EDITORIAL

Dermatophyte Treatment Failure: A Rapid Global Response to an Emerging Global Health Issue

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Dermatomycoses, or fungal infections of the skin, hair, and nails, affect nearly a billion people worldwide, especially in countries with a low sociodemographic index (SDI) and amongst vulnerable populations such as young children (1). Rising global rates of dermatophytosis impose a considerable burden on dermatology and primary care facilities worldwide, particularly on the Indian subcontinent. These infections, often perceived as minor, can severely impact quality of life, causing discomfort, social embarrassment, and contributing to poor sleep (2).

Superficial fungal skin infections are typically treated with topical or oral antifungals. In recent years, however, we have seen rising trends of increasing treatment failure, leading to recurrent and recalcitrant infections (3). Factors such as poor medication compliance, misuse of over-the-counter treatments, and variability in antifungal drug quality contribute to suboptimal treatment response. However, the most concerning cause of inadequate treatment response is the increasing number of dermatophyte strains demonstrating clinical and mycological resistance to widely used antifungal agents such as terbinafine (4). This makes treatment increasingly challenging and necessitates robust data collection and global awareness to tackle this growing problem effectively.

Dermatophyte treatment failure was initially reported to be an "epidemic"-like scenario by colleagues in India. The "epidemic" is no longer confined to India; recent reports indicate local transmission in North America, Germany, and South Africa. Earlier cases in regions like the Middle East, Europe, and Canada were mostly linked to travel or migration from high-risk areas such as India and Bangladesh (5, 6). However, recent findings suggest that *T. indotineae* may have been circulating in other countries undetected, necessitating a revaluation of its global spread and impact. The report in this issue from Sweden emphasizes the need for urgent assessment (7).

The earliest reports of dermatophyte resistance date back to the 1960s, but it was considered rare until recent years (8). Now, a sharp increase in cases of recalcitrant and recurrent dermatophyte infections is evident in numerous international publications.

In a recently published international survey, 91.7% of 260 dermatologists across 36 countries, outside of Europe, reported seeing cases of recurrent and recalcitrant dermatophyte infections in the preceding 3 years. Clinical features reported by respondents were consistent across regions, with the trunk and groin being the most commonly affected areas. The misuse of over-the-counter antifungal and potent steroid combinations is a significant contributing factor, particularly in India. Moreover, high rates of previous oral itraconazole usage were noted, with some regions reporting greater use of itraconazole than terbinafine, underscoring the pressing need for alternative therapeutic strategies (5).

The growing challenge of treating these infections has coincided with the emergence of *T. indotineae*, a newly identified species associated with high rates of antifungal resistance to terbinafine. *T. indotineae*, indistinguishable from *T. mentagrophytes* without molecular identification, is reported by some authors as the predominant species in India, often associated with terbinafine resistance (3, 4). This highlights the necessity for enhanced diagnostic capabilities and standardized methods for identifying and monitoring resistant strains.

T. indotineae is part of the *T. mentagrophytes* complex (genotype VIII) and is primarily transmitted through human-to-human contact. Identifying this organism is challenging, as it closely resembles other species in the complex and requires sequence-based identification. These investigations are expensive and available only at specialist centres. Additional challenges exist when trying to establish antifungal resistance. At present, there is no consensus agreement on breakpoints and epidemiological cut-off values for *T. indotineae* against common antifungals. Furthermore, many isolates are resistant to terbinafine, complicating management and necessitating alternative therapies like oral itraconazole, often at higher doses for extended periods. The emergence of azole resistance further complicates treatment regimens.

To address these challenges, international collaboration and surveillance are crucial. Diagnostic laboratories need to refer suspected cases to reference laboratories for precise identification and susceptibility testing. Additionally, comprehensive treatment guidelines and multidisciplinary patient care approaches are essential to manage extensive, drug-resistant dermatophytosis effectively. Organizations and departments must also promote local anti-fungal stewardship initiatives. Monitoring antifungal resistance at the population level through international surveillance programmes is also vital to understanding and combating this growing public health concern.

In response to this urgent need for a global disease registry and standardized data collection on treatment failure dermatophytosis, the American Academy of Dermatology (AAD) and the International League of Dermatological Societies (ILDS) have created an online international disease registry for cases of treatment failure dermatophytosis (www.aad.org/tinearegistry).

A concerted global effort and collaboration are essential to better understand and combat the emerging global threat of dermatophyte resistance.

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