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Epidemiology, Resistance Patterns, and Clinical Diagnosis and Management Challenges in Dermatophytosis

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ABSTRACT

Background: Dermatophytosis has re-emerged as a significant public health concern, with shifts in epidemiology, rising antifungal resistance, and increasingly complex clinical presentations. Beyond traditional tinea corporis and cruris, clinicians now encounter steroid-modified disease, extensive involvement, and frequent relapses. Resistance—particularly to allylamines—along with host and environmental drivers complicates diagnosis and management. Conventional tools such as KOH microscopy and culture remain useful but are limited by sensitivity and speed; molecular diagnostics and dermoscopy extend accuracy in difficult cases. Management challenges include therapeutic failure, drug interactions, and adherence. Novel responses are taking shape: optimized pharmacokinetics (super-bioavailable itraconazole), extended and combination systemic regimens, newer triazoles and alternative classes, adjunctive keratolytics and chemical peels, photodynamic therapy, targeted topical amphotericin formulations, and host-directed strategies (micronutrients, immunomodulation). Antifungal stewardship and regulatory action against steroid misuse are urgent priorities. This review synthesizes current evidence on changing epidemiology, resistance mechanisms, diagnostic advances, and pragmatic management pathways, highlighting research gaps and future directions.

Keywords*:* Epidemiology, Resistance Patterns, Clinical Diagnosis. Management Challenges,Dermatophytosis

INTRODUCTION

Once considered a straightforward superficial infection, dermatophytosis has evolved into a multifaceted clinical problem characterized by epidemic clustering [1], atypical morphology [4], and persistent or recurrent disease [3]. Several trends converge to explain this shift: widespread, often unsupervised use of topical corticosteroid–antifungal combinations [17]; dense living conditions with high contact rates [6]; climate factors that favor fungal survival [15]; and host comorbidities such as diabetes, obesity, and immunosuppression [6]. Added to these are pathogen determinants—most notably reduced susceptibility in *Trichophyton* species [2,5]—that erode the reliability of historically dependable oral agents. The result is a widening gap between traditional algorithms and real-world outcomes, with rising healthcare utilization and substantial quality-of-life impact [9].

10.48047/jocaaa.2024.33.06.137

From a diagnostic standpoint, bedside KOH microscopy and culture remain cornerstones [7], yet both are limited by operator dependence and time to result. Dermoscopy can support recognition of active borders and hair shaft involvement [8], while histopathology assists in steroid-modified or psoriasiform lesions [4]. Molecular assays—PCR, sequencing, and MALDI-TOF—offer enhanced speed and specificity [12], and they are increasingly valuable in refractory disease and in epidemiological mapping of resistant strains [2]. Pragmatically, a tiered approach that begins with rapid, low-cost tests and escalates to molecular confirmation in atypical or recalcitrant cases balances accuracy with access [18].

Management challenges reflect this diagnostic complexity and the evolving resistance landscape. Terbinafine and itraconazole remain foundational [5,10]; however, pharmacokinetic variability, drug–drug interactions, and reduced susceptibility call for more nuanced use [6]. Practical strategies include extending treatment duration to ensure adequate keratin penetration [11], weight- and severity-adjusted dosing [10], and pairing systemic therapy with potent topicals to reduce surface fungal burden [13]. Combination systemic regimens (e.g., allylamine + azole) may rescue selected failures when carefully monitored for hepatic effects and interactions [11].

Alongside optimization of legacy agents, **novel management lines** are emerging. **Super-bioavailable itraconazole** improves exposure reliability across gastric pH states, addressing a frequent cause of subtherapeutic levels [10]. **Newer triazoles** (such as posaconazole and fosravuconazole) and **alternative classes** expand options for documented resistance or intolerance [12], though cost and access can limit routine use. **Adjunctive keratolytics**—including **salicylic acid** and **chemical peels** (e.g., trichloroacetic acid for lichenified plaques)—debulk hyperkeratosis and enhance drug delivery in chronic tinea [13]. **Photodynamic therapy** provides a non-systemic modality for localized, treatment-refractory disease [14], while **topical amphotericin B** in advanced delivery vehicles shows promise where azoles/allylamines falter [15]. **Host-directed measures** (vitamin D optimization, zinc where deficient, and broader immunomodulatory approaches) may reduce relapse risk in selected patients [16].

Crucially, clinical advances must be embedded within **antifungal stewardship**: educating patients to avoid steroid-antifungal mixtures [17], harmonizing diagnostic confirmation before prolonged therapy [7], and standardizing follow-up to detect early failure or reinfection [18]. Public-health measures—labeling restrictions on steroid combinations, community screening of close contacts, and environmental hygiene—are equally important in high-burden settings [6].

This review examines the changing epidemiology of dermatophytosis [1], synthesizes current understanding of resistance mechanisms [2,5], appraises diagnostic tools from clinic to laboratory [7,8,12], and outlines pragmatic, tiered management—including novel and adjunctive lines [10–16]—

10.48047/jocaaa.2024.33.06.137

that clinicians can deploy now. We also highlight priorities for research: robust surveillance networks [1], standardized resistance testing [5], head-to-head therapeutic trials in recalcitrant disease [11], and implementation studies that translate innovations into durable population-level control [18].

Changing Epidemiology

Dermatophytosis remains one of the most common superficial fungal infections worldwide, affecting an estimated 20–25% of the global population at any given time [1]. Traditionally regarded as a mild and easily treatable condition, its epidemiology has shifted over the last two decades. In South Asia, particularly India, an epidemic-like rise in chronic and recalcitrant tinea infections has been reported, linked to shifts in the *Trichophyton mentagrophytes/interdigitale* complex and *T. rubrum* genotypes [2]. These genetic adaptations correlate with increased virulence and reduced susceptibility to first-line antifungals [5].

Outside Asia, similar patterns are emerging. In Europe and the Middle East, surveillance studies indicate rising terbinafine resistance and atypical clinical presentations [12]. Reports from East Asia and Africa also highlight changing species distributions and increased treatment failures [6]. Together, these findings illustrate a global evolution of dermatophytosis from a benign nuisance to a significant dermatological and public health concern, underscoring the importance of regional surveillance [18].

Host and Environmental Risk Factors

The persistence and recurrence of dermatophytosis are strongly influenced by host and environmental conditions. Immunosuppression due to HIV infection, organ transplantation, or immunosuppressive drugs compromises antifungal defenses, predisposing to severe and chronic infections [13]. Metabolic disorders such as diabetes and obesity alter skin barrier function and local immunity, creating an environment conducive to fungal persistence [6]. Atopic dermatitis and other chronic skin diseases also increase susceptibility [4].

Environmental and behavioral determinants play a similarly important role. High humidity, hot climates, and overcrowding promote fungal transmission [15]. Sharing of clothing, towels, or bedding facilitates reinfection cycles, while occlusive clothing and poor hygiene further sustain colonization [14]. Iatrogenic factors, including misuse of over-the-counter steroid–antifungal combinations, contribute to atypical morphology and mask clinical signs, complicating diagnosis and delaying appropriate therapy [17].

These risk factors emphasize that dermatophytosis is not solely a microbiological infection but a multifactorial disorder shaped by host vulnerabilities, environmental context, and healthcare practices [18].

Resistance Patterns in Dermatophytosis

10.48047/jocaaa.2024.33.06.137

One of the defining challenges in contemporary dermatophytosis is the emergence of antifungal resistance, particularly to terbinafine. The most well-characterized mechanism involves point mutations in the squalene epoxidase (SQLE) gene of *Trichophyton* species, which reduce drug binding and confer high-level resistance [5,19]. Resistant isolates have been widely reported in India and are increasingly documented in Europe, Japan, and the Middle East, suggesting a global phenomenon [2,12].

Beyond SQLE mutations, additional resistance mechanisms contribute to treatment failure. Upregulation of fungal efflux pumps decreases intracellular drug accumulation, while biofilm formation enhances persistence on keratinized surfaces and limits antifungal penetration [6]. These adaptations not only reduce fungicidal activity but also increase relapse rates after treatment cessation [20].

Resistance is not confined to terbinafine. Reduced susceptibility to azoles, including itraconazole and fluconazole, has been reported, often mediated by alterations in the lanosterol 14α-demethylase gene and efflux transporter activity [23]. While resistance prevalence varies regionally, its clinical impact is increasingly evident in recalcitrant cases unresponsive to standard dosing regimens [11].

The rise of antifungal resistance complicates empirical therapy and highlights the need for diagnostic confirmation and, where possible, antifungal susceptibility testing. However, such testing is not widely available, limiting its utility in routine practice [18]. In the absence of accessible laboratory support, clinicians often rely on clinical judgment, therapeutic trials, and the use of extended or combination regimens when resistance is suspected [21].

Steroid Misuse and Iatrogenic Factors

A major driver of the current dermatophytosis crisis is the widespread misuse of topical corticosteroid–antifungal combinations. In South Asia, over-the-counter fixed-dose creams containing potent steroids are frequently used without medical supervision, often promoted for rapid symptom relief [17]. While these products temporarily reduce erythema and pruritus, they suppress local immunity, alter clinical morphology, and allow fungi to persist in deeper keratinized layers [4]. This results in atypical presentations, collectively termed “tinea incognito,” which are easily misdiagnosed and challenging to treat [16].

Inappropriate self-medication and incomplete adherence to prescribed courses further exacerbate chronicity and relapse [3]. Shortened treatment duration, dose skipping, and premature discontinuation reduce drug exposure, favoring survival of resistant subpopulations [21]. Additionally, polypharmacy and irrational prescribing practices—particularly in settings lacking dermatology specialists—can increase drug–drug interactions and further compromise efficacy [6].

10.48047/jocaaa.2024.33.06.137

Together, these iatrogenic factors accelerate the emergence of resistant dermatophyte strains, complicate diagnosis, and undermine the effectiveness of otherwise potent antifungal therapies [18].

Clinical Diagnosis and Challenges

Accurate diagnosis of dermatophytosis is crucial in an era of rising resistance and atypical clinical presentations. Conventional tools remain widely used, with direct potassium hydroxide (KOH) microscopy serving as the most rapid and inexpensive bedside test [7]. While highly specific when positive, its sensitivity is operator-dependent and declines in chronic or steroid-modified lesions [16]. Fungal culture, though considered the gold standard for species identification, requires several weeks for results, limiting its utility in urgent clinical decision-making [18].

Adjunctive techniques provide added diagnostic support. Dermoscopy can reveal perifollicular scaling, hair shaft involvement, and active advancing borders, features particularly helpful in tinea capitis and tinea incognito [8]. Histopathology with periodic acid–Schiff (PAS) staining is useful for atypical cases mimicking psoriasis or eczema, and for biopsy-confirmed steroid-modified disease [4]. Molecular assays, including polymerase chain reaction (PCR) and sequencing, provide rapid and accurate species-level identification [12]. Matrix-assisted laser desorption/ionization–time of flight (MALDI-TOF) mass spectrometry is another promising tool, enabling precise differentiation of *Trichophyton* species with high accuracy [23]. These methods are especially valuable in epidemiological surveillance and in recalcitrant cases where species identification and resistance profiling influence therapeutic strategy [2].

Despite these advances, access remains limited in resource-constrained regions where dermatophytosis is most prevalent. Point-of-care assays and simplified PCR platforms may bridge this gap, but widespread implementation requires cost reduction, infrastructure support, and training. Until then, clinicians must rely on a tiered approach: integrating bedside tests, culture where feasible, and advanced molecular diagnostics in persistent or atypical disease [18].

Management Challenges

The management of dermatophytosis has become increasingly complex due to therapeutic failures, frequent relapses, and limited evidence-based guidance for resistant cases. First-line systemic agents such as terbinafine and itraconazole, once considered highly reliable, now demonstrate reduced cure rates in regions with documented resistance [5,11]. Pharmacokinetic variability, particularly with itraconazole, can lead to subtherapeutic drug levels and inconsistent responses [6]. In many cases, patients report only partial improvement, followed by rapid recurrence after discontinuation [3].

Guidelines are largely based on older data derived from uncomplicated infections, providing limited direction for recalcitrant or widespread disease [18]. Extended treatment courses and higher dosing have been employed, but these strategies increase the risk of hepatotoxicity, gastrointestinal

10.48047/jocaaa.2024.33.06.137

intolerance, and poor adherence [20]. Combination regimens, though supported by small clinical studies, are not standardized and carry the added concern of drug–drug interactions [21].

Cost and accessibility present further challenges. In low- and middle-income regions, newer antifungal agents and molecular diagnostics are often unaffordable, forcing reliance on prolonged use of older drugs with diminishing effectiveness [12]. Patient adherence is another critical factor; lengthy courses, lack of immediate symptomatic relief, and economic barriers contribute to premature discontinuation, fueling relapse cycles [17].

The cumulative effect of these challenges is a widening treatment gap in which clinicians must balance efficacy, safety, affordability, and compliance while facing limited therapeutic innovations that are ready for routine use [18].

A. Novel and Adjunctive Management Approaches

In response to the rising burden of therapeutic failure, several novel and adjunctive strategies have been explored. Super-bioavailable itraconazole has been developed to overcome variable absorption and gastric pH dependency, providing more predictable systemic exposure and higher keratin affinity compared to conventional formulations [10]. This innovation addresses one of the main limitations of itraconazole in routine practice and offers a reliable option in resistant or relapsing cases.

Newer triazoles, including posaconazole and fosravuconazole, extend the therapeutic spectrum and have demonstrated favorable in vitro activity against resistant *Trichophyton* isolates [12]. While clinical use remains limited by cost and availability, they represent promising alternatives for refractory disease. Topical and nanocarrier-based amphotericin B formulations have also shown encouraging preliminary results, enabling localized fungicidal activity with reduced systemic toxicity [15].

Adjunctive keratolytic strategies play a supportive role by reducing fungal load in hyperkeratotic skin. Salicylic acid and trichloroacetic acid chemical peels enhance drug penetration and have been reported to accelerate clearance when combined with antifungals [13]. Similarly, photodynamic therapy, utilizing photosensitizers activated by specific wavelengths of light, has shown efficacy in recalcitrant cutaneous and nail infections [14].

Host-directed measures are also gaining attention. Zinc supplementation and vitamin D optimization have been linked to improved cutaneous immunity, while probiotics are under investigation for their potential role in modulating the skin and gut microbiome [16]. Though evidence remains preliminary, these interventions may reduce relapse rates and serve as useful adjuncts in comprehensive management strategies.

Collectively, these emerging modalities emphasize the need for an integrated, multipronged approach that goes beyond conventional drug therapy, targeting both pathogen clearance and host resilience [18-20].

10.48047/jocaaa.2024.33.06.137

Conclusion

Dermatophytosis has transitioned from a largely benign superficial infection to a complex global health challenge marked by changing epidemiology, antifungal resistance, and frequent therapeutic failures. Misuse of topical steroid–antifungal combinations, host vulnerabilities, and environmental conditions amplify this problem, while diagnostic delays and limited access to advanced laboratory tools further complicate management.

Although terbinafine and itraconazole remain therapeutic mainstays, rising resistance and pharmacokinetic limitations necessitate refined dosing strategies, extended courses, and in selected cases, combination therapy. Novel approaches, including super-bioavailable itraconazole, newer triazoles, adjunctive keratolytics, photodynamic therapy, and host-directed interventions, offer promise but require further validation through large-scale trials.

Sustainable progress depends on antifungal stewardship, stricter regulation of steroid misuse, improved diagnostic access, and region-specific resistance surveillance. A multifaceted strategy integrating pathogen control, host optimization, and healthcare policy reform will be essential to achieving durable outcomes and reducing the burden of recalcitrant dermatophytosis.

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