

PREVALENCE OF FUNGAL INFECTION (DERMATOPHYTES) IN IMMUNOCOMPROMISED PATIENTS IN FAISALABAD

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DOI: <https://doi.org/10.5281/zenodo.15957658>

Received
08 April, 2025

Accepted
25 June, 2025

Published
16 July, 2025

ABSTRACT

The aim of the study was to determine the rate of dermatophytic fungal infection and pattern of antifungal resistance among immunocompromised patients in Faisalabad. Dermatophytes are a category of fungi that tend to cause skin, hair, and nail infections and are typically not serious in immune-competent people but can be severe in immunocompromised individuals by HIV/AIDS, cancer, diabetes, or organ transplants. Two hundred and fifty immunocompromised patients with clinical manifestations of dermatophytic infections were recruited involving various tertiary referral hospitals. The samples obtained were clinical samples which were prepared in KOH and grew fungus on Sabouraud Dextrose Agar. Dermatophyte species identification was based on colony growth and morphology and microscopic observation and antifungal susceptibility testing was conducted based on CLSI guidelines.

The most frequent clinical manifestations were tinea corporis (35.1%), tinea capitis (24.9%), tinea cruris (17.8%), onychomycosis (11.9%), and mixed-site infections (10.3%) of the 185 confirmed cases. There was also a high prevalence of scalp infections in Faisalabad and Tandlianwala, and body-site infections were most prevalent in Faisalabad and Jaranwala. Most patients were male (54.6%), and more than half of the young patients (21-40 years) were observed (53.0%) with 16.2 percent of pediatric patients. The frequency of antifungal resistance was 38.4 percent (fluconazole: 26.5 percent; terbinafine: 17.8 percent), similar to or higher than that reported in northern Pakistan; the increase in fluconazole-resistant *Trichophyton* across the world has been linked to mutation of *SQLE*, the relevant gene. Itraconazole (8.6%) and griseofulvin (5.9) resistance was low. These results indicate that there is a high burden of resistant dermatophyte infections in immunocompromised patients in Faisalabad and lack of routine susceptibility testing, focusing on antifungal stewardship, as well the development of region-specific treatment guidelines, is critical to improving patient outcomes.

INTRODUCTION

Dermatophytes are a kind of keratinophilic fungus that infect skin, hair and nail, causing superficial fungal infection usually known as dermatophytosis or tinea infections. Fungus infections, especially infections by dermatophytes are also a great health risk to the immunocompromised due to their weak immunological defence. Dermatophytes are a type of keratinophilic fungi that can grow on the skin, in hair,

and nails and cause superficial mycoses also known as tinea infections (Gupta et al., 2020). Such infections tend to be self-limiting in immunocompetent individuals but can be chronic, extensive, and recalcitrant in immunosuppressed groups, including human immunodeficiency virus (HIV) infection/acquired immunodeficiency syndrome (AIDS), cancers, diabetes mellitus, and individuals

undergoing immunosuppressive treatment (Ameen et al., 2021; Hay et al., 2018).

Dermatophytic infections have been increasing in global prevalence, and the World Health Organization has classified superficial fungal infections as a neglected tropical disease since they have high prevalence and high burdens on quality of life (WHO, 2023). This situation is also influenced by high humidity, poor hygiene, lack of access to dermatology services, and uncontrolled use of antifungals in South Asian nations, such as Pakistan (Khan et al., 2022). Faisalabad is an urban and industrial city that has a dense population, and, therefore, a definite set of problems with the ecology and socioeconomic factors might encourage the spread of dermatophyte fungi among more susceptible demographics.

Dermatophytes encompass infections of the human skin and hair, fingernails and toenails. Dermatophyte infections are becoming a growing concern over recent years. It complicates the management of antifungal infections due to the growing resistive rates in certain ethnic groups. When the infections are caused by dermatophytes, diagnostics should work by certain parameters, which distinguish between simple skin contaminations and these infections. These microorganisms affect skin, nail surfaces and surfaces on hands and feet. These fungi cause infections of the surfaces of the skin on the hands and the feet where they act as possible infectious agents (Chanyachailert et al., 2023).

The prevalence rates of dermatophyte infections among immunocompromised groups differed in various parts of Pakistan, as previous studies demonstrated that the prevalence rates ranged between 18% and more than 45%, depending on the type of diagnostics and characteristics of the population, as well as environmental aspects (Azeem et al., 2019; Ghazanfar et al., 2022). Nonetheless, very few region-specific data of Faisalabad exclusively target this high-risk group. The development of antifungal resistance and presence of clinical implications warrants the local prevalence assessment of dermatophytes in immunocompromised patients and makes an assessment timely and necessary.

The systemic antifungal medications are important in the medical management of both tinea capitis and tinea barbae. Tinea capitis and tinea barbae can be treated with the help of drug therapy that implies the use of griseofulvin the doses of which are typically 1525 mg/kg daily. Their therapy involves a period of eight weeks up to both clinical and mycological cure. Application of the treatments should be done twice

daily within 2-4 weeks on tinea corporis, tinea cruris, tinea faciei and tinea pedis. It has been reported that allylamine terbinafine demonstrates therapeutic effects within one week of administration, as a result of its fungicidal effects. Fluconazole or itraconazole within the triazoles and Griseofulvin can serve as an additional advantage in patients with diffuse, inflammatory, or immunocompromised infections of the infection (Mousavi et al., 2023).

T. interdigitale strains of tinea corporis or tinea cruris show resistance to terbinafine treatment. The study by Khurana and colleagues involving 64 patient strains showed that there was an increased minimum inhibitory concentration of terbinafine above 1mg/L on 39 resulting in 61 percent of the total strains under investigation. EUCAST AFST has determined epidemiological MIC cut-offs of 0.125 mg/L in *T. interdigitale* and 0.03 mg/L in *Trichophyton rubrum*. In testing, all of the isolated specimens were resistant to fluconazole but exhibited positive susceptibility to itraconazole (Kruithoff et al., 2023).

Three-quarters of all the 600 cases of invasive dermatophytosis were made up by 32.5 percent Majocchi granuloma cases, 55.6 percent deeper dermal dermatophytosis, 6.9 percent pseudomycetoma of invasive dermatophytosis and 5.0 percent disseminated dermatophytosis. The most common site of infection was unilateral lower limb at 16.9% followed by unilateral upper extremity at 9.4%. This was followed by bilateral lower limbs, face, scalp, trunk, groin(s), perineal region and head (both face, scalp), neck, breast and bilateral upper extremities in the order of 8.8%, 8.1%, 5.6% and 4.4% and 4.4% and 2.5% and 1.3% and 1.3% and 0.6% and 0.6% respectively. The invasive group of dermatophytosis showed overlapping infection in various body sites or extensive dermatophyte infection in thirty-two-point five percent of cases (Wang et al., 2021).

An accurate diagnosis is crucial to dermatophytosis due to its ability to provide timely treatment in addition to preventing the transmission of infections between humans and animals. When taking skin samples, it should be done close to the periphery of characterized lesions since materials found near the centre are non-viable or have low viability. The skin infections are poorly defined areas of the body where skin scrape testing should be employed by the various healthcare personnel in making a diagnosis. Therapeutic hair sampling necessitates both plucking and application of the so-called Mackenzie brushing techniques that animals get into heavily to carry out whole area examination. The patient is reported to

need two-three minutes of brushing, or until adequate amount of hair gathers in the brush. The medical personnel will collect entire nail clippings or post the desirable alternative of nail scrapings depending on the severity of fungal infection. As well as (Moskaluk & Vande Woude, 2022).

Antifungal resistance develops through mutation of genetic and biochemical systems in dermatophytes by changing drug targets and enhancing drug efflux pump to existing medicines. Terbinafine resistance may arise due to a single nucleotide substitution in the target gene of squalene epoxidase (sqle). The *T. rubrum* Sqle protein has four substitutions Leu393Phe, Leu393Ser, Phe397Leu, His440Tyr which are associated with terbinafine resistant phenotype. An increase in the expression of the salicylate 1-monooxygenase (SalA) gene along with the addition of additional copies of the SalA gene via transformation contributes to terbinafine resistance in *T. rubrum* (Martinez-Rossi et al., 2021).

MATERIAL AND METHODS:

Study design:

A prospective study was done in tertiary referral hospitals in Faisalabad in (n=185) immunocompromised patients (HIV/ AIDS, malignancy, diabetes, organ transplant) presenting with clinical features suggestive of dermatophytosis.

Microscopy and Collection of Specimen:

Samples of skin scrapings, nail clipping, and hair were taken aseptically by scraping the borders of active lesions. To confirm the presence of fungal elements, direct microscopic examination was done in 10-20% potassium hydroxide (KOH) solution under 10x and 40x objectives. Culture and Identification Specimens were inoculated into Sabouraud Dextrose Agar containing chloramphenicol and cycloheximide and incubated at 25 30 C up to 14 days. Colony appearance and microscopic examination of macro- and microconidia stain using lactophenol cotton blue were used to identify dermatophyte species (Dabas et al., 2017).

Antifungal Susceptibility Testing:

Vitro susceptibility testing was done as per the standard CLSI M38-A3 guidelines (Shakir et al., 2019).

Data recordings and analysis:

The demographic characteristics (age, sex) as well as clinical diagnosis (tinea corporis, capitis, cruris, onychomycosis, mixed) were recorded. Also, the distribution of the sites of infection was obtained. The percentage of the isolates whose intensity exceeded epidemiological cutoff values (ECVs), as outlined in the CLSI M38-A3 was used to calculate antifungal resistance rates in it.

Statistical Analysis

IBM SPSS version 26 was used to systematically organize and analyse the collected data. The frequency and percentage of dermatophytic hospital infections were calculated using descriptive figures.

RESULTS:

Infection region wise:

The bar chart shows regional distribution in dermatophyte infection under various body areas and parts-body, feet, other, and scalp among patients in various regions as shown if (Figure A). The most frequently occurring infection was in the scalp with Faisalabad (15 cases) and Tandlianwala (14 cases) both leading the pack followed by Muza (9 cases) indicating an increased exposure or transmission of the infection in these regions. In Faisalabad and Jaranwala, body infections were highest (12 cases each), and Tandlianwala had the lowest counts in most of the categories consistently. The distribution of feet infections was at near-median around a range of 2 to 4 cases in Chiniot and Faisalabad, and 4 in Tandlianwala. Sargodha (11) recorded the highest infections on other body sites as well as the lowest in Faisalabad (6). In general, the greatest burden of dermatophyte infections was found in Faisalabad, notably those of the scalp pointing towards possible environmental and lifestyles contributing to dermatophyte infections.

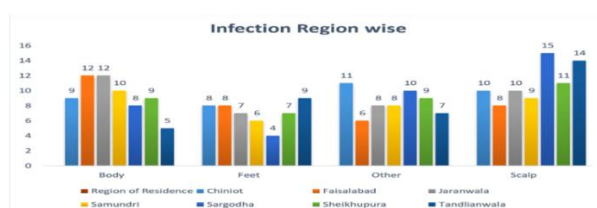


Figure A: region wise analysis

The Site of Dermatophyte Infection:

The most common clinical manifestations were tinea corporis as shown in (Figure B), which were 65 cases (35.14%), tinea capitis 46 cases (24.86%), and tinea

cruris 33 cases (17.84%). Onychomycosis (nail involvement) was identified in 22 patients (11.89%), whereas mixed-site infections were found in 19 patients (10.27%).

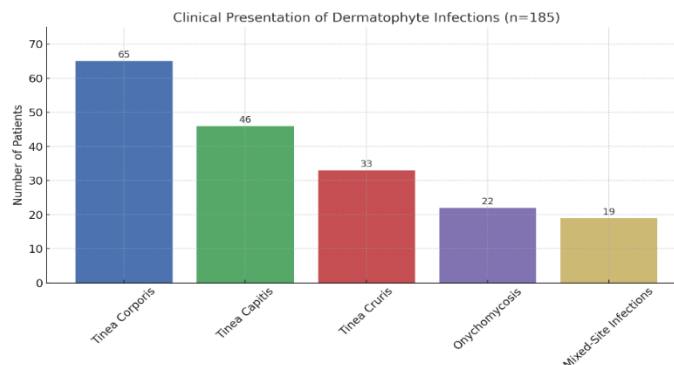


Figure B: Site of Dermatophyte Infection

Distribution on gender and age wise:

The gender-wise distribution indicated a pre-eminence among males (101 cases; 54.6%) as opposed to female (84 cases; 45.4%), but the difference was not statistically significant ($p > 0.05$). The 21-40-year age

group had the highest infection rate (98 cases; 53.0%), followed by the group over 40 years old and the lowest prevalence was found in the pediatric age group under 20years (30 cases; 16.2%) as shown in (Figure C).

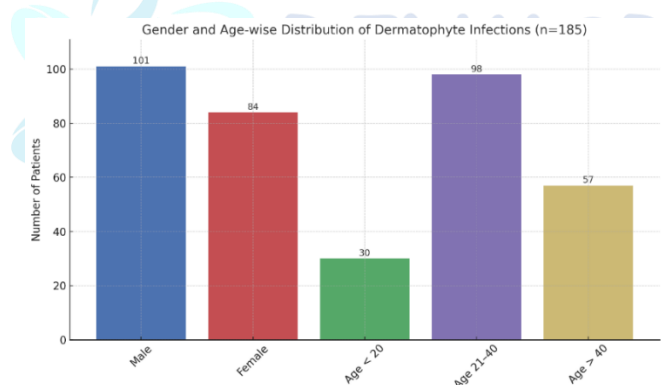


Figure C: Distribution on gender and age wise

Antifungal susceptibility pattern of dermatophytes:

Among 185 patients, 71 isolates (38.4%) had demonstrated reduced sensitivity to at least one of the commonly used antifungal agents. The most common was the fluconazole resistance that occurred in 49 cases (26.5%), terbinafine in 33 cases (17.8%). Itraconazole and griseofulvin proved to be superior, however, with

resistance rates was much lower at 16 cases (8.6%) and 11 cases (5.9%) respectively as shown in (Table 1). These results demonstrate new resistance patterns and increase the possibility of antifungal stewardship in clinical practices.

Table 1: Adjusted Antifungal Resistance Data (n = 185)

Antifungal Agent	Number of Resistant Isolates	Percentage (%)
Fluconazole	49	26.5%
Terbinafine	33	17.8%
Itraconazole	16	8.6%
Griseofulvin	11	5.9%
Total (Any Drug)	71	38.4%

Discussion:

The study offers a detailed survey of the epidemiology, clinical distribution, and antifungal resistances of dermatophyte infections in immunocompromised individuals in Faisalabad, Pakistan. The results indicate a high burden of dermatophytosis, a high diversity in clinical manifestations, age and gender stratification, geographical origin, and fungicide resistance. It was found that the commonest clinical manifestation out of 185 patients tested was tinea corporis (35.1 percent), tinea capitis (24.9 percent), and tinea cruris (17.8 percent).

There was also the observation of Onychomycosis and mixed-site infections but to a smaller degree. The current data correlate with the previous results of (Borgohain et al., 2021) who registered comparable dynamics in the Northern Pakistani population among immunocompromised patients. A similar pattern has also been found in India and other tropical nations, where tinea corporis and tinea capitis prevail due to favorable ecological conditions, including high humidity, poor hygiene, and overpopulation (Usman et al., 2021).

The immune system is weakened in immunocompromised hosts, especially individuals with diabetes, HIV/AIDS, or chemotherapy patients, weakening the skin barrier, which makes them vulnerable to superficial fungus infections (Ebert et al., 2020). The prevalence of the infection was maximal in the age category of 21-40 years (53.0 percent) with individuals older than 40 the following most-infected group (30.8 percent) and patients younger than 20 years of age had the least prevalence (16.2 percent). This age distortion can be related to lifestyle distinctions, profession, and immune response. Adults aged between 21-40 are generally more active at work and in social life, which causes a greater risk of exposure to shared amenities and facilities where infection by fungal culture can occur due to an unfriendly environment (Reisen et al., 2021). Likewise, these trends are reported in other regional studies (Reisen et al., 2021). Reduced rate of infection by children can be credited to enhanced parental protection and improved standard of hygiene at an initial stage of childhood.

Tinea capitis has been noted to be more prevalent in different settings, especially among school-going children, which indicates the presence of a cultural, environmental, and socioeconomic influence on the pattern of infection (Red Crescent Diagnostic Study, 2020). In gender ratio, there is a greater prevalence of

males (54.6) than females (45.4) although, the prevalence does not differ significantly ($p > 0.05$). This pattern has been regularly reported in analogous papers (Khurana et al., 2019) and conceivably is indicative of higher environmental contact, regular use of occlusive spacious dress, and outside occupations that encourage fungus development through perspiration and surface maceration. Nevertheless, the hormonal disparities and hygienic habits can also play a role in gendered vulnerability.

Faisalabad had the highest burden of infections basically in the region of the scalp and body. This might be because of crowding in the urban population, low housing standards, and high flux rates of movement of patients among the healthcare facilities which might stimulate transmission. On the other hand, lower infection rates were reported in some regions, such as Tandlianwala, which may have been caused by lower population density, or low access to health services. These conclusions are consistent with those of (Chanyachailert et al., 2023) who found regional disparities in fungal infections in rural Punjab and attributed them to the socio-environmental status. The antifungal susceptibility profile was a very crucial part of this study.

Disturbingly, the resistance of at least one of the antifungal agents in the isolates was at 38.4 percent. The highest resistance was caused by fluconazole (26.5 percent), followed by terbinafine (17.8 percent). Comparatively lower resistance was to itraconazole (8.6%), and griseofulvin (5.9%). These findings are in agreement with the rising global issue of dermatophyte resistance, especially in South Asia. The probability of acquiring resistance is stimulated by the over-the-counter availability of antifungal agents, noncompletion of the treatment course, and empirical writing habits (Ebert et al., 2020). Moreover, the presence of mutations in the squalene epoxidase (SQLE) gene correlates with terbinafine resistance and a decreased response to the drug due to the target structure being changed (Qureshi et al., 2019).

In conclusion, this work indicates that the incidence of dermatophyte infections is high, and the prevalence of antifungal resistance is threatening in immunocompromised patients in Faisalabad. Individuals aged 21-40 years were the most impacted with tinea corporis as the most prevalent clinical form. Resistance to fluconazole and terbinafine was also significant, which indicates the necessity of better diagnostic, treatment, and public health management measures. Further studies are necessary to track the

changing patterns of resistance and to formulate more potent management plans depending upon local situations.

Conclusion:

The research identifies a substantial burden of dermatophytic infection among the immunocompromised in Faisalabad with tinea corporis, tinea capitis, and tinea cruris as the most common clinical manifestations. Males had a slightly higher prevalence than females and adults aged 21-40 years were the most affected age group. The geographical patterns reported a denser infection in the cities such as Faisalabad than on the outskirts. The increasing trend of antifungal resistance, especially towards the common antifungal agents, fluconazole and terbinafine, is a major issue that was identified through the study. The finding of resistance in more than one-third of the isolates indicates the importance of antifungal susceptibility testing as a routine, rational prescription of the drugs, and increased clinical observation in the high-risk population. Such results underscore the necessity of enhanced facility-based diagnosis, adequate health education, and efficient antifungal stewardship initiatives to mitigate the incidence and relapse in dermatophyte infection.

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