

Antifungal Reistance in dermatphytosis:Emerging Challenges and the role of Pharmacist

Abstract:

Dermatophytosis is an example of one of the commonest superficial fungal infections, which traditionally could be easily managed by topical and oral antifungal medications respectively. Moreover, of late, resistance to antifungal agents, and more so terbinafine, poses alarming threats to successful, effective, and efficient management of the condition as of today. The development of resistance by some dermatophyte strains, such as *Trichophyton indotineae*, poses alarming threats, which include reduced successes and efficiency of management, particularly through successes and successes of returning or relapsing conditions, respectively. Causes of resistance include misuses of antifungal, readily available antifungal prescription from pharmacies, and non-adherence of patient strictness on administration of both topical and oral antifungal agents, respectively.

Keywords:Dermatophytosis; Antifungal Resistance; *Trichophyton* ;Terbinafine;

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Introduction:

Dermatophytosis results from keratinophilic fungi, termed Dermatophytes. Dermatophytosis has also been reported to be a superficial form of fungal infection typically affects skin, hair, and nails (Zorab, Amin, Mahmood, Mustafa, & Abdulrahman, 2023). Even though this infection is regarded as easily manageable, it emerged once again as a formidable disease due to antifungal resistance and changes in clinical disease manifestation(Rehman et al., 2018). There have been observed instances of chronic, recurrent, and intractable dermatophytosis in recent years, reported by practitioners in some parts of the world, especially in South Asia, over the past decade (Rehman & Hussain, 2012, 2013)

Resistance to antifungals among dermatophytes was considered to be exceptional, but recent molecular and clinical observations have made it clear that resistance is no longer exceptional but a new emerging trend worldwide (Alam et al., 2019). The heightened situations have been contributed by irrational use of antifungals, uncontrolled use of fixed dose combinations of creams that contain corticosteroids, and poorly enlightened patients (Shakeel et al., 2019).The pharmacists, who have the professional expertise in pharmacotherapy, can best deal with the above-mentioned situations(Sadia, Rehman, & Naveed, 2019).

Overview of Dermatophytes:

Classification of Dermatophytes:

The dermatophytes can be considered as fungi that take on a filamentous form and which fall under three major species according to their morphology and predilections: Trichophyton, Microsporum, and Epidermophyton (Manoyan, Gursheva, Gabuzyan, & Panin, 2024). These fungi possess the ability to infect keratinized tissues by breaking down.

Typical Species Causing Dermatophytes:

Fungal species most often analyzed in relation to infections in human beings which includes Trichophyton rubrum, T. mentagrophytes, T. interdigitale, and Microsporum canis (Chaumont, 2024). Recently, Trichophyton indotineae has been recognized as a distinct species in case of severe and resistant dermatophytosis, mainly in and around India subcontinent (Sattar et al., 2025).

Antifungal Drugs employed in Dermatophytes:

Topical Antifungal drugs:

Topical preparations of antifungal agents are nonetheless viewed as first-line therapeutic agent for localized dermatophytic infections. Among the most common agents of these categories drugs are following; azoles antifungals (clotrimazole, ketoconazole), allylamines (terbinafine), benzylamines (butenafine), and hydroxypyridones (ciclopirox). These agents act by inhibiting ergosterol synthesis or disrupting the integrity of fungal cell membrane (Xiao et al., 2022).

Systemic Antifungal Agents:

Systemic antifungal is also required in situations where the infections spread widely, or re-occur or donot respond to treatment. Oral antifungal agents include terbinafine, itraconazole, fluconazole, and griseofulvin. Although terbinafine has long remained the drug of choice because of its fungicidal property as well as pharmacokinetic properties, resistance has lately reduces its effectiveness (Khadim et al., 2024; Khadim et al., 2023; Mansoor et al., 2018).

Concept of Antifungal Resistance:

Definition of Antifungal Resistance:

Antifungal resistance refers to the reduced sensitivity exhibited by fungal pathogen against antifungal agents, thus reducing their effectiveness. Antifungal resistance may either be intrinsic or result of some sort of pathogenic gene mutations (Fisher et al., 2022).

Resistance vs. Treatment Failure:

It is important to differentiate between resistant organisms and failure of treatment due to lack of adherence, under-dosing, misidentification, and re-infection. Laboratory confirmation through susceptibility testing plays important role in proper classification (Rehman, Ahmed, Hashmi, & Jamil, 2017).

Antifungal Drugs Resistance

Epidemiology:

Global Trends:

Resistance in dermatophytes was a rarity in the past, though rising rates of resistance to terbinafine have recently been reported in Asia, Europe, and Africa (Sadia, Rehman, & Naveed, 2020).

Regional Patterns:

India has proven to be one of the main centers of resistance to antifungal agents among dermatophytoses, with various authors finding the rate of resistance to terbinafine to be above 30% in various parts of region(Benedict et al., 2021).

Evolution of *Trichophyton Indotineae:

T. indotineae has been found to be a genetically distinct species that has contributed significantly to aggressive infections as well as resistance to terbinafine (Jabet et al., 2023).

Mechanisms of Antifungal Resistance:

Genetic Mutation:

The (SQLE) gene encodes squalene epoxidase. Point mutations of the SQLE gene reduce the affinity of terbinafine, thus the mechanism of resistance conferred (Balkis, Leidich, Mukherjee, & Ghannoum, 2002).

Altered Drug Targets:

The structural variations occurring in the enzymes of ergosterol markedly decrease the effectiveness of antifungal agents.

Efflux Pump Over expression:

An increase in the expression of the ATP-binding cassette transporters results in an increase of the efflux of the drug out of the fungal cells.

Biofilm Formation:

Dermatophytes associated with biofilms show low susceptibility to antifungal agents owing to low penetration of antifungal agents(Sattar, Rehman, Naveed, Aziz, & Eraj, 2022).

Clinical Implications of Resistance:

Treatment Failure and Recurrence:

Resistant infections can take longer to be treated, thereby becoming a burden to patients.

Chronic and Extensive Diseases:

The resistant forms of Dermatophytosis can present with atypical morphology and repeated episodes, reoccurrence will be there.

Economic and Quality-of-Life:

Higher expenditure in healthcare, productivity loss, and distress can be serious effects (Rehman, Sattar, Mustafa, et al., 2024). Factors Contributing to Resistance Development:

Inappropriate Use of Antifungal:

Sub therapeutic doses and early dose cessation are factors in resistance

Over-the-Counter Availability:

Lack of control of antifungal distribution can lead to their abuse (Rehman, Sattar, Khan, et al., 2024)

Steroid-Antifungal Fixed-Dose Combination:

The improper use of creams that contain steroids impedes immunity and changes the presentation of illness.

Poor Patient Adherence:

In the event of insufficient levels of adherence, the therapeutic outcome will compromise(Sattar, Rehman, & Naveed, 2024) ₂

Dermatophytosis Diagnosis of Antifungal-Resistant:

Clinical Indicators:

If there is no response to conventional treatment, resistance should be suspected.

Mycological Confirmation:

KOH microscopy and fungal cultures remains to play an important role in diagnosis .

Antifungal Susceptibility:

CLSI and EUCAST procedures facilitate the detection of resistance and the management of treatment (Arendrup, Guinea, & Meletiadis, 2024).**Resistant Dermatophytosis Management:**

Alternate Therapeutic Strategies:

Regimens including itraconazole are progressively utilized

High dose or prolonged therapy:

Protracted periods of treatment may also be required

Combination Therapy:

Simultaneous or combination antifungal therapy may also show beneficial effects (Sattar, Naveed, Rehman, Usman, & Jamshed, 2024).

Antifungal Stewardship:

Principles of Stewardship:

Antifungal agents, dosage, and duration of use must be adequately optimized

Role of Pharmacists in Stewardship:

Pharmacists would help in evaluation, education, and monitoring (Rehman, Muskan, & Anum, 2025).

Role of the Pharmacist:

Rational drug selection:

Pharmacists play a vital role in promoting rational antifungal therapy choices, ensuring that the drug, dose, formulation, and duration are all evidence supported /as per guidelines and justified based on disease severity. Pharmacists can assist clinicians decide on systemic vs. topical therapy depending on the number, location, and nature of skin lesions. As terbinafine resistance has risen, other options such as itraconazole should be recommended to optimize therapy and avoid polypharmacy when possible and indicated(Jamil, Nohri, Sama, Malik, & Naveed, 2025; Naveed & Sadia, 2022; Sadia, Naveed, Rehman, Jamshed, & Dilshad, 2025; Zafar, Ahmed, Naz, & Naveed, 2012).

Education & Patient Counseling:

Patient counseling is of utmost importance and plays an important role in the effective management of the dermatophytosis infections. The patient education by the pharmacist on the right application of topical antifungals is paramount, further teaching on the importance of completing the treatment course is very vital. Patient education also involves debunking myths about quick *relief from infection by the* use of steroid-containing creams, while emphasizing the fact that improvement does not necessarily indicate microbiologic cure (Rehman et al., 2020).

Monitoring Adverse Effects:

Systemic antifungals relate to adverse reactions, such as hepatotoxicity and gastrointestinal symptoms, which pharmacists can use to monitor adverse reactions, assess follow-

through care related to blood work if necessary, and discuss interactions, especially with azoles. Monitoring and reporting adverse reactions related to systemic antifungals will promote patient safety and medication compliance (Sadia, Naveed, Rehman, & Jamshed, 2025).

Preventing OTC Misuse:

Over-the-counter and unrestricted use of antifungals and fixed-dose steroid combinations are important sources of resistance. A crucial tool in the control of tuberculosis in these areas appears to be the community pharmacist acting as a "gatekeeper" and dissuading and preventing self-medicating and irrational drug combinations and referring patients to consultants if they are repeat and extensive. These are important in areas that lack enforcement of control (Naveed, Hameed, Sharif, Urooj, & Mehak, 2014; Naveed, Sarwar, et al., 2014; Shakeel et al., 2021).

Improving Adherence:

Non-adherence is still a contributory cause of relapse in dermatophytes infections. Pharmacists must incorporate strategies to improve compliance, such as reduced dosing regimens and reminder and follow-up consultations. In addition to preaching about completion of treatment even when symptoms have diminished, pharmacists play an essential part in lessening recurrence and selective forces in resistance.

Pharmacists are essential in ensuring optimal evidence-based use of antifungal agents while preventing resistance (Rehman, Sattar, et al., 2025).

Regulatory and Public Health Perspectives:

Regulation of Fixed Dose Combinations:

The availability of irrational fixed-dose combinations of powerful corticosteroids, antifungals, and antibacterials has greatly impacted the epidemiology of dermatophytosis. A stiffer control regime is needed to make it difficult to find these combinations that tend to hide infections and encourage antifungal resistance. This is important to prevent misuse at the community level.

Guideline Development:

Region-specific clinical guidelines with standardized recommendations will be required to counter the rising resistance trends seen in some regions or countries. Future clinical guidelines should include recommendations on antifungal susceptibility testing and different regimens of therapy for antifungal resistance. They can be supplemented by the expertise of pharmacists and their drug utilization experience (Shakeel et al., 2022).

Policy Reforms:

The need for public health measures in regard to antifungal stewardship and prescription-only status and monitoring of resistance trends is a high priority. Aligning dermatophytosis with anti-microbial resistance strategies would optimize monitoring and resource allocation efforts. Synergistic efforts of policymakers and healthcare professionals and pharmacists would be essential to bring about a positive transformation in this regard (Ali et al., 2020).

Recent Advances and Future directions:

Molecular Diagnostics:

Improvements in molecular diagnostic technology, such as the polymerase chain reaction (PCR) and gene sequencing, have reduced the limitations in differentiating dermatophytes and mutations responsible for resistance. Mutations in the SQLE gene can be detected to identify early signs of resistance to terbinafine, therefore allowing customized treatment .

Novel Antifungal Agents:

New antifungal drugs and re-formulated drugs with improved pharmacokinetics are being studied for resistance. Drugs designed to target other pathways in the fungus or have higher activity against resistant isolates are currently promising drugs. Unfortunately, available clinical studies on their efficacy in the treatment of dermatophytosis are few.

Advanced Drug Delivery Systems:

New drug delivery systems, like liposomes, nanoparticles, and sustained-release creams, have been developed and focus on increased antifungal penetration in keratinized tissue.

This may prove useful in minimizing systemic side effects and the risk of resistance(Sadia, Naveed, Rehman, Jamshed, et al., 2025).

Research Gaps:

Despite the rising awareness of the existence of antifungal drug resistant cases of dermatophytosis, many gaps remain. There is a need for surveillance studies to be done on a large scale, designs for testing for susceptibility to be standardized, and intervention studies to be implemented by pharmacists(Sadia, Naveed, Rehman, & Jamshed, 2025).

Conclusion:

Antifungal resistance in dermatophytosis is an emerging health problem that is of importance to the well-being of people across the globe. The development of resistance among the dermatophyte species, mainly *T. indotineae*, highlights the importance of rational use of the antifungal agents, advancements in the diagnosis of the conditions, and the involvement of pharmacists, the medication experts, in the fight against the resistance.

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