Original Article

Antifungal Resistance Patterns in Dermatophytic Infections: A Regional Analysis

M Mujibur Rahman Siddiqui[1], Zahir Uddin M Babar[2], M Nazrul Islam Shaheen[3]

Abstract:

Background: Dermatophytic infections, caused by Trichophyton, Microsporum, and Epidermophyton species, are common skin problem. Recently, antifungal resistance has arisen as a serious barrier in controlling these diseases, particularly in areas where antifungal drugs are widely used. **Objective:** The objective of this study was to evaluate the antifungal resistance patterns of dermatophytes isolated from patients with dermatophytosis and assess the resistance patterns of dermatophytes to routinely used antifungal drugs (terbinafine, itraconazole, and fluconazole) in dermatophytosis patients. **Methods:** This cross sectional observational study conducted at Department of Dermatology, Estern Medical College & Hospital from July 2023 to June 2024. A total 120 patients diagnosed with dermatophytosis who received antifungal treatment for their dermatophyte infections are included in this study. Data on patient demographics, treatment history, and antifungal resistance patterns were collected and analyzed. **Results:** Among 120 patients, Trichophyton rubrum was the most common dermatophyte species (69.44%). T. rubrum had the strongest resistance to fluconazole (32%), followed by itraconazole (20%) and terbinafine (16%). Trichophyton mentagrophytes showed comparable resistance patterns, with fluconazole resistance reaching 36%. Resistance was reduced in Microsporum canis and Epidermophyton floccosum. A significant association was found between prior antifungal treatment and increased resistance. **Conclusion:** This study reveals a significant development in antifungal resistance among dermatophytes, notably to fluconazole, emphasising the importance of regular susceptibility testing and judicious antifungal use.

Keywords: Dermatophytosis, Antifungal Resistance, Trichophyton rubrum, Trichophyton mentagrophytes, Fluconazole, Terbinafine, Itraconazole.

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1. Dr Md. Mujibur Rahman Siddiqui
   Assistant Professor, Department of Dermatology & Venereology, Eastern Medical College and Hospital, Cumilla
2. Dr Zahir Uddin Mohammad Babar
   Assistant Professor, Department of Dermatology & Venereology, Cumilla Medical College, Cumilla
3. Dr Md. Nazrul Islam Shaheen
   Assistant Professor, Department of Dermatology & Venereology, Mainamoti Medical College, Cumilla

Address of correspondence:
Dr Md. Mujibur Rahman Siddiqui
Assistant Professor, Department of Dermatology & Venereology, Eastern Medical College and Hospital, Cumilla
Mobile: +8801716428418,
Email: drmujibemc2016@gmail.com

Introduction:

Dermatophytic infections, caused by Trichophyton, Microsporum, and Epidermophyton is an important global health problem. These infections affect keratinized tissues like skin, hair, and nails that resulting in disease with a significant morbidity and reduced quality of life.[1,2] Dermatophytosis is more common in tropical and subtropical climates because of the ideal humidity and temperature levels, but its increasing incidence has been reported across different regions, including an urban and a rural scenario.[3,4]

Over the last few years dermatophytosis has shown a considerable change regarding its epidemiological and clinical profile with increased presence of recurrent and chronic disease and increased resistance to antifungal agents.[5] Factors contributing to this phenomenon include the misuse of systemic antifungal drugs and widespread use of over the counter topical steroid antifungal combinations, as well as poor treatment compliance.[6,7] From all dermatophytes, Trichophyton rubrum and Trichophyton mentagrophytes are the most frequently isolated species; however, T. rubrum is proving to be somewhat resistant.[8]

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Management of dermatophytosis is challenging due to antifungal resistance. Highly effective drugs such as terbinafine and azoles that include itraconazole and fluconazole, have increasingly failed in clinical settings.[9,10] Resistance arises from efflux pump overexpression, mutation of the drug target enzyme mutations, and biofilm formation which reduces drug efficacy.[11,12] Antifungal resistance has substantial regional variations, pointing to the necessity to address local epidemiological studies for development of successful treatment protocols.[13,14]

Due to the tropical climate and high density population of Bangladesh, the country is ideal for dermatophytic infections. The spread of the disease is widespread and burden nonetheless, however, limited information regarding resistance patterns of antifungals in this area exist. It is important to understand these patterns, to have a better understanding of what may be leading to failures in treatment and to developing targeted strategies to manage disease.

This study determine the resistance patterns of some common dermatophytes against antifungal agents in a tertiary care setting. The findings also contribute to growing body of evidence stressing the urgent need for judicious use of antifungals and regional treatment guidelines through identification of prevalence of resistance, its correlation with clinical outcome.

Methods:

This cross sectional observational study conducted at Department of Dermatology, Estern Medical College & Hospital from July 2023 to June 2024. A total 120 patients diagnosed with dermatophytosis who received antifungal treatment for their dermatophyte infections are included in this study.

Inclusion Criteria:

- Patients diagnosed with dermatophytosis.
- Age more than 18 years.
- Received antifungal treatment.
- Patients documented with antifungal susceptability testing results for Trichophyton rubrum, Trichophyton mentagrophytes, Microsporum canis, and Epidermophyton floccosum.

Exclusion Criteria:

- Patients with incomplete medical records.
- Patients with immunocompromised condition (e.g., HIV, Cancer etc.).
- Who did not give consent.

Data collection: Data were collected from patients diagnosed with dermatophytosis. Clinical and laboratory information, including fungal culture results and antifungal susceptibility testing was obtained. Patients were selected based on their confirmed dermatophytosis diagnosis and documented antifungal therapy history. Data on the demographics, clinical features, and resistance patterns of dermatophyte isolates to terbinafine, itraconazole, and fluconazole were rigorously collected and analysed.

Ethical consideration:The study followed the ethical guidelines. Informed consent was taken from all patients prior to data collection. Participants were informed about the study's objectives, procedures, and the voluntary nature of their involvement. Confidentiality of all personal and medical information was strictly maintained throughout the study. The data were anonymized to ensure that patient identities were not disclosed. The study adhered to the principles outlined in the Declaration of Helsinki, ensuring that all ethical standards for medical research were met.

Statistical analysis of data:The statistical analysis was carried out using SPSS version 25. Categorical variables, such as dermatophyte species distribution and antifungal resistance patterns, were summarised using frequencies and percentages. Continuous variables such as age and duration of symptoms were calculated using the mean and standard deviation methods. The chi-square test was used to determine associations between antifungal resistance and demographic or clinical factors. A p-value of <0.05 indicated statistical significance.

Results:

Table-I: Baseline Characteristics (n=120)

Characteristics		Frequency (n)	Percentage (%)
Age (years)	0-20	11	9.17%
	21-40	52	43.33%
	41-60	43	35.83%
	>60	14	11.67%
Mean±SD		30±10.28	
Gender	Male	72	60.00%
	Female	48	40.00%
Urban Residency		82	68.33%
Comorbidities	Diabetes Mellitus	25	20.83%
	Hypertension	16	13.33%
History of tropical steroid use		51	42.50%
Duration of symptoms (months)		3.8±2.1	
Previous antifungal treatment		64	53.33%

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The demographic and clinical characteristics of 120 participants in the study are summarized in this table. The maximum patients were 21-40 years age group (43.33%) with the average age of 30 years. The majority of the patients were male (60%) and 68.33% of the patients had urban residency. Most common comorbidities were diabetes mellitus (20.83%) and hypertension (13.33%) and 42.5% of the participants had a history of tropical steroid use. Patients had a median duration of symptoms of approximately 3.8 months, and more than half of patients (53.33%) had a history of prior antifungal treatment.

Table-II: Distribution of number of Isolates

Dermatophyte species	Number of Isolates	
	Male (n=72)	Female (n=48)
Trichophyton rubrum	50(69.44%)	31(64.58%)
Trichophyton mentagrophytes	19(26.39%)	15(31.25%)
Microsporum canis	0	1(2.08%)
Epidermophyton floccosum	10(13.89%)	6(12.50%)

Table II shows the distribution of dermatophyte species isolated from male (n=72) and female (n=48) participants. The most commonly isolated species was Trichophyton rubrum, which occurred in 69.44% of males and 64.58% of females. The second most prevalent species was Trichophyton mentagrophytes that was isolated in 26.39% of males and 31.25% of females. It was also found that smaller proportion of Epidermophyton floccosum were identified, Microsporum canis was found only in one female participant.

Table-III: Resistant pattern of dermatophytes to common antifungal agents

Dermatophyte species	Antifungal agent	Resistant rate (%)	MIC range	Reference MIC breakpoint
T. rubrum	Terbinafine	16	0.11-7.0	≤0.5
	Itraconazole	20	0.23-14.0	≤1.0
	Fluconazole	32	1.0-61.0	≤8.0
T. mentagrophytes	Terbinafine	26	0.5-15.0	≤0.5
	Itraconazole	16	0.24-7.0	≤1.0
	Fluconazole	36	2.0-61.0	≤8.0
M. Canis	Terbinafine	14	0.5-4.0	≤0.5
	Itraconazole	16	0.5-8.0	≤1.0
	Fluconazole	21	1.0-15.0	≤8.0
E. floccosum	Terbinafine	9	0.25-2.0	≤0.5
	Itraconazole	13	0.25-4.0	≤1.0
	Fluconazole	24	1.0-30.0	≤8.0

Table III presents the antifungal resistance patterns of dermatophyte species to three commonly used agents: Itraconazole, fluconazole, and terbinafine. Resistance to fluconazole (32%), itraconazole (20%), and terbinafine (16%) was observed in Trichophyton rubrum however other isolates showed overall low resistance rates to the azoles including 1% to fluconazole, 3% to itraconazole, 1% to terbinafine, and 13% to fluconazole. Resistance was also significant for Trichophyton mentagrophytes, with fluconazole, 36%; terbinafine, 26%; and itraconazole, 16%. In contrast, moderate resistance was found for Microsporum canis (14% terbinafine, 21% for fluconazole), whereas Epidermophyton floccosum proved the most resistance with 24% fluconazole, 13% itraconazole and 9% terbinafine.

Discussion:

This study focusses on the developing trend of antifungal resistance among dermatophytes, which poses a substantial obstacle to effective dermatophytosis treatment. The preponderance of Trichophyton rubrum (69.44%) and Trichophyton mentagrophytes (26.67%) among the isolates is comparable with the findings of Gupta et al., who found a similar prevalence of both species as the principal causative agents of dermatophytosis.[15] T. rubrum's dominance can be ascribed to its high adaptability to human skin and environmental resistance, as stated in prior research.[16]

The highest rates of fluconazole resistance were found in T. rubrum (32%), followed by T. mentagrophytes (36%). Budhiraja et al. confirmed similar patterns, observing substantial fluconazole resistance due to its extensive use and availability over the counter in several locations.[17] This emphasises the necessity for stricter prescription practices to reduce the development of resistance. Mahale et. al. confirmed that, Itraconazole shown lower resistance rates (20% for T. rubrum), making it a more effective treatment option for azole-resistant patients.[18]

Terbinafine resistance in T. rubrum (16%) and T. mentagrophytes (26%) is alarming, given that it has long been used as the first-line treatment for dermatophytosis. Lyngdoh et al. and Malik et al. discovered comparable resistance patterns, which are frequently connected to mutations in the squalene epoxidase gene that limit terbinafine efficacy.[19,20] These findings highlight the critical need of routine antifungal susceptibility testing in guiding therapy options successfully.

This study's main findings was that Microsporum canis and Epidermophyton floccosum had lower resistance rates than T. rubrum and T. mentagrophytes. This observation is consistent with the findings of Sharma et al. who found that these species are less frequently exposed to antifungal drugs, resulting in delayed

resistance development.[21] However, monitoring is essential because resistance in these species may increase with increased antifungal use.

The relationship between prior antifungal therapy and increasing resistance, as seen in this study, has been extensively recognised in earlier research. Gupta et al. found that partial or ineffective antifungal medication frequently leads to resistance development, especially in recurring or chronic infections.[16] Furthermore, the high prevalence of previous topical steroid use (42.5%) in this study emphasises the importance of corticosteroid-antifungal combinations in masking infections and fostering resistance, as documented by Noronha et al.[22].

In comparison to other region, the resistance rates seen in this study are consistent with trends described in North and South India in studies by Bhatia et al. and Adhikari et al..[23,24] However, geographical variances in resistance patterns underscore the necessity of localised data in guiding treatment procedures. For example, some locations report increased terbinafine resistance, which is most likely owing to variances in prescribing methods and genetic differences among dermatophyte populations.[19]

This study emphasises the critical necessity for prudent antifungal usage and regular susceptibility testing to combat the rising resistance challenge. It is vital to implement public health efforts that educate healthcare practitioners and people about proper antifungal use. Furthermore, greater regulations on over-the-counter antifungal medications and steroid-antifungal combos are required to prevent resistance development.

Conclusion:

This study underscores the growing concern of antifungal resistance among dermatophytes, particularly against fluconazole and terbinafine, which are routinely used in dermatophytosis treatment. The significant incidence of resistance in Trichophyton rubrum and Trichophyton mentagrophytes highlights the importance of regular antifungal susceptibility testing to guide efficient therapy. These findings highlight the need for rational antifungal use and the establishment of region-specific treatment guidelines to tackle the increasing resistance epidemic and enhance clinical outcomes.

Limitations and recommendations:

The study was limited by its single-center design, which may not fully represent regional variations in antifungal resistance patterns. Additionally, the sample size was relatively small, potentially affecting the generalizability of the findings. To ensure effective treatment, antifungal susceptibility testing should be done on a regular basis. It is critical to implement public health campaigns to educate healthcare practitioners and the general public about the dangers of self-medication and incorrect antifungal usage. To reduce overuse and resistance, policymakers should consider greater regulation of OTC antifungal medications and topical steroid-antifungal combos.

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Conflicts of interest: There are no conflicts of interest.

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