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Original Research Article

Clinico-etiologic Profile and Antifungal Sensitivity Patterns of Dermatophytosis: An Observation Study

Rakesh Ranjan Kumar Rahul[1], Babita Kumari[2]

[1]Assistant Professor, Department of Skin &VD, Sri Krishna Medical College and Hospital, Muzaffarpur, Bihar, India

[2]Assistant Professor, Department of Obstetrics and Gynaecology, Nalanda Medical College and Hospital, Patna, Bihar, India

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Corresponding author: Dr. Rakesh Ranjan Kumar Rahul

Conflict of interest: Nil

Abstract

Aim: The aim of the study was to assess the etiological prevalence of pathogenic dermatophytes, clinical types of dermatophyte fungal infections, and in vitro antifungal drug susceptibility testing against dermatophytes to understand the variation in minimum inhibitory concentrations (MICs) levels of antifungals among dermatophytes.

Methods: The present study was conducted in the Department of Skin and VD, for one year . All patients with dermatophyte infections visiting the outpatient department during this period were screened. A total of 150 consecutive patients aged between 18 and 65 years with recurrent cases of tinea and other atypical presentations, receiving antifungal treatment, and willing to have minimum three days washout period before antifungal drug susceptibility testing of the clinical specimen (fungal isolate), were recruited.

Results: Male preponderance was observed (60%) among 150 cases studied. The mean age of the study population was 36.6 ± 13.76 years. Most patients were in the 18–30 years group (n = 60), followed by 31 to 40 years (n = 30), > 50 years (n = 35) and 41 to 50 years (n = 25). Itching (92%), scaling (89.33%), dryness (78%) and inflammation (46%) were the most common clinical presentations. Antifungal susceptibility testing was done for all 100 culture-positive patients. Griseofulvin reported the least mean MIC values, followed by luliconazole, eberconazole, sertaconazole, amorolfine and itraconazole. The mean MIC value of terbinafine (0.05 [0.043] µg/mL) was above the reference range. However, it was noted only in 15 (15%) out of total culture-positive patients. The individual high MIC values were reported up to 0.256 µg/ml [range: 0.001–0.03 µg/ml]. Higher MIC values were reported for terbinafine for both T. mentagrophytes (0.256 µg/ml) and T. rubrum (0.256 µg/ml).

Conclusion: Dermatophytosis is a prevalent problem in the Indian scenario due to the hot and humid climate and low socio-economic status. Varied etiological agents, along with regional variations, make the management of this common cutaneous condition challenging. T. rubrum was found to be the most common, and T. mentagrophytes the emerging/codominant fungal isolate.

Keywords: Antifungal, Coastal Areas, Dermatophytes, Tinea Infection, Trichophyton.

Introduction

Dermatophytes are the most commonly encountered fungi in humans and other vertebrates that spread through direct contact with infected humans, animals, and soil.[1] Infections due to these agents are usually restricted to the stratum corneum and are generally referred as 'tinea' or 'ringworm' (tinea capitis; tinea barbae; tinea corporis; tinea cruris; tinea manuum; tinea pedis and tinea unguium).[2,3] Dermatophytes belong to 3 closely related genera-Trichophyton, Microsporum and Epidermophyton.[4] High prevalence rates of tinea pedis and onychomycosis have been recognized in certain occupational groups like a marathon runner (22-31%), miners (21-72.9%), and soldiers (16.4-58%).[5,6] Trichophyton species are the major causative agents responsible for dermatophytosis with a prevalence rate of 70-90% for onychomycosis and 53-86% for rest of the tinea infections.[7,8]

The various antifungal agents currently available in clinical use against dermatophytes are terbinafine, itraconazole, fluconazole, luliconazole, etc. Even though antifungal agents' inappropriate use may result in resistant strains, their activity against dermatophytes has not yet been fully explored. The research outlining the antifungal susceptibility of common dermatophyte species in India is inadequate, posing a therapeutic challenge to practitioners.[9] Furthermore, despite the high incidence and clinical relevance, multicentric evidence depicting the present day clinico-

epidemiological patterns of dermatophytosis across India is scarce. The magnitude of the concern thus demands studies across different geographic locations within India to increase the generalizability of the data.

Treatment options for dermatophytosis are topical as well as systemic antifungal drugs. But during course of time dermatophytes have also evolved drug resistance for single as well as multiple drug simultaneously. Studies conducted worldwide show that resistance among dermatophytes is not uncommon.[10,11] Due to high temperature and increased humidity, there are increased cases of dermato phytosis and other fungal infections especially in terrain and hilly region of Western Nepal. Since there was increased incidence of drug resistance observed over a period of time to the antimycotic drugs commonly used for the treatment i.e., fluconazole, terbinafine and clotrimazole, the need for testing of antifungal susceptibilities of dermatophytes has become apparent.

The aim of the study was to assess the etiological prevalence of pathogenic dermatophytes, clinical types of dermatophyte fungal infections, and in vitro antifungal drug susceptibility testing against dermatophytes to understand the variation in minimum inhibitory concentrations (MICs) levels of antifungals among dermatophytes.

Methods

The present study was conducted in the Department of Skin and VD, Sri Krishna Medical College and Hospital, Muzaffarpur, Bihar, India for one year. All patients with dermatophyte infections visiting the outpatient department during this period were screened. A total of 150 consecutive patients aged between 18 and 65 years with recurrent cases of tinea and other atypical presentations, receiving antifungal treatment, and willing to have minimum three days washout period before antifungal drug susceptibility testing of the clinical specimen (fungal isolate), were recruited.

Patients with a non-mycotic pathology in the area of fungal infection or any condition that, in the investigator's opinion, does not justify the patient's inclusion in the study were excluded from the study. All patients provided written consent in the patient authorization form to participate in the study. A detailed history was obtained from all patients, who were then subjected to clinical examinations and investigations, including a wet preparation for direct microscopic examination, fungal culture and antifungal susceptibility tests.

Sample processing

All the 300 scraping samples were collected, and the specimens were shipped to a central facility. The primary identification of dermatophytes was done using direct microscopy with 10% potassium hydroxide (KOH) mount. Direct microscopic examination of the wet-mount was performed under a microscope, under ×10 and ×40 for fungal hyphae, spores or yeast cells. The Sabouraud dextrose agar (SDA) was used for isolation and identification of fungal isolates. Specimens were cultured on SDA media (Micro Master Laboratories Pvt. Ltd) with 0.05% chloramphenicol alone (Micro Master Laboratories Pvt. Ltd), or with 0.5% cycloheximide (HiMedia Laboratories Pvt. Ltd) and 0.05% chloramphenicol (Micro Master Laboratories Pvt. Ltd) and incubated at 30°C for up to four weeks. Cultures were examined once a week and professed negative if no growth was observed until 6 weeks. Identification of dermatophytes to the species level was done by assessing the colony morphology, microscopy (Lactophenol Cotton Blue Mount), and physiological and biochemical tests. Further antifungal drug susceptibility testing was performed, and the minimum inhibitory concentration (MIC) of the drugs was determined.

Antifungal drug susceptibility testing

Antifungal drug susceptibility testing was performed as per the microbroth dilution technique of Clinical and Laboratory Standards Institute Guidelines (CLSI M38-A).[12,13] The antifungal drug susceptibility testing was done for seven antifungal agents, namely, luliconazole, sertaconazole, eberconazole, itraconazole, terbinafine, griseofulvin and amorolfine. The MIC for the antifungals was interpreted according to the CLSI M38-A guidelines.

Statistical analysis

All the data from cases was fed in MS Excel (Microsoft office 2018) and then analyzed by Statistical Package for Social Service (SPSS) for window version; SPSS 22, Inc., Chicago, IL). All data were expressed in terms of percentage.

Results

Table 1: Demographic details

Gender	**N%**
Male	90 (60)
Female	60 (40)
Age in years	
18-30 years	60 (40)
31-40 years	30 (20)
41-50 years	25 (16.66)
>50 years	35 (23.34)

Male preponderance was observed (60%) among 150 cases studied. The mean age of the study population was 36.6 ± 13.76 years. Most patients were in the 18–30 years group (n = 60), followed by 31 to 40 years (n = 30), > 50 years (n = 35) and 41 to 50 years (n = 25).

Table 2: Clinical features

Category	Male (n=100) (%)	Female (n=50) (%)	Total (n=150) (%)
Itching	94 (94)	44 (88)	138 (92)
Dryness	76 (76)	41 (82)	117 (78)
Inflammation	52 (52)	17 (34)	69 (46)
Scaling	91 (91)	43 (86)	134 (89.3)
Pustules	6 (6)	3 (6)	9 (6)
Erythema	40 (40)	17 (34)	57 (38)
Alopecia	3 (3)	1 (0.5)	4 (2.66)
Local hair loss	2 (2)	2 (4)	4 (2.66)
Lesion with central clearing surrounded by an advancing, red, scaly and elevated border (Ring worm lesions)	20 (10)	23 (46)	43 (28.66)
Annular patches of inflammatory or non-inflammatory alopecia	3 (3)	1 (1)	4 (2.66)
Erythema and mild scaling on the dorsal aspect of the hands	1 (1)	1 (0.5)	2 (1.33)

Itching (92%), scaling (89.33%), dryness (78%) and inflammation (46%) were the most common clinical presentations.

Table 3: Antifungal susceptibility testing among culture positive patients

Category	Culture positive (n = 100)
Terbinafine	
High MIC	15 (15)
Susceptible	85 (85)
MIC (µg/mL), mean (SD)	0.05 (0.043)
MIC90	0.001–0.03
Griseofulvin	
High MIC	0
Susceptible	100 (100)
MIC (µg/mL), mean (SD)	0.19 (0.082)
MIC90	0.25–3.0
Itraconazole	
High MIC	0
Susceptible	100 (100)
MIC (µg/mL), mean (SD)	0.84 (0.252)
MIC90	0.05-1.0
Luliconazole	
High MIC	0
Susceptible	100 (100)
MIC (µg/mL), mean (SD)	0.29 (0.286)
MIC90	0.05-1.0
Sertaconazole	
High MIC	0
Susceptible	100 (100)
MIC (µg/mL), mean (SD)	0.36 (0.372)
MIC90	0.05-1.0
Amorolfine	
High MIC	0
Susceptible	100 (100)
MIC (µg/mL), mean (SD)	0.60 (0.306)
MIC90	0.05-1.0
Eberconazole	
High MIC	0
Susceptible	100 (100)
MIC (µg/mL), mean (SD)	0.32 (0.251)
MIC90	0.05-1.0

Antifungal susceptibility testing was done for all 100 culture-positive patients. Griseofulvin reported the least mean MIC values, followed by luliconazole, eberconazole, sertaconazole, amorolfine and itraconazole. The mean MIC value of terbinafine (0.05 [0.043] µg/mL) was above the reference range. However, it was noted only in 15 (15%) out of total culture-positive patients. The individual high MIC values were reported up to 0.256 µg/ml [range: 0.001–0.03 µg/ml]. Higher MIC values were reported for terbinafine for both T. mentagrophytes (0.256 µg/ml) and T. rubrum (0.256 µg/ml). The MIC values for itraconazole were within the range; while griseofulvin had the lowest mean MIC (0.25–3.0 µg/mL). The MICs of itraconazole, luliconazole, amorolfine, sertaconazole and eberconazole were within the reference range.

Discussion

Dermatophytosis continues to be the most common cause of superficial fungal infection worldwide.[14,15] Reports indicate that the epidemiology of dermatophytes varies among countries and even within different regions in the country.[15] It is more prevalent in developing, particularly in tropical and subtropical countries like India, evidently due to the hot and humid climatic conditions.[16] In addition to climatic factors, geographic location, health-care system, overcrowding, urbanization, population migration, environmental and personal hygiene culture, the prevalence of virulent species, socioeconomic conditions, individual immune system, etc., may also affect the epidemiology and incidence of dermatophyte infections.[16,17]

Male preponderance was observed (60%) among 150 cases studied. The mean age of the study population was 36.6 ± 13.76 years. Most patients were in the 18–30 years group (n = 60), followed by 31 to 40 years (n = 30), > 50 years (n = 35) and 41 to 50 years (n = 25) which was comparable with India's reported literature on dermatophytosis-centric studies.[18-20] The higher incidence in young males could be attributed to their increased physical activity, predisposing them to increased sweating. The lower incidence among females seen in this study could be attributed to their hesitation to consult physicians and the financial dependence on males. To prevent the unnecessary usage of toxic drugs, regular surveillance of antifungal susceptibility patterns in patients should be carried out in their long-term interest.[21] Itching (92%), scaling (89.33%), dryness (78%) and inflammation (46%) were the most common clinical presentations. Antifungal susceptibility testing was done for all 100 culture-positive patients. Griseofulvin reported the least mean MIC values, followed by luliconazole, eberconazole, sertaconazole, amorolfine and itraconazole. The mean MIC value of terbinafine (0.05 [0.043] µg/mL) was above the reference range. However, it was noted only in 15 (15%) out of total culture-positive patients. The individual high MIC values were reported up to 0.256 µg/ml [range: 0.001–0.03 µg/ml]. Higher MIC values were reported for terbinafine for both T. mentagrophytes (0.256 µg/ml) and T. rubrum (0.256 µg/ml). The MIC values for itraconazole were within the range; while griseofulvin had the lowest mean MIC (0.25–3.0 µg/mL). The MICs of itraconazole, luliconazole, amorolfine, sertaconazole and eberconazole were within the reference range. Hence, the clinician must consider the plausible reasons such as virulence potential of the infecting species, clinical type of dermatophytosis and external factors such as heat, humidity, sweating, type of clothing and the pharmacological factors such as the quality of the drug, compliance, pharmacokinetics and absorption of the drug to understand the recalcitrant infection better.[22]

This indicates the need to optimize the use of itraconazole, emphasizing on the right dose and duration of treatment, considering the present effectiveness of oral itraconazole in our routine clinical practice. Moreover, this is the last drug in the current armamentarium, and hence rational use of itraconazole is the need of the hour. Vardai Pai et al. had also reported lower MIC of systemic griseofulvin and topical amorolfine than fluconazole.[23] The clinician must consider the plausible reasons such as virulence potential of the infecting species, clinical type of dermatophytosis and external factors such as heat, humidity, sweating, type of clothing and the pharmacological factors such as the quality of the drug, compliance, pharmacokinetics and absorption of the drug to understand the recalcitrant infection better.

Conclusion

Dermatophytosis is a prevalent problem in the Indian scenario due to the hot and humid climate and low socio-economic status. Varied etiological agents, along with regional variations, make the management of this common cutaneous condition challenging. T. rubrum was found to be the most common, and T. mentagrophytes the emerging/codominant fungal isolate. Tinea corporis was the most common clinical type of dermatophytosis. Various techniques are available for antifungal susceptibility testing of dermatophytes but only broth microdilution technique is currently accepted to determine in-vitro susceptibility of dermatophytes. As this technique is laborious and need expertise, only few mycology laboratories can perform this test. However, further studies on larger samples are warranted to correlate the MIC values with clinical outcomes to define the MIC breakpoints which will help adapt to therapeutic choices with high chances of success.

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