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Research Article

Clinical and Epidemiological Profile of Pathogenic Moulds Causing Systemic Mycoses in Patients Receiving Immunosuppressive Therapy and Their Antifungal Susceptibility in a Tertiary Care Hospital

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ABSTRACT
Background: Invasive mould infections remain a serious problem in immunosuppressed patients because the disease often evolves rapidly, presents with nonspecific features, and demands early antifungal selection.
Aim: To describe the clinical and epidemiological profile of pathogenic moulds causing systemic mycoses in patients receiving immunosuppressive therapy and to assess their antifungal susceptibility pattern.
Materials and Methods: This prospective cross-sectional study was conducted in a tertiary care teaching hospital in Chennai over 12 months in the year 2022.Three hundred immunosuppressed adults with suspected systemic mycosis were evaluated using conventional mycological methods. Mould isolates were identified by culture characteristics and lactophenol cotton blue microscopy. Antifungal susceptibility testing was performed by the CLSI M38-A2 broth microdilution method.
Results: Systemic mycoses were confirmed in 28 of 300 patients, yielding an incidence of 9.3%. Men constituted 67.9% of confirmed cases, and the 41-60-year age group was most affected (60.7%). Thoracic Medicine contributed the largest share of cases (39.3%). Aspergillus spp. were the predominant isolates (57.1%), followed by Mucor spp. (25.0%) and Rhizopus spp. (17.9%). All proven mould infections occurred among corticosteroid-exposed COVID-19 patients, with a significant association between steroid regimen and proven mycosis within that subgroup (chi-square=24.7411, p=0.000001). Amphotericin B showed 100% in-vitro susceptibility across all isolates. Voriconazole retained excellent activity against Aspergillus spp., whereas itraconazole and posaconazole showed reduced activity against Mucorales.
Conclusion: Systemic mould infections in immunosuppressed patients in this setting were driven mainly by Aspergillus spp. and Mucorales, with a clear concentration among steroid-exposed patients. Species-level identification and routine antifungal susceptibility testing remain important for timely and appropriate therapy.

Keywords: Amphotericin B, Antifungal Susceptibility, Aspergillosis, Immunosuppression, Mucormycosis, Systemic Mycoses.

INTRODUCTION

Invasive fungal disease is no longer confined to a narrow group of profoundly immunocompromised hosts. The at-risk population has widened steadily with the expanding use of chemotherapy, organ transplantation, corticosteroids, biological agents, and intensive care support. That therapeutic progress has improved survival, but it has also created a larger clinical space in which opportunistic fungi can invade, disseminate, and cause severe disease.[1]

The change is not merely quantitative. The spectrum of fungal disease has also shifted, with more reports of difficult mould infections, new host profiles, and therapeutic uncertainty in patients whose immune defects are treatment-related rather than classical.[2] In routine practice, these infections are troublesome because the presenting features are rarely specific. Fever, cough, sinus symptoms, or altered sensorium may initially

resemble bacterial or viral disease, so microbiological confirmation often arrives late.[3]

Aspergillus remains the dominant invasive mould in many hospital settings, especially in patients with haematological disease, prolonged steroid exposure, or critical illness. Its clinical relevance extends beyond pulmonary disease because delayed recognition may lead to angioinvasion and systemic spread.[4] Mucorales are equally important for a different reason. Although less frequent in many series, they progress aggressively, show a marked affinity for vascular invasion and tissue necrosis, and often require urgent treatment decisions before laboratory certainty is complete.[5]

The post-COVID period added further complexity in India. COVID-19-associated mucormycosis emerged at an exceptional scale, driven by a combination of corticosteroid exposure, diabetes, prolonged hospitalisation, and altered host immunity.[6] At the same time, COVID-19-associated pulmonary aspergillosis became a recognised complication in critically ill patients, reminding clinicians that severe viral illness and intensive care support can themselves create conditions favourable for invasive mould disease.[7]

Against this background, antifungal susceptibility testing has become more than a laboratory adjunct. It provides context for therapeutic choices, helps detect reduced azole susceptibility, and supports stewardship in high-burden settings where empirical treatment alone may not be enough.[8] Indian data on invasive fungal infections also continue to show important variability in pathogen distribution and susceptibility patterns across centres, underlining the need for hospital-level evidence.[9]

The present study was therefore undertaken to characterise the clinical and epidemiological profile of pathogenic moulds causing systemic mycoses in patients receiving immunosuppressive therapy, and to evaluate their antifungal susceptibility pattern in a tertiary care setting.

Aim

To study the clinical and epidemiological profile of pathogenic moulds causing systemic mycoses in patients receiving immunosuppressive therapy, and to evaluate their antifungal susceptibility pattern.

MATERIALS AND METHODS

Study Design and Setting: A prospective cross-sectional study was conducted from August 2021 to August 2022 in the Institute of Microbiology, Madras Medical College, in collaboration with the Departments of Haematology, Medical Oncology, and Nephrology at Rajiv Gandhi Government General Hospital, Chennai.

Study Population: Adults aged more than 18 years who were receiving immunosuppressive therapy and had clinical features suggestive of systemic mycosis were eligible. The study population included patients on corticosteroids, individuals receiving chemotherapy for haematological or solid organ malignancy, renal transplant recipients, and critically ill patients with prolonged intensive care exposure. A total of 300 suspected cases were evaluated.

Inclusion Criteria: Immunosuppressed patients with clinical suspicion of invasive or disseminated fungal infection were included.

Exclusion Criteria: Patients not meeting the clinical criteria for suspected systemic mycosis and those with incomplete microbiological work-up were not considered for final analysis.

Sample Collection and Processing: Clinical specimens included sputum, bronchoalveolar lavage, cerebrospinal fluid, urine, blood, bronchial wash, and tissue samples obtained under aseptic precautions. Respiratory specimens were inoculated onto Sabouraud dextrose agar and incubated at 25 degrees C and 37 degrees C. Cerebrospinal fluid and urine samples were centrifuged before culture. Blood samples were first inoculated into brain-heart infusion broth and later subcultured onto Sabouraud dextrose agar. Cultures were observed for up to four to six weeks before being considered negative.

Identification of Mould Isolates: Preliminary screening was performed using 10% potassium hydroxide wet mount. Definitive identification was based on colony morphology, growth characteristics, pigmentation, and lactophenol cotton blue microscopic features. The clinical significance of isolates was judged using repeated isolation, specimen type, and clinicomicrobiological correlation.

Antifungal Susceptibility Testing: Antifungal susceptibility testing for mould isolates was performed by the CLSI M38-A2 broth microdilution method. Amphotericin B, voriconazole, itraconazole, and posaconazole were tested. Conidial suspensions were prepared from 48-hour cultures on potato dextrose agar, standardised spectrophotometrically, inoculated into RPMI-

1640 medium, and incubated at 35 degrees C. Minimum inhibitory concentration was taken as the lowest concentration showing complete visual inhibition of growth.

Statistical Analysis: Data were entered in Microsoft Excel and analysed using SPSS software. Frequencies, percentages, and distributions were used for descriptive analysis. Chi-square testing was applied for categorical associations. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Among 300 immunosuppressed patients evaluated for suspected systemic mycosis, 28 were confirmed microbiologically, giving an incidence of 9.3%. Men accounted for 19 cases (67.9%), while women accounted for 9 cases (32.1%). Middle-aged adults formed the largest affected group, with 17 of 28 patients (60.7%) belonging to the 41-60-year category [Table/Fig-1].

Department-wise distribution showed that Thoracic Medicine contributed the greatest number of confirmed cases, followed by the IMCU and ENT/Surgery. This pattern suggests a strong respiratory and critical-care concentration of disease in the present cohort [Table/Fig-1, Fig-1].

Table/Fig-1: Demographic and Clinical Distribution of Confirmed Systemic Mycosis Cases (N=28).

Domain	Variable	n	%
Age group	20-40 years	4	14.3
Age group	41-60 years	17	60.7
Age group	>60 years	7	25.0
Area	West Chennai	10	35.7
Area	West suburbs of Chennai	9	32.1
Area	South Chennai	2	7.1
Area	Central Chennai	1	3.6
Area	North and north suburbs	6	21.4
Department	Thoracic Medicine	11	39.3
Department	IMCU	7	25.0
Department	ENT/Surgery	6	21.4
Department	High Dependency Unit	2	7.1
Department	Neurology ICU	1	3.6
Department	Medicine	1	3.6
Sex	Male	19	67.9
Sex	Female	9	32.1

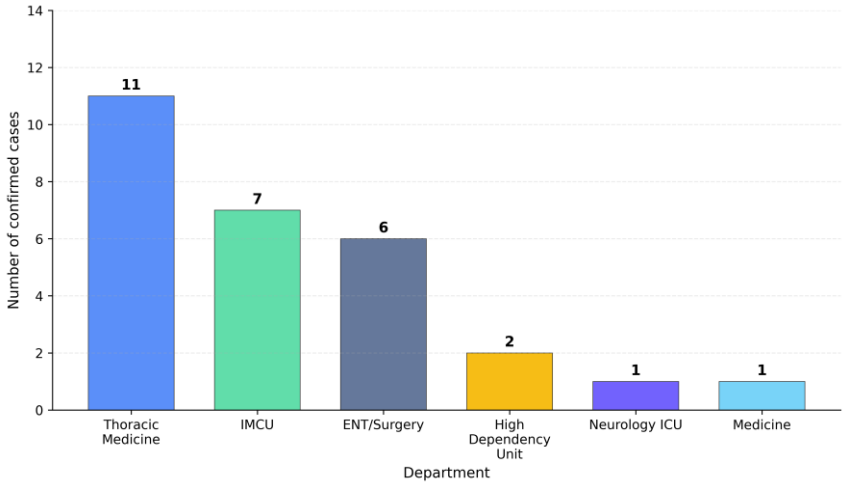

Fig. 1: Department-Wise Distribution of Confirmed Systemic Mycosis Cases.

The bar chart depicts the distribution of confirmed cases across major treating departments; values above bars indicate the number of cases.

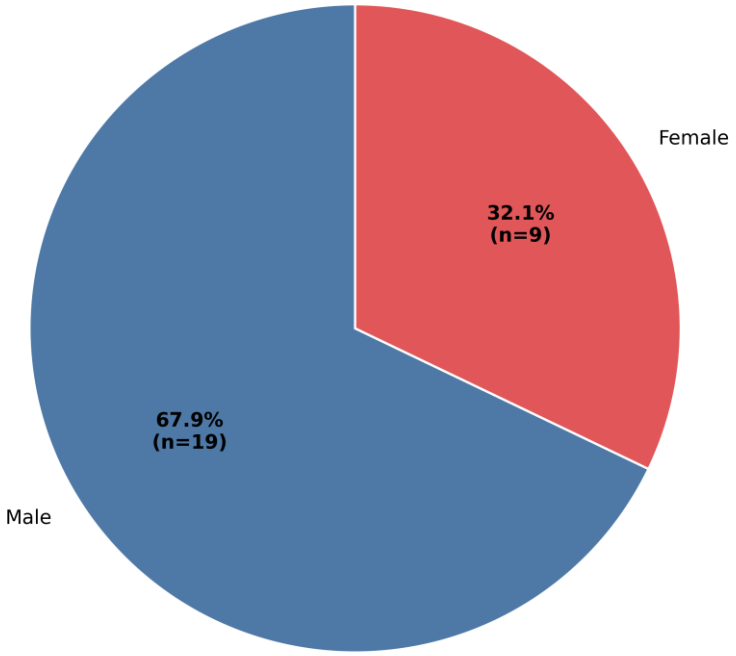

Fig. 2: Sex Distribution among Confirmed Systemic Mycosis Cases.

The pie chart shows the proportion of male and female patients among the 28 confirmed cases. All proven systemic mould infections occurred among corticosteroid-exposed COVID-19 patients. Within that subgroup, 24 proven cases were associated with methylprednisolone exposure and 4 with dexamethasone exposure, yielding a significant association between steroid regimen and proven mycosis (chi-square=24.7411, p=0.000001) [Table/Fig-2]. No proven mould infection was documented in the transplant or haematological malignancy subgroups during the study period.

Table/Fig. 2: Type of Immunosuppressive Therapy and Proven Systemic Mycosis among Suspected Cases.

Clinical subgroup	Immunosuppressive agent	Suspected cases (n)	Proven mycosis (n)	Proven among exposed (%)
COVID-19	Dexamethasone	170	4	2.4
COVID-19	Methylprednisolone	100	24	24.0
Solid organ transplantation	Tacrolimus	6	0	0.0
Solid organ transplantation	Mycophenolate mofetil	4	0	0.0
Haematological malignancy	Vincristine	6	0	0.0
Haematological malignancy	Cytarabine	4	0	0.0
Haematological malignancy	Doxorubicin	3	0	0.0
Haematological malignancy	Etoposide	3	0	0.0
Haematological malignancy	Azathioprine	2	0	0.0
Haematological malignancy	Tacrolimus + mycophenolate mofetil	2	0	0.0

Within the COVID-19 subgroup, the association between steroid regimen and proven systemic mycosis was statistically significant (chi-square=24.7411, p=0.000001).
Aspergillus spp. were the predominant moulds isolated, accounting for 16 of 28 cases (57.1%). Mucor spp. constituted 7 cases (25.0%), and Rhizopus spp. accounted for 5 cases (17.9%) [Table/Fig-3, Fig-3]. The isolate pattern supports the continued predominance of Aspergillus, while also showing a substantial contribution from Mucorales in this immunosuppressed population.

Table/Fig-3: Spectrum of Pathogenic Mould Isolates Among Confirmed Cases (N=28).

Organism isolated	n	%
Aspergillus spp.	16	57.1
Mucor spp.	7	25.0
Rhizopus spp.	5	17.9

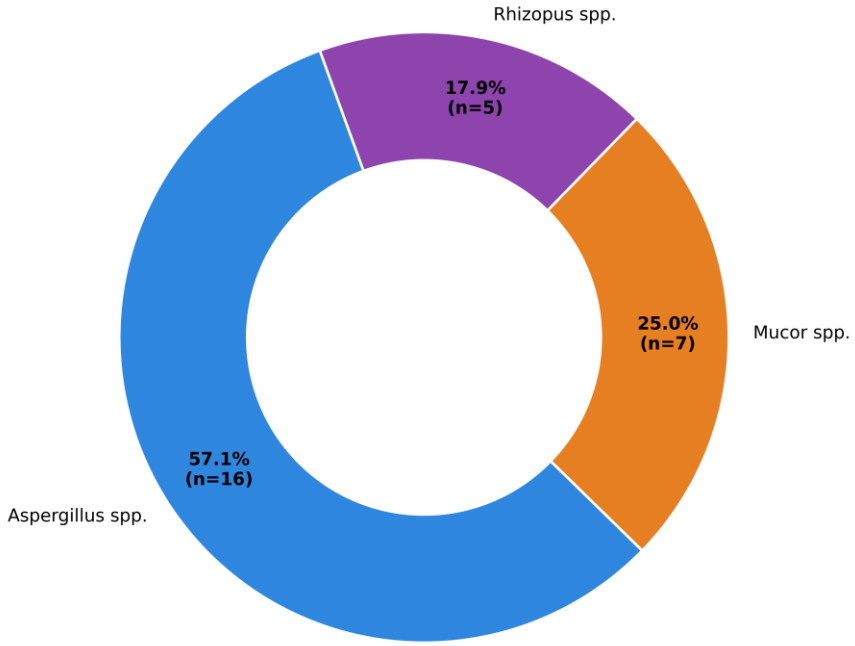

Fig. 3: Distribution Of Pathogenic Mould Isolates Among Confirmed Systemic Mycosis Cases.

Donut chart summarises the relative contribution of Aspergillus spp., Mucor spp., and Rhizopus spp. to the confirmed mould burden.

Antifungal susceptibility testing showed complete in-vitro susceptibility to amphotericin B across all tested mould isolates. Aspergillus flavus and Aspergillus fumigatus also retained complete susceptibility to voriconazole, while susceptibility to itraconazole and posaconazole declined mainly among Mucorales. Rhizopus spp. showed susceptibility rates of 40.0% to itraconazole and 80.0% to posaconazole, whereas Mucor spp. showed 28.6% susceptibility to itraconazole and 42.9% susceptibility to posaconazole [Table/Fig-4, Fig-4].

Table/Fig. 4: Antifungal Susceptibility Profile of Mould Isolates by CLSI M38-A2 Broth Microdilution.

Antifungal	A. flavus (n=8)	A. fumigatus (n=8)	Rhizopus spp. (n=5)	Mucor spp. (n=7)
Amphotericin B	S 8 / R 0	S 8 / R 0	S 5 / R 0	S 7 / R 0
Voriconazole	S 8 / R 0	S 8 / R 0	S 4 / R 1	S 5 / R 2
Itraconazole	S 6 / R 2	S 8 / R 0	S 2 / R 3	S 2 / R 5
Posaconazole	S 7 / R 1	S 8 / R 0	S 4 / R 1	S 3 / R 4

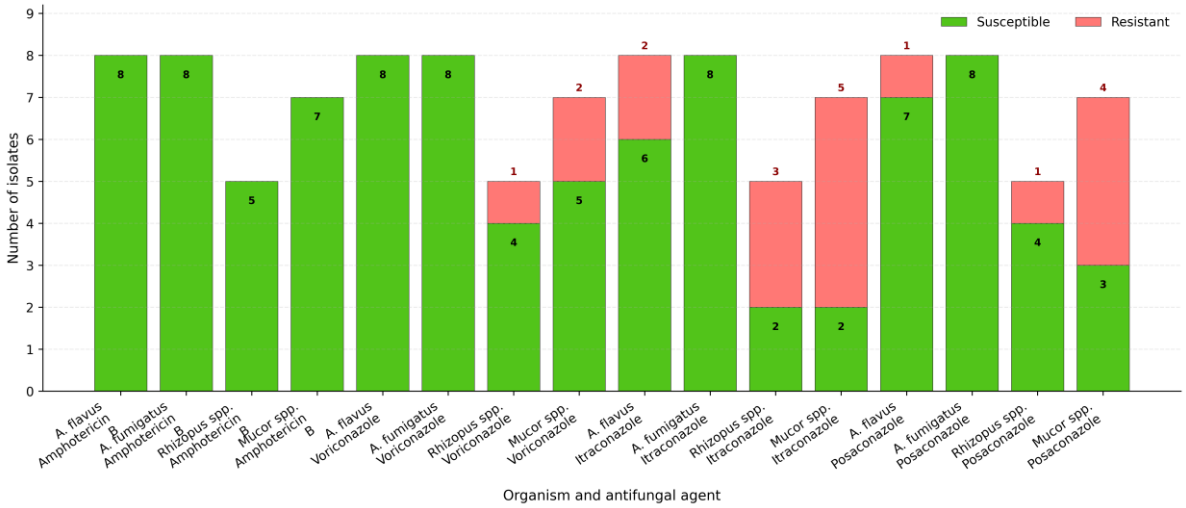

Fig. 4: Susceptible And Resistant Isolate Counts Across Antifungal Agents And Mould Species.

The stacked bar chart displays susceptible and resistant counts for each species-drug combination; bold labels indicate isolate numbers

DISCUSSION

The present study captures a hospital pattern that has become increasingly familiar in recent years. Invasive mould disease is now seen in a broader and more treatment-exposed host population than before, and Indian tertiary-care data have similarly shown considerable heterogeneity in pathogen distribution across centres.[9] Here, the burden was concentrated among steroid-exposed patients, with respiratory units contributing the largest share of confirmed cases.

The predominance of Aspergillus spp. in this series is biologically and clinically plausible. Aspergillus continues to occupy the leading position in invasive mould disease because inhaled conidia readily exploit impaired local and systemic host defences.[4] That observation is also consistent with treatment guidance, where voriconazole remains a core agent for invasive aspergillosis when the isolate profile and clinical context are supportive.[10]

Mucorales formed a smaller but still substantial fraction of isolates. That finding matters because mucormycosis behaves differently from aspergillosis, both clinically and therapeutically. International guidance continues to emphasise rapid recognition, surgical assessment when indicated, and amphotericin B-based treatment because delayed active therapy can carry serious consequences.[11] The reduced azole susceptibility seen in the present isolates, especially with itraconazole and posaconazole, follows the same broad therapeutic concern.

The clustering of proven cases in corticosteroid-exposed COVID-19 patients reflects the post-pandemic Indian experience. Reviews of COVID-19-associated mucormycosis from India have described the same convergence of steroid exposure, altered glycaemic control, prolonged admission, and immune dysregulation.[6] Severe COVID-19 has also been linked to pulmonary aspergillosis, and pooled data suggest that mortality is substantial when CAPA complicates critical illness.[12] The present findings fit within that wider clinical picture.

From a laboratory standpoint, the study also reinforces why culture and susceptibility data still matter. Even when amphotericin B remains broadly active, therapy cannot be guided safely on taxonomy alone, especially when clinicians are dealing with mixed risk profiles and variable azole performance. Recent reviews on mucormycosis and invasive fungal diagnosis have likewise stressed that early organism-level recognition and timely laboratory support are central to outcome-oriented care.[13,14]

The study should be read with its limits in mind. It was conducted at a single tertiary centre, the number of confirmed cases was modest, and species identification remained morphology-based. Clinical outcome correlation was not available for every isolate, and some subgroup counts were small. Still, the pattern that emerges is clinically useful. In an immunosuppressed patient with suspected systemic mould infection, species-level diagnosis and susceptibility testing can meaningfully sharpen the initial therapeutic decision.

Limitation(s)

The study was single-centre in design, included a relatively small number of confirmed systemic mycoses, and relied on conventional phenotypic identification without routine molecular confirmation. Outcome-based correlation with antifungal response was also limited.

CONCLUSION

Systemic mycoses in immunosuppressed patients in this tertiary-care setting were dominated by Aspergillus spp., with Mucorales contributing a clinically important secondary burden. The concentration of proven cases among corticosteroid-exposed patients highlights the continuing relevance of careful risk stratification in the post-COVID era. Amphotericin B retained universal in-vitro activity, while azole susceptibility varied across mould groups, particularly among Mucorales. These findings support routine species-level identification, timely antifungal susceptibility testing, and closer integration between clinical teams and the microbiology laboratory when invasive mould disease is suspected.

Source of Funding

None.

Conflict of Interest

None declared.

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