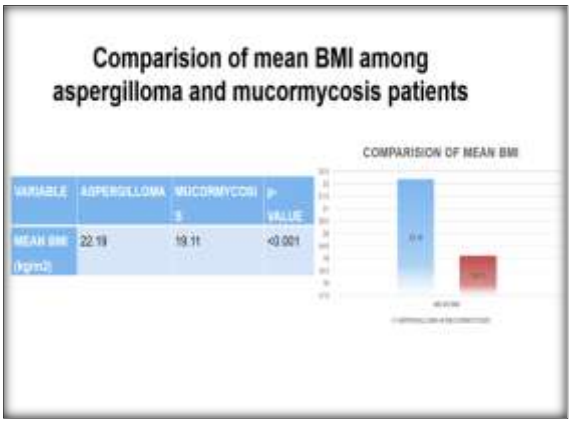
Descriptive Analysis of different variables between two groups using an independent t-test

Variable	Mean±SD		t Value	P Value
	Mucormycosis	Aspergilloma		
Age	47.55±9.77	51.83±7.89	1.11	0.28
BMI	19.11±1.55	22.19±2.64	3.09	<0.001*
ANC	4698.22±1010.88	5490.00±1174.02	1.62	0.12
AEC	449.66±280.22	452.58±267.70	0.02	0.98









In the current study involving 23 patients, 17 (73.9%) were males and 6 (26.1%) were females; 6 (26.1%) were underweight, 14 (60.9%) had normal weight, and 3 (13.0%) were overweight. The observed risk factors included Post-COVID-19 status in 5 patients (21.7%), Diabetes Mellitus in 10 (43.5%), and Hypertension in 8 (34.8%); addictions comprised smoking in 9 (39.1%) and alcohol use in 5 (21.7%). The severity of hemoptysis was moderate in 9 patients (39.1%), severe in 13 (56.5%), and massive in 1 (4.3%). Histopathological examination revealed Aspergilloma in 12 cases (52.17%), Mucormycosis in 9 (39.13%), mixed infection in 1 (4.32%), and inconclusive findings in 1 (4.32%). Perioperative complications included stump leak in 5 patients (21.7%) and intraoperative bleeding in 6 (26.1%).

In the comparative analysis, 7 of 9 patients with mucormycosis (77.8%) and 9 of 12 patients with aspergilloma (75%) were male, while 2 of 9 mucormycosis patients (22.2%) and 3 of 12 aspergilloma patients (25%) were female. Among those with mucormycosis, 4 patients (44.4%) were underweight and 5 (55.6%) had normal weight, with none being overweight, whereas among aspergilloma patients, 2 (16.7%) were underweight, 8 (66.7%) had normal weight, and 2 (16.7%) were overweight. Risk factors in patients with mucormycosis vs aspergilloma are COVID-19 4(44.4%) vs 1(8.3%); DM 6 (66.6%) VS 4(33.3%); HTN 2 (22.2%) VS 4(33.3%); Smoking 5(55.6%) vs 3(25.0%); Alcohol 2(22.2%) vs 2(16.7%).

In patients with mucormycosis compared with those with aspergilloma, moderate hemoptysis occurred in 0 (0%) vs 8 (66.7%), severe hemoptysis in 8 (88.9%) vs 4 (33.3%), and massive hemoptysis in 1 (11.1%) vs 0 (0%). Stump leak was observed in 4 (44.4%) vs 1 (8.3%). The mean age was 47.55 ± 9.77 years vs 51.83 ± 7.89 years, and the mean BMI was 19.11 ± 1.55 vs 22.19 ± 2.64. Intraoperative bleeding occurred in 4 (44.4%) vs 2 (16.7%).

Post-COVID-19 status was significantly more frequent in patients with mucormycosis (44.4%) compared with those with aspergilloma (8.3%; $p = 0.05$). Diabetes mellitus was also more common among mucormycosis cases (66.6%) than aspergilloma cases (33.3%; $p = 0.19$). Patients with mucormycosis had a lower BMI (19.11 ± 1.55) compared with those with aspergilloma (22.19 ± 2.64; $p < 0.001$). Severe to massive hemoptysis occurred more often in the mucormycosis group ($p < 0.001$). Stump leak was another perioperative complication noted more frequently in mucormycosis cases (44.4%) than in aspergilloma cases (8.3%; $p = 0.05$).

DISCUSSION

The study involved 23 patients presenting with recurrent hemoptysis following bronchial artery embolization (BAE) and exhibiting the air crescent sign in pre-existing post-tubercular cavities, all of

whom underwent VATS lobectomy. Histopathological examination revealed the following: Mucormycosis in 9 cases (39.13%), Aspergilloma in 12 cases (52.17%), a combination of Mucormycosis and Aspergilloma in 1 case (4.32%), and inconclusive findings in 1 case (4.32%). A rare case was reported where one patient exhibited both mucormycosis and aspergilloma, a notably rare occurrence that poses significant challenges for management with medical therapy alone.[5]

Radiological Indicators in Mycetoma: The air crescent sign is most commonly associated with pulmonary aspergilloma. The reversed halo sign is highly suggestive of pulmonary mucormycosis in neutropenic patients, although it is typically an early and transient finding. Other radiological features—such as consolidation, nodules, halo sign, micronodules, mass, cavitation, and pleural effusion are non-specific.[6]

Clinical Features: In the study by Jeong et al., pulmonary mucormycosis and aspergilloma present with non-specific symptoms such as fever, cough, dyspnea, chest pain, and hemoptysis, rendering them clinically indistinguishable.[3] Severe to massive hemoptysis, however, occurs more frequently in pulmonary mucormycosis. In our study, pulmonary mucormycosis was significantly more associated with severe to massive hemoptysis compared to aspergilloma ($p < 0.001$).

Risk Factors-Pulmonary Mucormycosis: The incidence of post-COVID status was significantly higher in mucormycosis patients (44.4%) compared to those with pulmonary aspergilloma (8.3%; $p = 0.05$). Patients with mucormycosis also had a lower body mass index (BMI) (19.11 ± 1.55) than aspergilloma patients (22.19 ± 2.64; $p = 0.001$). Diabetes mellitus was more prevalent among mucormycosis cases (66.6%) compared to aspergilloma (33.3%; $p = 0.19$). In the Indian context, Prakash et al. identified several risk factors for mucormycosis, including hematologic malignancies, solid organ transplants, diabetes mellitus, COVID-19 infection, malnutrition, post-pulmonary tuberculosis, and chronic kidney disease.[6] This pattern aligns with findings from multiple pulmonary fungal infection studies, which consistently report higher prevalence among males, attributed to greater exposure to occupational risk factors, higher rates of smoking, and increased prevalence of comorbidities among men.[7] Studies by various authors on pulmonary aspergilloma cohorts have similarly documented male proportions ranging from 60% to 80%.[8,9]

Perioperative Complications: Stump Leaks: Significantly more common in pulmonary mucormycosis (44.4%) compared to aspergilloma (8.3%; p=0.05). Benjamin SR et al conducted a small case series of pulmonary mucormycosis: reported substantially higher post-surgical morbidity including prolonged air-leak/stump problems; authors note higher morbidity/mortality for mucormycosis vs other fungal pulmonary disease.[10]

Diagnosis: Radiological investigations; Microbiological: Sputum and BAL KOH, fungal cultures; Serological: Aspergillus/mucorale-specific IgG, Galactomannan antigen assay; Histopathology, Biopsy evaluation.

Treatment: The treatment goals for both mucormycosis and aspergilloma focus on alleviating symptoms, minimizing hemoptysis, and preventing pulmonary fibrosis.[6]

Mucormycosis Treatment

- First-line therapy: Liposomal amphotericin B.
- Step-down therapy: Oral isavuconazole or posaconazole.
- Additional considerations: Address underlying disease and consider surgery when necessary.

Aspergilloma Treatment

- Antifungal therapy:
  - Systemic: Itraconazole or voriconazole.
  - Local: Amphotericin B deoxycholate (AMB-D) or ketoconazole.
  - Surgical intervention: Recommended for recurrent hemoptysis following bronchial artery embolization (BAE).
- Conservative management: Regular follow-up for non-severe cases.

The study highlights the importance of differentiating between aspergilloma and mucormycosis in patients with post-tubercular cavities presenting with an air crescent sign. While the air crescent sign is traditionally associated with aspergilloma, Sharma S et al,[11] the study found a significant proportion of mucormycosis cases presenting with this radiological feature. This underscores the necessity for comprehensive diagnostic evaluations, including microbiological, serological, and histopathological analyses, to identify the fungal pathogen accurately.

Risk factors such as post-COVID-19 status, low BMI, and diabetes mellitus were more prevalent in mucormycosis patients, aligning with existing literature identifying these as significant risk factors for mucormycosis. Additionally, the higher incidence of severe to massive hemoptysis and increased perioperative complications in mucormycosis cases highlight the aggressive nature of this infection compared to aspergilloma.

CONCLUSION

While the air crescent sign on CT imaging is a hallmark of pulmonary aspergilloma, it is not pathognomonic. A multidisciplinary approach involving clinical, microbiological, bronchoscopic, serological, and histopathological evaluations is essential to distinguish between aspergilloma and mucormycosis. Recognizing the specific fungal etiology is critical, as mucormycosis demands prompt and aggressive treatment due to its association with higher morbidity, mortality, and perioperative complications.

Clinicians should maintain a high index of suspicion for pulmonary mucormycosis in patients presenting

with fungal balls and an air crescent sign, especially when accompanied by risk factors such as post-COVID status, low BMI, and severe hemoptysis.

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