

# Clinicopathological characteristics of Fungal infections with special emphasis on Dematiaceous Fungi: A Cross-sectional study

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## ABSTRACT

### Background

Fungal infections are seen mostly as opportunistic infections in immunocompromised patients and as traumatic infections in immunocompetent individuals. In recent times, there is increasing trends of fungal infections in immunocompetent patients without any history of trauma. There are very few studies available in India on dematiaceous fungi in clinical settings.

### Aims and Objectives:

To analyse the clinico-histopathological features of dematiaceous fungal infections in comparison with other fungal infections among patients in a tertiary care hospital.

### Materials and methods

This cross-sectional study included all the fungal infections reported in histopathology during the 8 years period from January 2015 to December 2022. Hematoxylin & Eosin (H&E) stained histopathology slides were reviewed and special stains like Periodic Acid Schiff (PAS) & Gomori Methenamine Silver (GMS) were carried out for confirmation in all the fungal infections.

### Results

A total of 60 patients diagnosed with fungal infections by histopathological examination were analyzed. There was male preponderance (61.7%) with peak incidence in 41-60 years. Of the total 60 fungal infections, Aspergillosis (36.7%) was the common type with dematiaceous fungi accounting for 13.4% (8 cases) of infections. Among the 8 cases of dematiaceous fungi, phaeohyphomycosis constituted 7 cases (87.5%) while chromoblastomycosis constituted one case (12.5%). Around 75% of the dematiaceous fungal infections showed foreign body granulomatous host tissue response while cystic changes occurred only in dematiaceous fungicompared to other fungal infections.

### Conclusion

Awareness about the histopathological features of this rare group of dematiaceous subcutaneous mycoses is important in arriving at the correct diagnosis. Histopathology aided by special stains provides a rapid, cost-effective and definitive diagnosis in most of these cases.

### Keywords

Phaeohyphomycosis, Chromoblastomycosis, histopathology, Clinical features

immunocompromised individuals <sup>[1]</sup>. These

### Introduction

Fungal infections represent a significant and growing public health concern, particularly among infections can range from superficial skin conditions to severe systemic diseases, posing diagnostic and therapeutic challenges due to their varied clinical presentations and the limited availability of effective antifungal therapies <sup>[2]</sup>. Among the diverse array of pathogenic fungi, dematiaceous fungi stand out due to their distinct pigmentation and ability to cause a broad spectrum of infections, collectively grouped under the two categories namely phaeohyphomycosis and chromoblastomycosis, even in immunocompetent individuals <sup>[3,4]</sup>.

Dematiaceous fungi, characterized by their darkly pigmented hyphae and spores, are responsible for a variety of clinical manifestations, from localized cutaneous infections to life-threatening invasive cerebral and disseminated conditions <sup>[5]</sup>. The melanin pigment present in these fungal hyphae is responsible for the pathogenicity

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of these infections by scavenging free radicals and inhibiting phagocytosis [5]. Phaeohyphomycosis is characterised by septate pigmented hyphae while chromoblastomycosis show round non-budding yeast forms referred to as medlar bodies / sclerotic bodies or muriform cells with copper penny appearance [6]. These infections are often chronic and resistant to treatment, complicating clinical management. The tissue response in these dematiaceous fungal infections is not specific making histopathological diagnosis a definite challenge [7]. In some cases, these pigmented fungal infections can break through cutaneous tissue and disseminate to other sites like brain with bad prognosis [8]. It is estimated that 1.7 million deaths have occurred from fungal diseases in 2020 [1]. Despite their clinical significance, there is a relative paucity of comprehensive studies detailing the clinicopathological characteristics of infections caused by these melanized fungi.

This cross-sectional study aims to fill this gap by systematically examining the clinicopathological features of fungal infections, with a particular emphasis on those caused by dematiaceous fungi.

Understanding the unique aspects of dematiaceous fungal infections is crucial for developing targeted interventions and improving patient prognosis in this challenging area of infectious disease.

## AIMS AND OBJECTIVES

To analyze the clinico-histopathological features of dematiaceous fungal infections in comparison with other fungal infections among patients in a tertiary care hospital.

## METHODOLOGY

This was a cross-sectional study carried out in the Department of Pathology, Karpaga Vinayaga Institute of Medical Sciences and Research Centre. The study was approved by the Institutional Ethics Committee for Human Studies, Karpaga Vinayaga Institute of Medical Sciences and Research Centre (approval no.: KIMS/PG/07/09/2023). Purposive sampling was followed and all the fungal infections reported in histopathology during the 8 years period from January 2015 to December 2022 were included in the study. Patients of any age and gender diagnosed with fungal infections by histopathological examination were included in the study. Other granulomatous infections like tuberculosis,

leprosy etc. and poorly fixed necrotic lesions without definite fungal structures were excluded in the study.

Relevant clinical and pathological data were retrieved from the medical records of Department of Pathology. Corresponding Hematoxylin & Eosin (H&E) stained histopathology slides were reviewed and special stains like Periodic Acid Schiff (PAS) & Gomori Methenamine Silver (GMS) were carried out for confirmation in all the cases.

Statistical analysis was carried out using SPSS 23. Pearson Chi-Square test was used to analyze the association between site distribution and type of fungal infections. A p-value of <0.05 was considered to be statistically significant.

## RESULTS

In this study of total 60 fungal infections, there was a male predominance (61.7%) with the highest incidence observed in the 41-60 years age group (53.3%) (Table 1).

Among the fungal infections, Aspergillosis was the most common type, representing 36.7% of cases. Dematiaceous fungi were responsible for 13.4% (8 cases) of the total fungal infections. Within the dematiaceous fungi category, phaeohyphomycosis accounted for 7 cases (87.5%) and chromoblastomycosis accounted for only one case (12.5%). Other fungal infections identified included mucormycosis (23.3%), rhinosporidiosis (10%), maduramycosis (6.6%), dermatophytes (5%) and candida (5%).

Both PAS and GMS stains consistently showed positivity in all fungal infections, including those caused by dematiaceous fungi. The fungal elements appeared magenta-coloured structures after PAS staining while GMS imparted a black colour to the fungal hyphae and yeast forms (Figure 1).

Among the dematiaceous fungal infections, 75% exhibited a foreign body granulomatous tissue response. Additional histological changes in dematiaceous fungal infections included necrosis (62.5% of cases), eosinophil infiltrates (50% of cases), neutrophilic microabscesses (25% of cases), cystic changes (25% of cases), and xanthogranulomatous inflammation (25% of cases). These histological responses were similar to those observed in other fungal infections, except for the cystic changes, which were exclusive to dematiaceous

subcutaneous fungal infections.

The site distribution of dematiaceous fungi varied significantly ( $p < 0.007$ ) from other fungal infections. Upper extremities (75%) were the most common site for dematiaceous fungi while nasal cavity and paranasal sinuses were the most common site for other fungal infections with 42 cases (80.8%) occurring in that site (Table 2).

## DISCUSSION

Fungal infections impact over one billion individuals annually, with a global distribution. Around 130 fungal species belonging to 70 genera have been implicated as causative agents in humans. Despite the high mortality associated with these infections, many, including mycetoma, chromoblastomycosis, and sporotrichosis, are often neglected [9]. Dematiaceous fungi, known for causing a variety of infections, pose significant diagnostic challenges [10].

The current study revealed that approximately 53.3% of fungal infection cases were in patients aged 41-60 years, with a male predominance of 61.7%. This aligns with the findings of M. Sridevi et al [11], where the mean age was 45 years, and males comprised 63.8% of the cases.

Aspergillosis emerged as the most common fungal infection in the present study accounting for 36.7% of cases while dematiaceous fungi were responsible for 13.4% of cases. Abilash et al [12], from South Tamil Nadu reported a higher incidence of rhinosporidiosis (27.78%) and equal occurrences of Aspergillosis (16.67%) and phaeohyphomycosis (16.67%). In contrast, M. Sridevi et al [11], from North Tamil Nadu reported 38.3% of cases of phaeohyphomycosis among the fungal infections. These differences highlight the regional variations in the prevalence of dematiaceous fungal infections, which are often more prevalent in tropical and subtropical areas globally. In India, dematiaceous fungal infections have been reported from extreme northern states to southern states except for the western region since the climate ranges from tropical to temperate over these prevalent areas.

Histopathological evaluation of fungal lesions reveals a spectrum of non-specific host tissue responses. Verma S et al [13] from North East India reported foreign body granulomas in 66% of dematiaceous fungal infection cases. But in the present study 75%

of dematiaceous fungal infections exhibited a foreign body granulomatous reaction in tissues. Subhashini R et al [14] reported cystic changes in 72% of dematiaceous fungal infections, whereas only 25% of such infections in the current study showed cystic changes.

Clinically, phaeohyphomycosis often presents as a solitary cystic swelling in the distal extremities. Some of the cutaneous lesions may be even nodular or verrucous in nature. [14] It is reported that implantation of vegetable matter or wood splinter following traumatic injury especially among those in agricultural occupation is considered to be the source of dematiaceous infections, since majority of these organisms are saprophytes found in soil. In the current study, the upper extremities were the most common site for dematiaceous fungal infections (75%), differing from Pradhan, et al [15], where foot was the most frequently affected site.

## Limitation:

The study does not incorporate the fungal culture results for identifying the exact causative organism among the various species in the group of dematiaceous fungi. Also, the clinical patients' profile including immune status, occupation history or any other known predisposing factors for fungal infections were not available since the data were retrieved from laboratory records. Further research incorporating the fungal culture data and clinical risk factors will help in better understanding of the characteristics of this rare group of fungal infections.

## CONCLUSION

Awareness about the histopathological features of this rare group of dematiaceous subcutaneous mycosis is important in arriving at the correct diagnosis since clinically they are often mistaken for ganglion or dermoid cysts. Histopathology aided by special stains provides a rapid, cost-effective and definitive diagnosis in most of these cases.

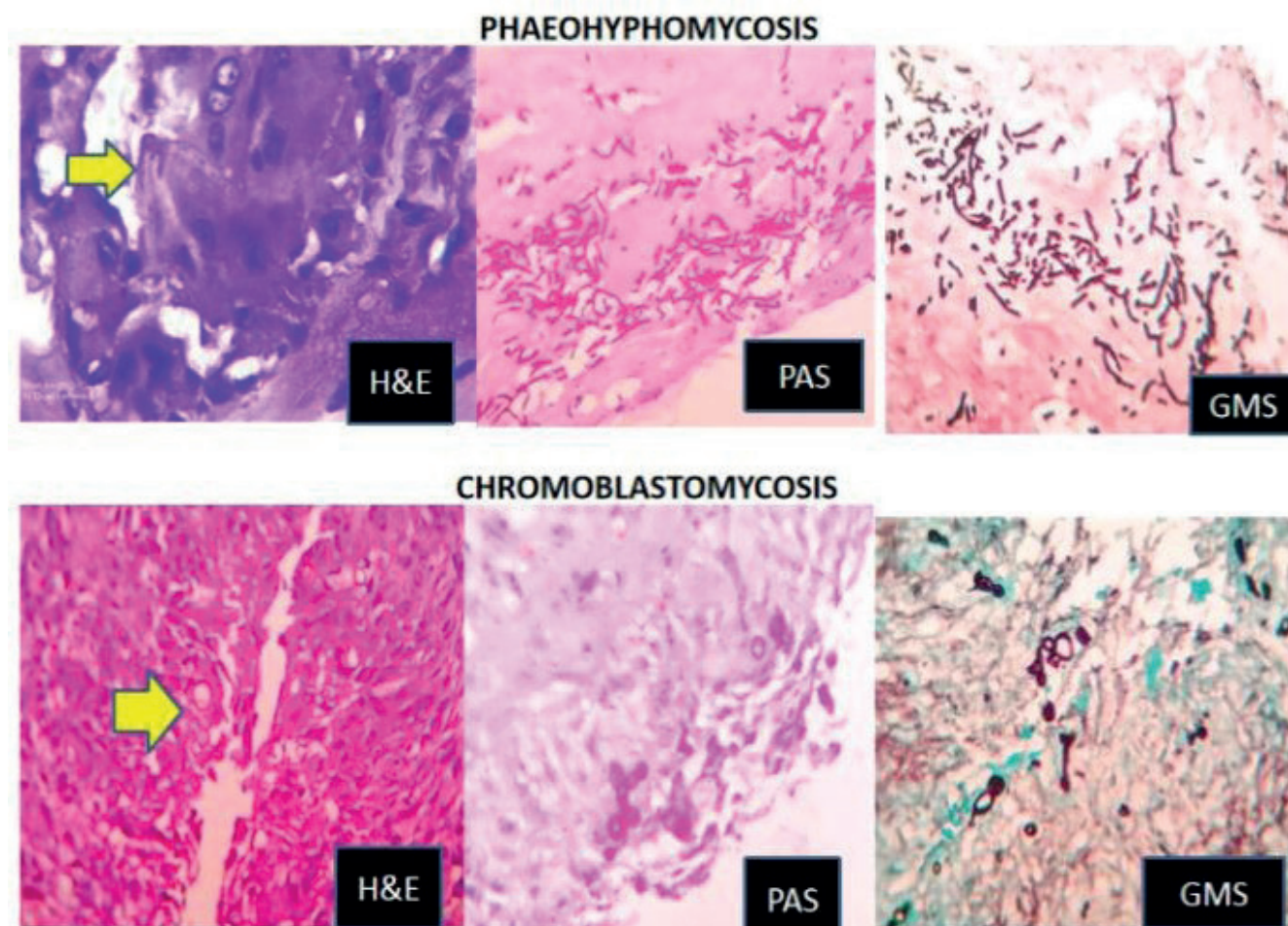
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There are no conflicts of interest. Ethical conduct of research This study was approved by the institutional ethics committee (KIMS/PG/07/09/2023).

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**Figure 1:** Histopathological features of dematiaceous fungi

**Fig 1A:** Phaeohyphomycosis-Shows brown pigmented septate hyphae in H&E, which appears magenta in PAS and black in GMS stained sections.

**Fig 1B:** Chromoblastomycosis- Shows brown yeast forms in H&E, which appears magenta in PAS and black in GMS stained sections.

**Table 1:** Demographic of the patients (Total=60)

Parameters	Number (n)	Percentage(%)
Age (Years)		
>60	8	13
<60	52	86.7
Sex		
Male	37	61.7
Female	23	38.3

**Table 2:** Correlation of site distribution with histological type of fungal infections

Site	Dematiaceous fungal infections (n=8)	Other fungal infections (n=52)	Pearson Chi-square test
Upper extremities (Forearm, Hands, Elbows)	6	2	P-value- <0.007 *Highly significant
Other Sites (Nose & PNS, Foot, Genital tract, Face)	2	50	
Total (60)	08	52	

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