

Prevalence of Dermatophytes and Their Antifungal Susceptibility to Itraconazole in Clinically Suspected Patients of Tinea Corporis

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Author's Contribution

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ABSTRACT

Objective: To assess the prevalence and clinico-mycological characteristics of dermatophyte species in tinea corporis, and determine the susceptibility of isolated dermatophyte species to Itraconazole.

Methodology: This cross sectional study was conducted in Department of Microbiology, Basic Medical Sciences Institute, Karachi from June 2018 to June 2019. A total of 301 samples of skin scraping of the suspected cases of tinea corporis were taken from the patients who visited dermatology OPD of Jinnah Postgraduate Medical Centre. The specimens were taken by scrapping the margin of lesions with a sterile surgical blade and were processed for potassium hydroxide (KOH) mount test. The mycological culture was performed on Sabouraud's dextrose agar with and without antibiotics and on dermatophyte test medium. Lactophenol cotton blue mount, cellophane tape mount, and biochemical testing were used to identify the species of dermatophytes. The antifungal susceptibility testing was done by micro broth dilution method according to the guideline of Clinical and Laboratory Standard Institute.

Results: The males were affected more than females. Redness/ Erythema was the most common presenting complaint (n= 192, 63.8%) while the most common clinical type was an annular lesion (n= 133, 44.2%). The most common isolated dermatophytes was *T. mentagrophytes* (n= 38, 45.2%). There was no resistance seen towards itraconazole for any isolates, though the MICs of itraconazole was within the range in the upper limit for almost every isolate. This indicates the need to optimize the use of itraconazole. Furthermore, because itraconazole is the last medicine in the existing arsenal, so itraconazole must be used wisely

Conclusion: *Trichophyton* formed the commonest etiological agent and *T. mentagrophytes* and *T. rubrum* were found to be the principal causative agent of tinea corporis in our region. Isolates were found to be susceptible to itraconazole, however the MICs were found to be in the upper range

Keywords: Tinea corporis, dermatophytes, Itraconazole, sensitivity.

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Introduction

Fungi are a group of organisms having several species capable of causing disease in humans. Fungal infections are very common in humans. Approximately more than 50,000 species are present, but only 100 to 150 species

are capable of infecting humans and around 25 species because the most of human diseases.¹ Fungal infections are categorized into three broad types: Superficial mycoses, subcutaneous mycoses and systemic mycoses. Dermatophytosis is one of the earliest and the most prevalent superficial mycoses. According to WHO,

global prevalence of superficial mycoses is around 20-25% and approximately 30 to 70% of adults are asymptomatic carrier of this disease.^{2,3} Simultaneously in the past 4-5 years there is rise in recurrent, recalcitrant, and chronic cases of superficial and endemic fungal infections have been observed.⁴

These are a group of fungi that is physiologically, morphologically and antigenically related to each other and usually they are named as ringworm fungi.⁵ These are non-motile, filamentous, ascomycetes having septate hyphae, require keratin for growth so they are usually found on skin, nails, scalp and moist areas of body and are unable to penetrate mucus membrane. More than 100 species are identified and around 40% of these are responsible to cause diseases in humans. The incubation period of dermatophytes on the human skin is from one to two weeks.⁶ Dermatophytes have ability to penetrate in the superficial stratum corneum with minimal or no inflammatory response. Recent studies also have observed increased number of cases in close contacts. The probable reason behind these increased cases could be chronicity and recurrent infection in families. To prevent the chronicity and recurrence, proper history should be taken and all family members should be treated simultaneously.⁷ It affects all age groups, irrespective of gender but young adults are commonly infected. Dermatophytes affect roughly 10 to 15% of people worldwide at some point during their lifetime.⁸

Tinea corporis typically presents as well-demarcated, erythematous, scaly patches with raised margins and a ring-like shape due to the rash spreading outward. Lesions may have annular or irregular borders with papules, pustules, or vesicles.^{9,10} The face and limbs are more commonly affected due to greater exposure, while immunosuppressed patients may experience widespread lesions.¹¹

Fungi are eukaryotic organisms and have many molecular and cellular drug targets similar to human beings so development of antifungal agents is very demanding, complex and carries a significant risk of host toxicity. Trend of antifungal treatment is changing now with increasing use of local guidelines as compared to past when more generalized approach was used worldwide. Currently triazoles and Allylamines are also incorporated in antifungal regimen in addition to long standing common use of imidazoles in past. Itraconazole is used for management of dermatophytosis and has proven superior to other agents due to its oral bioavailability, hydrophobic nature, high molecular weight, high protein

binding capacity and wider spectrum. The mechanism of action of itraconazole is by inhibiting C-14 α demethylation of lanosterol which disrupts fungal cell membrane synthesis by inhibiting synthesis of ergosterol.¹² Itraconazole is metabolized in the liver by cytochrome CYP3A4 isoenzymatic system and excreted through kidneys. The minimum inhibitory concentration (MICs) of itraconazole is very low in comparison to other oral antifungals. It has been observed by many studies that clinical resistance to terbinafine, griseofulvin and fluconazole is increasing. There has been no evidence of drug resistance mutation in dermatophytes species; if there had been, the MIC levels would have been substantially higher than they are now.¹³ It has been used globally on a huge population of patients due to good safety profile.

Itraconazole can be considered as one of the most effective azoles for treating dermatophytes despite the fact that azoles resistance to dermatophytes is on the rise. Resistance may be due to various mechanisms like decreased uptake of drug, over expression of genes encoding ABC transporters resulting in increase in drug efflux, decreased drug uptake, activation of signaling pathways to antifungal stress response and target alterations.¹⁴ Over expression of genes encoding drug efflux pumps is one of significant system for developing resistance and failing to treat a condition, especially azoles agents. Biofilm formation by the dermatophytes also demonstrates resistance by acting as a physical barrier that prevents antifungal and host immune cells from reaching the microbes.⁷ Tinea corporis, a common dermatophytosis, is prevalent in hot, humid regions, including developing countries. In Pakistan, cases with chronic, atypical presentations, frequent relapses, and treatment failures are increasing. Limited studies exist on its epidemiology and antifungal susceptibility in the region. This study aims to identify predominant dermatophytes species, assess risk factors, and evaluate antifungal susceptibility to itraconazole, providing data for improved diagnosis, treatment, and prevention strategies.

Methodology

This cross-sectional study was carried out in Department of Microbiology, Basic Medical Sciences Institute (BMSI), and Jinnah Postgraduate Medical Centre (JPMC) Karachi in collaboration with the department of Dermatology (JPMC) for collection of study samples from June 2018 to June 2019. Ethical approval from Institutional Review Board (IRB) was taken from

committee of Jinnah Postgraduate Medical Centre (JPMC), Karachi vide letter no (F.2-81/2019-GENL/33048/JPMC). Informed consent was obtained from all participants. Data which obtained was kept highly confidential. The study included all patients suspected of having tinea corporis, regardless of their gender or age. The patients who were getting active treatment for last two weeks with oral or topical antifungal agents and patients who gave refusal for consent were excluded. Detailed medical history of every patient was taken from each case. A careful sample collection, and rigorous laboratory procedures were done for diagnosing and analyzing tinea corporis. Lesion sites were cleaned with ethanol, and specimens were collected by scraping lesion margins. Direct microscopic examination using potassium hydroxide (KOH) revealed fungal structures by breaking down keratin. Specimens were cultured on Sabouraud Dextrose Agar (SDA) and Dermatophyte Test Medium (DTM), incubated at 25°C and 37°C, and observed for six weeks. Fungal growth was analyzed for colony morphology, pigmentation, and microscopic features using Lactophenol Cotton Blue (LPCB) and cellophane tape mounts. Urease tests and stock culture preservation via oil overlay and water culture techniques ensured accurate species identification and long-term viability. Antifungal susceptibility to itraconazole was assessed using a microbroth dilution assay per CLSI guidelines, with drug solutions prepared meticulously for testing, aimed to enhance diagnosis, treatment, and understanding of tinea corporis. All the information was collected via structure proforma. The development and analysis of this database was done on Statistical Package for Social Sciences (SPSS, version 21)

Results

The study included 301 patients with *tinea corporis*, showing a slight male predominance (56.8% males vs. 43.2% females). The most affected age group was 21–30 years (34.9%), followed by 31–40 years (20.9%) and 41–50 years (15.0%), while the least affected were children aged 1–10 years (6.6%). Most participants (94.6%) belonged to the low socioeconomic class, with only a small fraction from middle (4.6%) and high-income groups (0.66%). Regarding occupations, laborers/manual workers constituted the largest group (48.8%), followed by housewives (25.6%), other professions (17.3%), and students (8.3%). clinical attributes of the study population (n=301) revealed that the majority had a disease duration of more than 5 months (36.5%), followed by 4-5 months

(31.8%), and 2-3 months (26.9%), with only 4.6% reporting less than 1 month. A history of recurrence was observed in 72.7% of cases, and 45.5% had a family history of the condition. Sharing household items was reported by 56.8%, and 37.8% had exposure to pets. Additionally, 34.2% of the participants had co-morbidities. On the distribution of signs and symptoms among patients with tinea corporis (n=301) showed that most lesions were localized (76.1%) rather than generalized (23.9%). The lesions were predominantly annular (44.2%), followed by discrete (25.2%), confluent (17.6%), and eczematous (13.0%). Redness was observed in 63.8% of patients, itching in 58.5%, scaling in 56.5%, and papules in 53.8%. Less commonly, vesicles (30.6%) and pustules (15.6%) were present.

On the distribution of fungal isolates among different age groups revealed that the highest prevalence of fungal infections was in the 21-30 years age group (34.9%), followed by 31-40 years (20.9%) and 41-50 years (15.0%). Among fungal types, dermatophytes, non-dermatophytes, and culture-negative samples were most common in the 21-30 years group. Lower prevalence was noted in the 1-10 years group (6.6%) and individuals older than 50 years (11.3%). The distribution was statistically significant with a p-value of 0.01. Table. 1

Table I: Distribution of fungal isolates among different age groups.

Age (years)	Type of Fungi			Total	p-value*
	Dermato-phytes	Non Dermato-phytes	Culture Negative samples		
	n (%)	n (%)	n (%)	n (%)	
1–10	7 (8.3)	4 (7.6)	9 (5.4)	20 (6.6)	0.01*
11–20	9 (10.7)	6 (11.5)	19 (11.5)	34 (11.3)	
21–30	29 (34.5)	18 (34.6)	58 (35.1)	105 (34.9)	
31–40	18 (21.4)	10 (19.2)	35 (21.2)	63 (20.9)	
41–50	12 (14.2)	8 (15.3)	25 (15.1)	45 (15.0)	
>50	9 (10.7)	6 (11.5)	19 (11.5)	34 (11.3)	

Based on clinical presentation of *Tinea corporis* varies by fungal species. *T. mentagrophytes* most frequently causes redness (95.1%) and itching (89.2%), with moderate scaling (44.5%) and vesicles (21.3%). *T. rubrum* is associated with lower itching (44.2%) and redness (81.6%) but has similar rates of vesicles (22.3%) and pustules (21.2%). *T. tonsurans* causes high itching (91.2%) and redness (88.6%) but less scaling (38.4%) and vesicles (8.9%), with slightly higher pustule formation (22.5%). These findings indicate species-specific variability in symptoms. Table II

Table II. Clinico-etiological Correlation of *Tinea Corporis*.

Species	Redness (%)	Itching (%)	Scaling (%)	Papule (%)	Vesicle (%)	Pustule (%)
<i>T. mentagrophytes</i>	95.1	89.2	44.5	12.1	21.3	20.8
<i>T. rubrum</i>	81.6	44.2	39.5	18.4	22.3	21.2
<i>T. tonsurans</i>	88.6	91.2	38.4	17.3	8.9	22.5

On the comparison between KOH microscopy and culture for diagnosing *Tinea corporis* showed that 76.5% of KOH-positive cases were also culture-positive, while 63.1% of KOH-positive cases were culture-negative. Among KOH-negative cases, 23.5% were culture-positive, and 36.9% were culture-negative. The correlation between KOH and culture results was statistically significant ($p = 0.01$). Table III

Table III: Comparison between KOH and Culture.

KOH	Culture				<i>p-value*</i>
	Positive		Negative		
	n	%	n	%	
Positive	104	76.5	104	63.1	
Negative	32	23.5	61	36.9	0.01

According to the antifungal susceptibility profile of dermatophytes against itraconazole showed variation among species. *T. mentagrophytes* had the highest susceptibility, with 44.8% of isolates showing MIC values across a range from 0.06 to 0.5 $\mu\text{g/ml}$, predominantly at higher concentrations. *T. rubrum* accounted for 32.7% of isolates, with MIC values primarily clustering between 0.25 and 0.5 $\mu\text{g/ml}$. *T. tonsurans* comprised 22.4% of isolates, displaying susceptibility across all MIC ranges, with fewer isolates at higher concentrations. The overall findings were statistically significant ($p < 0.05$). Table IV.

Table IV: Antifungal susceptibility profile of dermatophytes against Itraconazole.

Species	MIC value of Isolates ($\mu\text{g/ml}$)					Total	<i>p-value</i>
	0.03	0.06	0.125	0.25	0.5		
<i>T. mentagrophytes</i>	0	6	6	10	16	38 (44.8%)	0.55
<i>T. rubrum</i>	3	2	4	7	11	27 (32.7%)	
<i>T. tonsurans</i>	3	6	3	4	3	19 (22.4%)	

* $p < 0.05$ was considered statistically significant

Discussion

Tinea corporis is a common form of dermatophytosis, accounting for approximately 22% of all cases globally. Recent years have seen significant epidemiological shifts,

with some causative species showing global prevalence while others remain regionally distributed. The rising trend of recurrent and chronic *Tinea corporis* infections underscores its growing public health relevance. Antifungal susceptibility testing plays a vital role in guiding treatment protocols, understanding drug resistance mechanisms, and adjusting therapies to prevent resistant strains and recurrent infections.¹⁵ This study aimed to identify the predominant species causing *Tinea corporis* in the region and assess their antifungal susceptibility. Results revealed that the most affected age group was 21-30 years (34.9%), with the lowest prevalence in the 1-10 years group (6.6%). These findings align with studies by Matehkolaei et al,¹⁶ and Basak et al¹⁷ reported similar trends. Kalsi AS et al¹⁸ in India also identified peak prevalence in individuals aged 16-30 years (50%).

Gender-wise, the study showed a male predominance (56.8%), consistent with findings by Shakir et al¹⁵ in Pakistan (66.6%), Islam et al in Bangladesh, and Sengupta et al¹⁹ in India. Studies suggest that *Tinea corporis* is more common in young males due to factors such as outdoor professions, excessive sweating, exposure to infection, shared accommodations, and less attention to personal. Additionally, societal norms and hormonal differences, including higher androgen levels in women that inhibit fungal growth, contribute to this gender disparity. Contrastingly, studies by Bhise et al²⁰ in India and Araya et al²¹ in Ethiopia found female predominance (59.4% and 52.8%, respectively), attributing this to factors like cosmetic use, tight-fitting clothing, housework-related sweating, and shared clothing habits. These contrasting findings highlight the need for region-specific analyses of *Tinea corporis* epidemiology.

In our study, dermatophytes were isolated from 27.9% of the samples, with non-dermatophytes accounting for 17.2%, and 54.8% showing no growth. The focus of our research was on dermatophytes, with the *Trichophyton* genus being the most prevalent. Among the dermatophytes, *T. mentagrophytes* was the most commonly isolated species (44.8%), followed by *T. rubrum* (32.7%) and *T. tonsurans* (22.4%). The distribution of dermatophytosis and its etiological agents varies significantly between countries and even within different regions of the same country, indicating the diverse and variable nature of dermatophyte prevalence.¹⁵ This regional variation was also highlighted by Hayette and Sachelli et al¹⁴ who noted that different regions have

unique patterns in terms of species prevalence. In line with our findings, *T. mentagrophytes* is reported as the leading cause of *Tinea corporis* in the Middle East and has also been identified as the most common isolate in studies conducted in Lahore, Pakistan,¹⁵ Iran,²² and Hong Kong.¹⁰

In this study, 80.6% of samples were KOH positive, and 68.9% were culture positive (including both dermatophytes and non-dermatophytes). These findings are consistent with the studies by Fatima et al²³ and Kaur et al²⁴. The sensitivity of KOH versus fungal culture has shown conflicting results in various studies, with some highlighting higher culture positivity, indicating its superiority for fungal identification. However, while mycological culture remains the gold standard for fungal infection diagnosis, it takes 2-3 weeks to yield results, making it impractical for immediate clinical use. In contrast, KOH mount is a simple, rapid, and essential tool for preliminary diagnosis, allowing for prompt treatment and helping to prevent the spread of dermatophytosis.²³

Regarding antifungal susceptibility, all our isolates were susceptible to itraconazole. However, the majority of patients had minimum inhibitory concentrations (MICs) near the higher limit. This finding aligns with studies by Sardana et al¹³ and Tahiliani et al.²⁵ Given the ongoing efficacy of itraconazole in clinical practice, it is crucial to optimize its use by ensuring appropriate dosing and treatment duration. Since itraconazole is one of the last available antifungal options, its careful use is essential to avoid the emergence of resistance. The lack of widespread resistance in dermatophytic isolates suggests that such infections should not be categorized as "resistant," but rather as "recalcitrant," highlighting the need for better management strategies.²⁵ Although study possess several limitations include a limited sample size, a single-center design, as well as a focus just on itraconazole susceptibility, which may restrict the findings' generalizability and knowledge of resistance patterns. Lack of long-term follow-up and assessment of environmental factors further limits the depth of the study. Future studies should include larger, multi-center trials, more comprehensive antifungal susceptibility testing, and long-term follow-up to assess recurrence. Addressing the environmental factors and seeking combination therapies or alternative treatments may enhance the management of the condition.

Conclusion

As per the study conclusion species, *T. mentagrophytes* was the most common, followed by *T. rubrum* and *T. tonsurans*, each exhibiting distinct clinical features, with redness and itching being the most prevalent symptoms. The antifungal susceptibility testing revealed that all isolated species demonstrated varying degrees of susceptibility to itraconazole, with *T. mentagrophytes* showing the highest susceptibility. Results underscore the importance of species-specific diagnosis and targeted antifungal therapy for effective management of *Tinea corporis*. However future studies recommended to validate findings with larger studies, expand antifungal testing, use molecular methods for accuracy, and link susceptibility profiles to treatment outcomes. Evaluation of the resistance mechanisms, environmental factors and preventive strategies are also important better management of *Tinea corporis*.

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