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Original Article

Defining 'difficult dermatophytosis' beyond chronic/ recurrent forms: A clinico-etiological analysis from a teaching hospital in Northern India

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Abstract

Objective We aimed to study and define "difficult dermatophytosis" encountered frequently; as well as examine demography, patient practices and clinico-etiological pattern among these patients.

Methods A prospective, cross-sectional study was conducted to include 93(n) cases (after informed consent) from the patients attending the outpatient department in the Department of Dermatology, Venereology and Leprology between August 2019 and August 2020. The inclusion criteria were: - age >12 years and fulfilling one or more criteria defining "difficult dermatophytosis' i.e. multiple/ large lesions, multifocal, recurrent therapy, multiple relapses, clustering and chronicity. The clinico-demographic data was recorded in a pre-designed pro forma, a KOH examination for skin scraping and fungal culture was done for all cases. Data was analysed with SPSS version 20.

Results Males outnumbered females (M: F =1.2:1) and majority (67.8%) of patients were <40 years (Mean=34.13±11.5; Median=31yrs.). Body Mass Index (BMI) was higher than 25 in 55.9% cases; mean BMI seen in the study was 25.17±4.60. Multiple/large lesion (90.3%) was most common inclusion criteria followed by multifocal lesions (84.9%). All patients had tinea cruris; tinea corporis was most commonly associated followed by tinea faciei lesions. A significant proportion (76.3%) of cases had ≥4 family members cohabiting with them (Mean=5.07±0.03); more than half (56.98%) had an affected family member (Mean=0.90±1.00). The most common co-morbid condition seen was atopy seen in 16 (17.2%) patients. Presentation for dermatology consult was delayed by >1 month in 81.7% cases; >6 months in 47.3% cases and >1 year in 26.9% cases. A strong statistical association was found of multiple relapses with 'delay in dermatology consults' (p value=0.002). A significant association of delay was also seen with chronicity (p value=0.046) was also seen. Nearly three-fourth study participants (72%) reported prior use of topical corticosteroid; oral (11.8%) and parental (20.4%) use were also reported. Prior use of luliconazole (40.8%) was most commonly reported among topical drugs, whereas itraconazole was used by 46% patients previously. Irrational use of anti-fungals was seen in 75%; including inappropriate doses (18%), inappropriate duration (34%), poly-pharmacy (6%) and non-compliance (1%). A statistically significant association of irrational use was found with multiple/large lesions (p value=0.008).

Conclusion We propose this definition for the unusual presentations of the disease, particularly in the Indian sub-continent. Better access to clinical dermatology services and rational use of systemic anti-fungals as a means to mitigate difficult dermatophytosis.

Key words
Dermatophytes; Trichiphyton; Epidemiology; Dermatophytosis.

Introduction

Dermatophytosis, has stealthily reached epidemic proportions in the last decade, with a remarkable resilient pattern and frequent replapses.[1] The terms "chronic" "recalcitrant" or "recurrent" dermatophytic infections have been the 'buzzwords' gaining considerable traction in dermatology circles. "Chronic dermatophytosis" has been defined as persistence of infection for

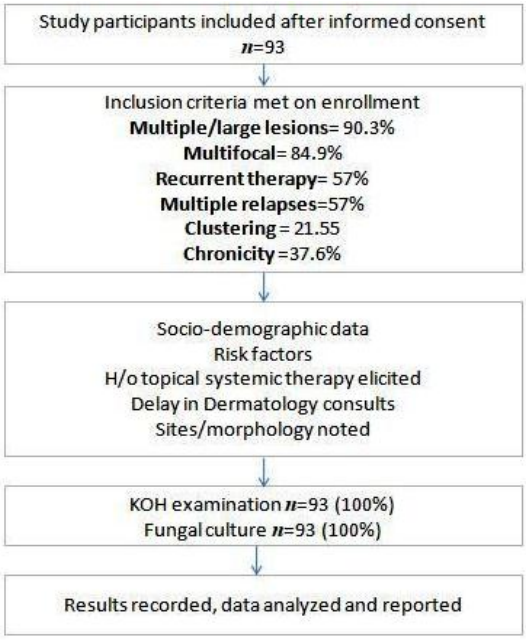

Figure 1 Flow diagram of study design

more than 1 year with several relapses or for a total duration of >1 year in spite of treatment.[2] Another proposed definition for is an infection lasting more than 6 months to 1 year despite regular treatment; on the other hand 'recurrent' type is referred to dermatophytosis that runs a protracted course with multiple exacerbations/ remissions.[1,3] Dogra *et al.* was the first prospective study to focus on 'recurrent' tinea (defined as an episode of relapse within 4 weeks of stopping treatment in the last 6 months) where Trichophyton mentagrophytes was identified as causative agent.[4] They concluded that the resistance or high MIC (Minimum inhibitory concentration) could not explain the disease, as most isolates were not resistant, a fact reported by other authors form North India.[4,5]

We propose here a definition for "difficult dermatophytosis" to include not just chronic or recurrent forms; but also extensive/ multifocal disease/ familial clustering presenting to dermatologist. We also examine socio-demographic factors, practices, previous therapy, disease pattern and aetiology among these patients.

Patients and Method

A prospective, cross-sectional study was conducted after appropriate ethical clearance to include ninety-three (n=93) consecutive patients with "difficult dermatophytosis" from patients attending the outpatient department of Dermatology, Venereology and Leprology between August 2019 and August 2020 (**Figure 1**). Patients ≥12 years with "difficult dermatophytosis" (excluding pregnant/lactating females) fulfilling one or more of six inclusion criterion were included (**Table1)**.

The demographic data, relevant history and examination were recorded in a pre-designed pro forma (**Figure 2**).

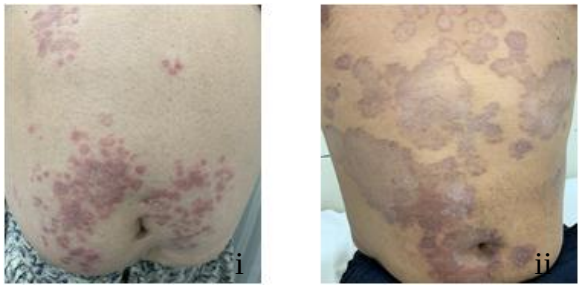

Figure 2 a Atypical clinical presentations (i) Psoriasis-like lesions (ii) Pityriasis rosea-like lesions.

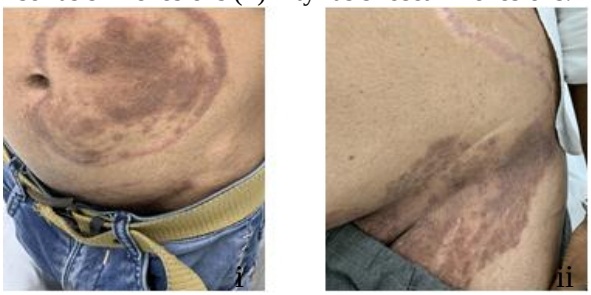

Figure 2 b Steroid-based creams resulting in dermatophytosis with:- (i) Pseudo-imbricate pattern of tinea corporis (ii) Pigmentation and atrophy of skin.

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Table 1 Inclusion criteria for 'difficult dermatophytosis' definitions used in the study.

1.	Multiple/ large lesions More than 4 lesions or a single lesion >10 cm in diameter.
2.	Multi-focal More than two anatomical sites involved: groin, buttock, thighs, axilla, inframammary fold, face, scalp/ hair, nails, abdomen/ back, pubo-genital.
3.	Recurrent therapy Received more than two courses of systemic antifungals in the last 3 months.
4.	Multiple relapses More than 3 recurrences in last one year.
5.	Clustering More than 2 family members affected.
6.	Chronicity Lesions persisting with/without treatment for more than 3 months.

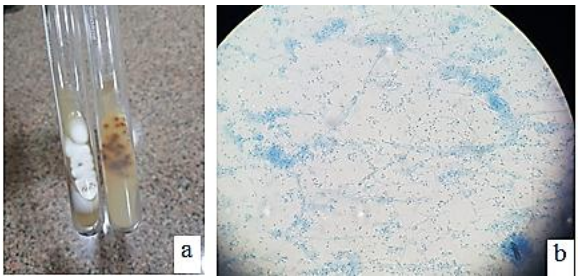

Figure 3 Co-existing conditions seen among study participants.

A skin scrapping was done with the blunt edge of a 23 No. blade; a portion of the skin scrapings was used for a KOH examination to look for fungal hyphae (10% KOH under light microscopy (400×)); remaining were sent for fungal culture **(Figure 3)**. Specimens were inoculated on four tubes of Sabaraud's dextrose agar (SDA) with and without cycloheximide and incubated at 25°C and 37°C. The SDA slants were examined for growth daily for first week and twice a week for subsequent period of 4 weeks. Fungal growth obtained was identified on the basis of colony morphology, rate of growth, colour, texture, pigmentation and findings on Lactophenol cotton blue (LCB) mount examination. The data was recorded in an Excel sheet and statistical analysis was done with SPSS version 20.

Results

Males outnumbered females (M:F=1.2:1) and majority (67.8%) of patients were < 40 years (Mean=34.13±11.5; Median=31yrs). Body Mass Index (BMI) was higher than 25 in 55.9% cases; mean BMI seen in the study was 25.17±4.60. Multiple/ large lesion (90.3%) was most common inclusion criteria followed by multifocal lesions (84.9%) (**Figure 1**).

Most (56.6%) had disease duration >1 year; of these cases a considerable number had disease for >2 years (20%). All patients had tinea cruris; tinea corporis was most commonly associated followed by tinea faciei lesions (**Table 2**).

Animal exposure

Thirty-nine percent (38.7%) cases reported regular animal contact; most common being cattle (20.4%), household pets (8.6%), poultry (1.1%) and pigs (1.1%). No statistically significant association was seen with any inclusion criteria (multiple large lesions (p value=0.73), multifocal (p value=0.77), recurrent therapy (p value=0.83), multiple relapses (p value=0.83), clustering (p value=0.70) and chronicity (p value=0.52).

Most patients (90.3%) reported regular daily bathing; clothe sharing was reported by 20.4% patients. Fifteen patients (16%) reported some physical activity in the form of gym/ swimming/ team sports/ athletics. Twelve patients (12.9%) had long duty hours (>10 hours). There was a statistically significant association seen with physical activity (p value=0.024).

Table 2 Clinical diagnosis and gender distribution seen in the study.

Clinical manifestation	*Cases seen n (%)*	*Sex n (%)*	
		Male	*Female*
Tinea corporis	87 (93%)	45 (48%)	42 (45%)
Tinea ungiuum	2 (2.2)	1 (1%)	1 (1%)
Tinea facei	33 (35%)	18 (19%)	15 (16%)
Tinea cruris	93 (100%)	47 (50%)	39 (42)

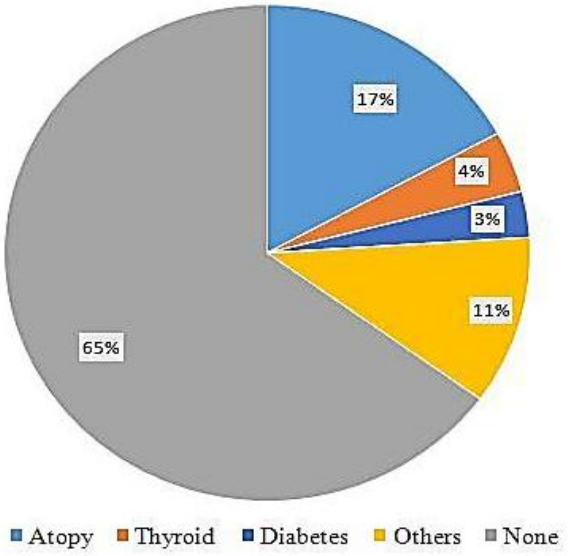

Figure 4 Co-existing conditions seen among study participants.

A significant proportion (76.3%) of cases had ≥4 family members cohabiting with them (Mean= 5.07±0.03); more than half (56.98%) had an affected family member (Mean=0.90±1.00). The most common co-morbid condition seen was atopy seen in 16 (17.2%) patients, however no statistically significantly association was seen with any of the inclusion criterion.

Other associated diseases seen in the study populations were hypothyroidism 4 (4.2%), hypertension 5 (5%), chronic liver disease 4 (4%), diabetes 3 (3%) and tuberculosis 2 (2%) (**Figure 4**).

Seventy-six (81.7%) cases presented to a dermatologist after >1 month of self-treatment/ treatment by non-specialist. Nearly half (47.3%) of the patients first consulted a dermatologist 6 months after the onset of lesions. A significant number 25(26.9%) had a delay of >1 year after disease onset.

A strong statistical association was found of multiple relapses with delay in dermatology consults (p value=0.002). A significant association of delay was also seen with chronicity (p value=0.046) was also seen. However, no statistical significant association of delay in specialist care with multiple large lesions (p value=0.4120), multifocal (p value=0.716), recurrent therapy (0.082), clustering (0.652) was found.

A significant number of patients (35.5%) had previously taken alternative medical systems (Homeopathy/ Ayurveda/ others) before moving to allopathic treatment; however, no significant association seen (multiple large lesions p value=1.00), multifocal (p value=0.364), recurrent therapy (p value=0.51), multiple relapses (p value=0.66), clustering (p value=0.30) and chronicity (p value=0.50) (**Figure 5**).

Nearly three-fourth study participants (72%) reported prior use of topical corticosteroid (TCS) either alone or in combination with antibiotics/ anti-fungals; while some even took oral or parental steroids (**Figure 5)**. Half of the study participants 47 (50.5%) had used over-the-counter (OTC) topical formulation (antifungal-steroid or TCS) in combinations with oral steroids

No significant associations were seen with steroid use with inclusion criteria (multiple large lesions (p value=0.68), multifocal (p value=0.72), recurrent therapy (p value=1.00), multiple relapses (p value=0.79), clustering (p value=0.54) and chronicity (p value=0.60).

We could elicit a history of topical anti-fungal use in 64.5% study participants; luliconazole cream was the most commonly used followed by terbinafine and (**Figure 6**). Concurrent or consecutive use of ≥2 anti-fungal creams was reported by 11 (8%) patients. Topical anti-fungals use was denied by 31 (33.5%) while nature of topical drug was not known in 25 (26.9%) patients.

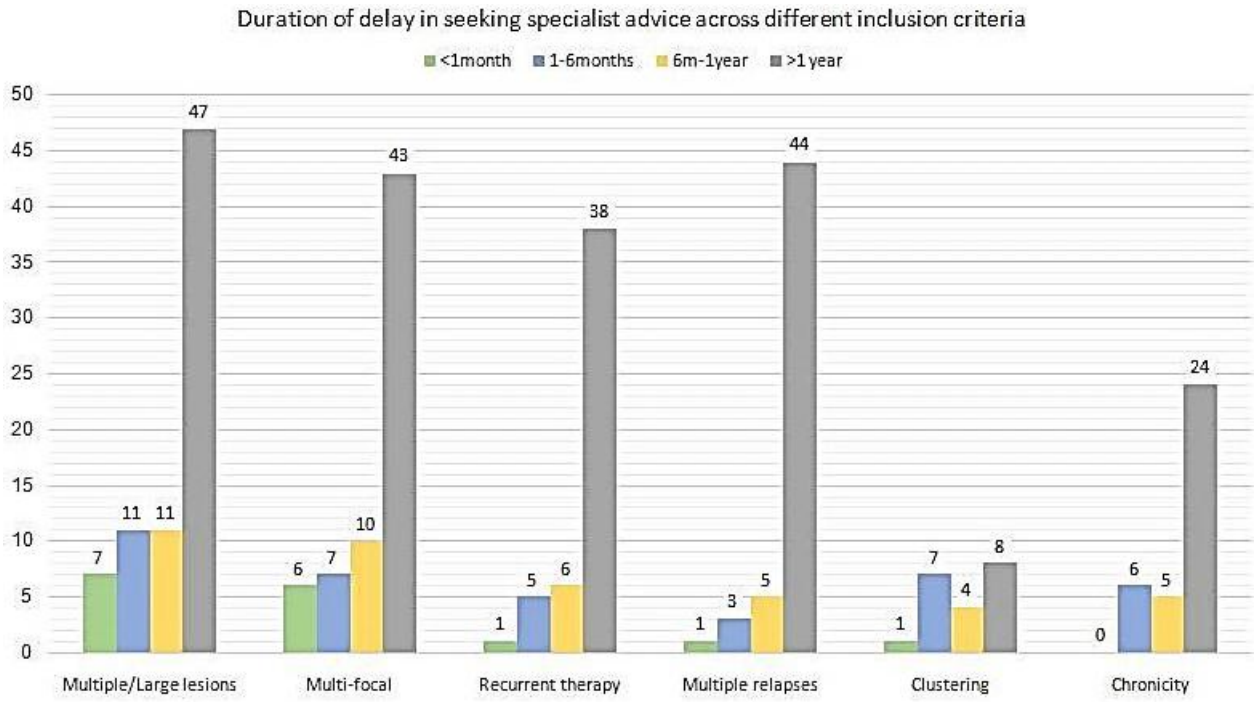

Figure 5 Duration of delay in seeking specialist advice across different inclusion criteria.

Twenty four patients (25%) reported topical application for ≥1 month while two (2.2%) of had used them >1 year at presentation. Twenty-three patients (24.7%) could not recall the duration of anti-fungal use

Seventy-one (76.3%) patients had previously received oral antifungals, the most commonly prescribed anti-fungal was itraconazole followed by fluconazole, terbinafine and griseofulvin (**Figure 5**). Twenty-eight (30.4%) patients gave history of intake of ≥2 oral antifungals. The nature of oral medication was unknown in 14 (17.5%) patients.

The patients' treatment history was assessed and only 25% patients had rational use of systemic anti-fungals (**Figure 7**). Of these 75%, the reason for irrational use were inappropriate doses (18%), inappropriate duration (34%), poly-pharmacy (6%) and non-compliance (1%). The only statistically significant association of irrational use was found with multiple/ large lesions (p value=0.008). (Multifocal (p value=0.343), recurrent therapy (p value=0.634), multiple relapses (p value=1.00), clustering (p value=0.578) and chronicity (p value= 0.634)).

Fungal hyphae could be identified on KOH examination in 74% patients while it was negative in 26% patients. A statistically significant association of positive KOH mount with multiple large lesions (p value=0.04600) and multifocal (p value=0.043) disease was seen. (Recurrent therapy (p value=0.226), multiple relapses (p value=0.527), clustering (p value=0.926) and chronicity (p value=0.636). Out of the 93 patients growth on SDA was obtained in 56 cases, all were identified as Trichophyton rubrum.

Discussion

The patients with dermatophytosis seen in dermatology tertiary care centres represent just the tip of the iceberg; a vast majority continues to be treated by non-specialist and unfortunately at times by non-doctors. Though, attempts have

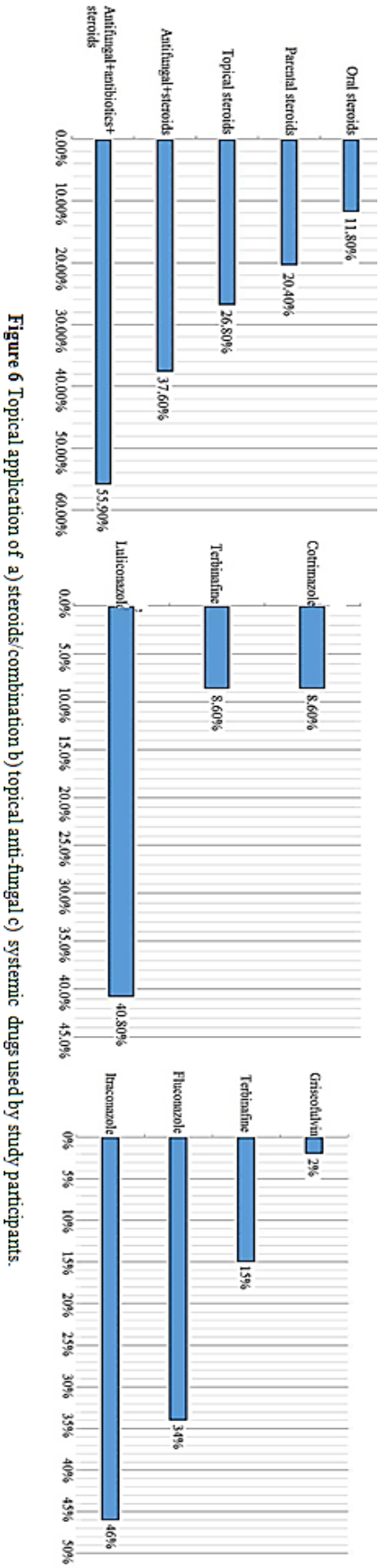

Figure 6 Topical application of a) steroids/combination b) topical anti-fungal c) systemic drugs used by study participants.

been made to categorise the disease as recurrent/ chronic; many patients seen in dermatology clinics that may not fall in these categories, yet have an unusual or atypical presentation.[6] Various authors have reported a prevalence of recurrent dermatophytosis among all patients of dermatophytosis ranging from 9.3 to 65.3% in Indian patients.[7,8]

We found most study participants were <40 years (mean=34.13±11.5); this concurs with findings reported previously, possible attributable to more active lifestyle and therefore more risk of exposure to infection.[9,10] A slight male preponderance; many authors have reported no gender predilection/ slight predilection for the male gender.[11] Anatomical differences, active lifestyles and different sickness behaviour predispose men to so called 'jock itch'.[12-14]

Previous recommendations advising antifungal-steroid combination to tide over the inflammation and provide rapid relief continue to be followed by some general physicians.[15,16] Patients also self-medicate with topical steroid based creams, 72% cases in this study had used topical steroids alone or in combination. This makes it harder for dermatologists to treat the infections when these patients present.[11] Delay in Dermatology consults had a statistically significant association with multiple relapses as well as chronicity. The authors wish to stress upon early intervention by a qualified dermatologist; however this may be easier said than done.

The national body of dermatologists in India has a membership of ~12,000 doctors, when divided with the population of over 1.32 billion is grossly inadequate.[17] Also, urban clustering as well as retired or semi-retired members further add to the scarcity.[17] In the USA, almost 500 dermatologists enter the workforce each year;

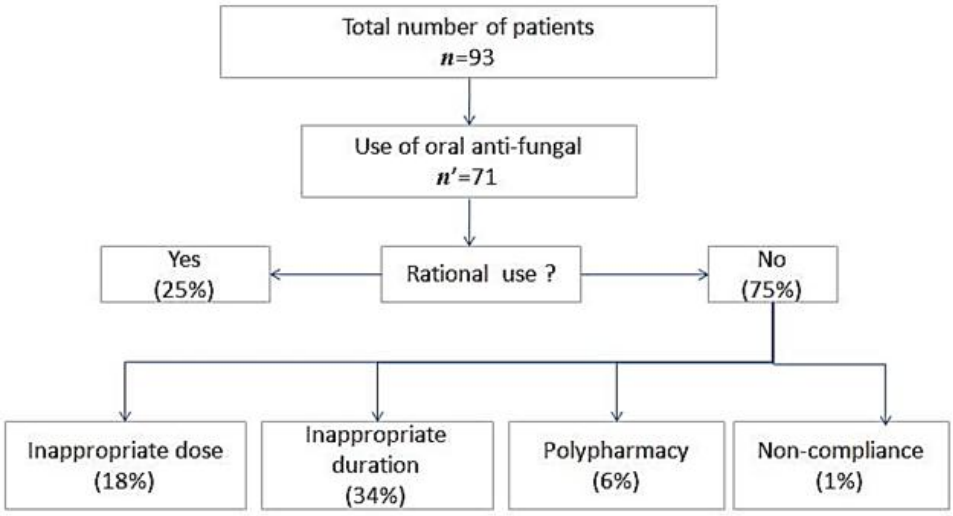

Figure 7 Flow diagram showing systemic anti-fungals use among study participants.

and with an estimated 9,600 dermatologists spread over a significantly smaller population (approximately 320 million) leads to a far better specialist ratio compared to India.[18]

T.rubrum was the most frequent fungal isolate; this concurs with findings by similar Indian studies.[19] T.mentagrophytes has been also been increasingly reported by various authors in recent studies.[20,21]

We found irrational use of systemic anti-fungals in 75% cases; there was a significant association with multiple large lesions. Rampant and at times reckless use by unqualified healthcare providers as well as unregulated availability of Schedule-H drugs should be checked by robust legislation. Non-dermatologists at times even prescribe reserve drugs like voriconazole/ posconazole for treating recalcitrant tinea, which are potentially life-saving drugs for other indications.[1,22]

Government should incentivise to encourage and increase dermatology services and training in underserved areas. A good clinical dermatologist is an asset for the community and better career opportunities and adequate compensation will encourage trainees to practice clinical dermatology rather than a cosmetology oriented practice.

In conclusion, we propose better access to dermatology services and rational use of systemic anti-fungals as a means to mitigate the increase in difficult dermatophytosis.

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