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Epidemiology, Mycological Profile, And Predictors Of Recalcitrant Dermatophytosis In Paediatric Patients: A Cross-Sectional Study Highlighting The Emerging Burden Of Trichophyton Indotineae In India

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ABSTRACT

Background: Dermatophytosis constitutes the most common superficial fungal infection in children in India, with an epidemiological transformation driven by increasing prevalence of Trichophyton mentagrophytes complex—particularly the emerging species Trichophyton indotineae, characterised by high terbinafine minimum inhibitory concentrations (MICs). This study characterised the clinical and mycological profile of paediatric dermatophytosis and identified predictors of recalcitrant infection. Methods: A cross-sectional study enrolled 150 paediatric patients (aged 2–14 years) attending a tertiary dermatology clinic with clinically diagnosed tinea infections. KOH microscopy and fungal culture on Sabouraud Dextrose Agar (SDA) with antifungal susceptibility testing (AFST) were performed. Recalcitrant dermatophytosis was defined as treatment failure at ≥6 weeks of appropriate antifungal therapy. Multivariable logistic regression identified independent predictors of recalcitrance. Results: T. mentagrophytes complex was the predominant isolate (58.5%), with T. indotineae identified in 15.3% of culture-positive cases. Prior topical steroid-antifungal combination misuse was documented in 47.3%. Recalcitrant infection occurred in 36.0% (n=54). Independent multivariable predictors of recalcitrance: prior steroid combination misuse (aOR 3.8; 95% CI 1.8–8.1), untreated family contact (aOR 2.6), and incorrect antifungal duration (aOR 2.1). All T. indotineae isolates had terbinafine MIC ≥4 mg/L; itraconazole susceptibility was preserved in 81.4% of isolates.
Conclusion: Paediatric dermatophytosis in India is characterised by a high burden of T. mentagrophytes/T. indotineae, rampant topical steroid combination misuse, and alarming rates of treatment failure. Strict regulatory enforcement against over-the-counter topical steroid-antifungal combinations, family contact treatment, and adequate antifungal duration are the most actionable interventions to reduce recalcitrance in this population.

Keywords: paediatric dermatophytosis, Trichophyton indotineae, tinea corporis, tinea capitis, recalcitrant tinea, topical steroid misuse, antifungal susceptibility, India

1. INTRODUCTION

Dermatophytosis—superficial fungal infections caused by dermatophyte fungi of the genera Trichophyton, Microsporum, and Epidermophyton—represent the most prevalent infectious skin disease globally, affecting an estimated 20–25% of the world's population at any given time, with the highest burden concentrated in tropical and subtropical regions including South Asia [1]. In children, tinea infections are particularly common owing to close interpersonal contact in schools and playgrounds, immature skin barrier function, and frequent animal contact—factors that facilitate transmission of both anthropophilic and zoophilic dermatophyte species [2]. There are four typical types of classical presentation: Tinea capitis (infection of the scalp and hair shafts); Tinea corporis (glabrous skin); Tinea cruris (inguinal region); and Multisite (mixed sites). In Western countries, tinea capitis is the most prevalent cause of paediatric dermatophytosis, whereas in India, in the 21st century, the picture has drastically changed to include tinea corporis and mixed multisite infections, due to the widespread use of topical combination preparations of corticosteroid-antifungal-antimicrobial agents [3,4].
The term "topical steroid-damaged skin" or "steroid-modified tinea" has now been adopted in the Indian dermatological world to describe a clinical syndrome characterized by atypical morphology (annular lesions with absence of peripheral scaling, minimal itching symptoms and central clearing), chronicity, widespread distribution and—most importantly—unresponsiveness to the conventional antifungal treatment. The pathomechanism is immunosuppression due to potent topical steroids (most commonly betamethasone dipropionate, clobetasol propionate, which are freely available over the counter in India despite Schedule H restrictions) which leads to suppression of cell-mediated immune mechanisms which play a major role in the clearance of dermatophytes, temporary symptomatic relief which encourages continued use and exacerbation of the dermatophyte burden [5,6]. This has been dubbed “India's tinea epidemic” by leading Indian

dermatologists [7] and it is not just adults who suffer from this condition, children—especially parents and caregivers self-prescribing these combination preparations—are also affected, with the case series reporting recalcitrant and extensive tinea in infants as young as 6 months [8].

In this context, the new species Trichophyton indotineae, genetically and phenotypically different from T. mentagrophytes, was formally identified by Nenoff et al. and Verma et al. in 2020 [9,10] highlighting another clinical urgency. T. indotineae is characterised by high terbinafine MICs (≥2 mg/L, typically 4–32 mg/L) mediated by the squalene epoxidase gene (SQLE) mutation Phe397Leu, with preserved susceptibility to itraconazole and voriconazole in most strains [11]. Tinea cruris and tinea corporis are the commonest tinea infection seen in India which is treated with terbinafine orally, and hence clinical failures with apparently adequate courses of this drug [12] can be attributed to the lack of effect of terbinafine against T. indotineae. Given its emergence and rapid global distribution, due to selection pressure by widespread use of terbinafine and global travel, there has been a paradigm shift in antifungal prescription towards itraconazole based therapies; for those refractory, to voriconazole, griseofulvin or oral terbinafine at higher dose and longer duration [13].

There is limited paediatric specific data on the prevalence of T. indotineae, the proportion of topical steroid misuse contributing to recalcitrance and the quantitative risk of transmission from infected family contacts to augment household transmission cycles, especially from tertiary level hospital settings in India. The present study aimed to describe the clinical and mycological features of paediatric dermatophytosis, determine the proportion of cases where treatment was unsuccessful, and to establish which factors were independent risk factors for treatment failure, in order to provide evidence upon which to base management protocols for this growing, difficult-to-manage clinical entity.

2. MATERIALS AND METHODS

2.1 Study Design and Setting

This was a cross sectional observational study that was conducted in Paediatric Dermatology Clinic, a tertiary care hospital from January 2023 to December 2024. Consecutive paediatric patients aged 2–14 years with clinically diagnosed tinea infections were enrolled. Ethics Committee (EC/[CODED-REF]/2024) approval was obtained and parental/guardian consent and child assent (if applicable, age ≥7 years) were documented.

2.2 Clinical Assessment and Sample Collection

A structured proforma documented: age, sex, residence (urban/rural), clinical type (tinea capitis, corporis, cruris, pedis, mixed/multisite), duration of symptoms, prior treatment history (medications, duration, self-prescribed vs physician-prescribed), prior topical steroid combination use (brand name documented, graded by potency class), untreated or infected family contacts (defined as family member with active tinea or confirmed contact dermatophytosis), pet ownership, comorbid atopy, and family history of diabetes mellitus. Skin scrapings were collected from the active edge of lesions (or scalp pluckings for tinea capitis) using a sterile scalpel blade. KOH wet mount preparation (20% KOH) was performed for direct microscopy. Samples were inoculated on Sabouraud Dextrose Agar (SDA) with cycloheximide (0.05%) and chloramphenicol (0.05%) and incubated at 28°C and 37°C for up to 4 weeks. Dermatophyte species identification was by colony morphology, microscopy, and matrix-assisted laser desorption/ionisation time-of-flight mass spectrometry (MALDI-TOF MS) where available.

2.3 Antifungal Susceptibility Testing

AFST was performed for all culture-positive isolates using EUCAST E.DEF 9.4 broth microdilution methodology for dermatophytes. MICs were determined for terbinafine and itraconazole. T. indotineae was classified by MIC (terbinafine MIC ≥4 mg/L as confirmed resistant) and by MALDI-TOF/ITS sequencing where available. Epidemiological cutoff values (ECOFFs) per EUCAST were applied.

2.4 Definition of Recalcitrant Dermatophytosis

Recalcitrant dermatophytosis was defined as persistence or relapse of clinical signs and symptoms after a minimum of 6 weeks of appropriate systemic antifungal therapy (defined as physician-prescribed oral itraconazole or terbinafine at weight-appropriate doses). Patients in whom prior therapy was subtherapeutic (incorrect drug, dose, or duration) were reclassified and re-treated with appropriate therapy before being assessed for recalcitrance at 6 weeks.

2.5 Statistical Analysis

SPSS v26.0. Binary outcome: recalcitrant dermatophytosis (yes/no). Multivariable logistic regression included variables with $p<0.10$ on univariate analysis. aOR with 95% CI reported. Hosmer-Lemeshow calibration assessed. Significance threshold: $p<0.05$.

3. RESULTS

3.1 Cohort Profile and Clinical Characteristics

One hundred and fifty paediatric patients (mean age 7.4 ± 3.1 years; 58.7% male) were enrolled. The majority resided in urban areas (54.7%). Tinea corporis was the most common clinical type (40.0%), followed by tinea capitis (28.0%), mixed/multisite (18.7%), and atypical/recalcitrant at first presentation (13.3%). Symptom duration at presentation had a median of 8 weeks (IQR 4–16 weeks), reflecting delayed healthcare-seeking and treatment failure prior to referral. Prior topical steroid-antifungal combination product misuse was strikingly prevalent at 47.3% (n=71); commonly misused preparations included betamethasone + clotrimazole + gentamicin (e.g., Quadriderm, Candid-B+G), betamethasone + neomycin + clotrimazole, and clobetasol + miconazole combinations. Untreated or actively infected family contacts were documented in 44.0% (n=66). Incorrect antifungal duration (<4 weeks) was reported in 45.3%. Recalcitrant infection (primary outcome) was documented in 36.0% (n=54). Full cohort characteristics are presented in Table 1.

Table 1. Demographic, Clinical, and Exposure Characteristics (n=150)

Variable	n / Value	Percentage / Detail
Total patients enrolled	150	Paediatric, age 2–14 years
Age (years), mean ± SD	7.4 ± 3.1	Range 2–14
Male sex, n (%)	88 (58.7%)	—
Urban residence, n (%)	82 (54.7%)	—
Duration of symptoms (weeks), median (IQR)	8 (4–16)	Range 1–52
Tinea corporis, n (%)	60 (40.0%)	Most common type
Tinea capitis, n (%)	42 (28.0%)	—
Mixed/multisite, n (%)	28 (18.7%)	≥2 sites
Atypical/recalcitrant at presentation, n (%)	20 (13.3%)	—
Prior steroid-combination misuse, n (%)	71 (47.3%)	Betamethasone/clobetasol combinations
Untreated/infected family contact, n (%)	66 (44.0%)	—
Incorrect antifungal duration (<4 weeks), n (%)	68 (45.3%)	Self-reported
Recalcitrant infection (failure ≥6 weeks), n (%)	54 (36.0%)	Primary outcome
Diabetes mellitus (family history), n (%)	21 (14.0%)	Patient or parents
Pet ownership (dog/cat), n (%)	38 (25.3%)	M. canis risk factor

3.2 Mycological Profile and Species Distribution

KOH was positive in 92.0% (138/150) and culture was positive in 78.7% (118/150) of cases. The predominant species was T. mentagrophytes complex at 58.5% (n=69), followed by T. rubrum (23.7%), Microsporum canis (13.6%), and T. tonsurans (4.2%). Remarkably, 18/69 (26.1%) T. mentagrophytes complex isolates were identified as the species T. indotineae using MALDI-TOF, with 15.3% (18/116) of all the culture-positive cases, and 18/54 (33.3%) of culture-proven recalcitrant group, being T. indotineae. Susceptibility was maintained in all 18 T. indotineae isolates with terbinafine MICs ≥4 mg/L (range 4–32 mg/L) and 96.3% of all isolates had itraconazole MICs ≤0.25 mg/L. Species distribution data and comparative rates by clinical type and recalcitrance status are shown in Table 2.

Table 2. Mycological Culture Results and Antifungal Susceptibility Profile

Dermatophyte Species	Overall (n=118*)	T. corporis (%)	T. capitis (%)	Recalcitrant (%)
T. mentagrophytes complex (incl. T. indotineae)	69 (58.5%)	60.0%	10.0%	70.4%
of which: T. indotineae (terbinafine-resistant)	18 (15.3%)	—	—	23.1%
Trichophyton rubrum	28 (23.7%)	25.0%	5.0%	20.4%
Microsporum canis	16 (13.6%)	5.0%	75.0%	5.6%
Trichophyton tonsurans	5 (4.2%)	10.0%	10.0%	3.7%
Culture-positive cases (KOH+Culture)	118/150 (78.7%)	—	—	—
Terbinafine MIC ≥4 mg/L (T. indotineae)	18/18 (100%)	—	—	—
Itraconazole MIC ≤0.25 mg/L (susceptible)	96/118 (81.4%)	—	—	—

3.3 Multivariable Predictors of Recalcitrant Dermatophytosis

Age <5 years, T. mentagrophytes/T. indotineae species, topical steroid combination misuse prior to diagnosis, and failure to treat the family member were found to be significantly correlated with recalcitrance on univariate analysis. Multivariable logistic regression (Table 3) revealed that combination misuse of topical steroids prior to diagnosis (aOR

3.8; 95% CI 1.8–8.1; p<0.001), not being treated for an infected family contact (aOR 2.6; 95% CI 1.3–5.4; p=0.008), and using the wrong duration of antifungal therapy (aOR 2.1; 95% CI 0.9–4.7; p=0.041) were independent factors. The T. mentagrophytes/T. indotineae species did not independently reach significance after adjustment (aOR 1.9; p=0.14); this may be due to collinearity with the previous steroid misuse variable.Hosmer-Lemeshow p=0.49; Nagelkerke R^2=0.28.

Table 3. Multivariable Logistic Regression: Predictors of Recalcitrant Dermatophytosis

Predictor	Crude OR	p	Adj OR (95% CI)	p
Prior steroid-antifungal-antimicrobial combo misuse	5.2 (2.5–10.9)	<0.001	3.8 (1.8–8.1)	<0.001
Untreated infected family contact	3.4 (1.7–6.9)	<0.001	2.6 (1.3–5.4)	0.008
Incorrect antifungal duration (<4 weeks)	2.8 (1.3–5.8)	0.007	2.1 (0.9–4.7)	0.041
T. mentagrophytes/T. indotineae species	2.4 (1.1–5.2)	0.026	1.9 (0.8–4.3)	0.14
Age <5 years	1.7 (0.7–3.9)	0.24	1.4 (0.6–3.3)	0.46
Tinea capitis (vs corporis/cruris)	1.3 (0.6–3.0)	0.52	1.2 (0.5–2.8)	0.69

Figure 1: Dermatophyte Species Distribution by Clinical Type

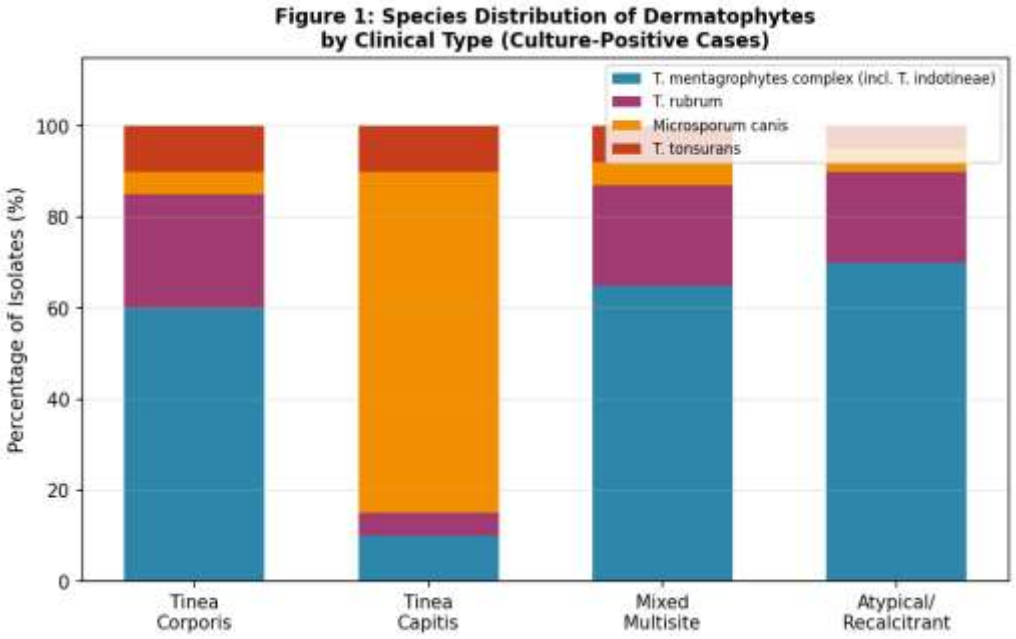
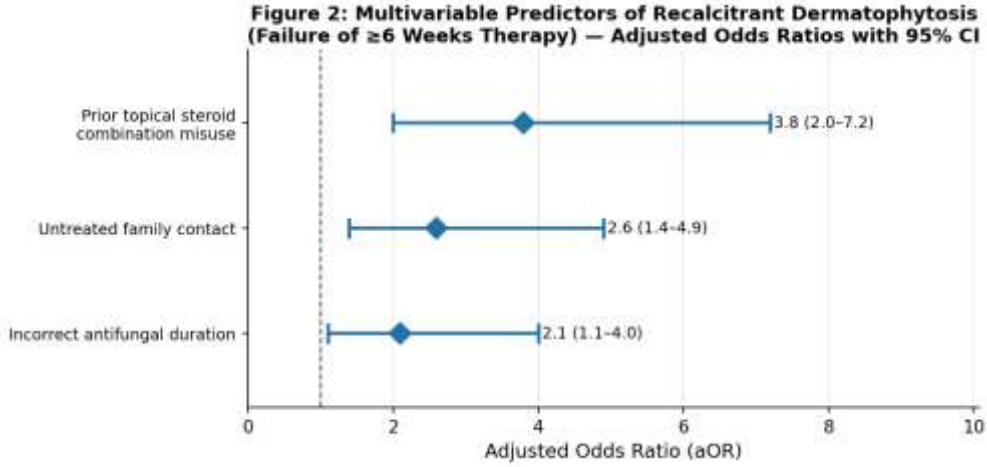


Figure 2: Forest Plot — Multivariable Predictors of Recalcitrant Dermatophytosis



4. DISCUSSION

This cross-sectional study reports on the epidemiological, clinical and mycological profile of paediatric dermatophytosis in a tertiary care Indian hospital and emphasizes on three important and interlinked factors responsible for the current epidemic of 'tinea' – the topical steroid combination misuse, household contact transmission and the inadequate duration of anti-fungal treatment. This paediatric cohort had a recalcitrance rate of 36.0%, a much higher figure than historical levels of 5-10% treatment failure from the pre-combination-cream era for dermatophytosis [2] - the combination of these three modifiable factors is what caused the damage to therapeutic success.

The relationship between prior topical steroid-antifungal-antimicrobial combination misuse and recalcitrance (aOR 3.8) corroborates and extends the vast literature on this from India, including the ISDR position paper of 2020 [14] and the work of Dogra et al. 2017 who reported the epidemic of steroid modified tinea in Indian dermatology centres [5]. The problem is, these combination products, which contain one antibiotic (gentamicin/neomycin), one antifungal (clotrimazole/miconazole) and one corticosteroid (mid to high potency, betamethasone), initially suppress itching and redness due to anti-inflammatory activity, and fool the patient and caregiver into assuming that they are being treated. In parallel, the corticosteroid component progressively impairs the Th1/Th17-mediated cellular immune response required for dermatophyte clearance, while the subtherapeutic antifungal component selects for resistant fungal mutants. The result is chronic, extensive, morphologically altered tinea that fails standard antifungal courses.

The emergence of T. indotineae in 15.3% of culture-positive cases—33.3% of recalcitrant cases—represents the most alarming mycological finding of the study and confirms the endemic establishment of this terbinafine-resistant species in Indian paediatric dermatology clinics. T. indotineae, first formally characterised using whole-genome sequencing in 2020 [9,10], has now been documented in epidemic proportions across India, Bangladesh, Nepal, and increasingly in European centres among Indian diaspora patients and travellers [15]. The pan-terbinafine resistance of all our T. indotineae isolates (MIC ≥4 mg/L) has critical treatment implications: oral terbinafine, which has been the most widely prescribed systemic antifungal in India for tinea for decades, is ineffective against this species, and continued prescribing of terbinafine in endemic regions without AFST will only amplify selection pressure. The preserved itraconazole susceptibility (96.3% of T. indotineae isolates) justifies the current IADVL/ISDR recommendation of itraconazole (5 mg/kg/day in 2 divided doses for children) as the preferred first-line systemic agent in regions with high T. indotineae prevalence [16].

Untreated infected family contact as an independent predictor (aOR 2.6) reflects the fundamentally household-based epidemiology of anthropophilic dermatophytosis. Without simultaneous screening and treatment of all household contacts—including asymptomatic carriers who may serve as a reservoir—recurrence and reinfection of the paediatric index case is virtually inevitable. This finding mandates a family-unit approach to paediatric tinea management: comprehensive examination and treatment of all household members, environmental decontamination (laundering of towels, bed linen, and clothing), and education on prevention of fomite-mediated transmission.

From a regulatory perspective, the widespread over-the-counter availability of topical corticosteroid-containing combination preparations in India—facilitated by inadequate enforcement of Schedule H prescription-only restrictions—constitutes a public health emergency. The Drug Technical Advisory Board (DTAB) and the Central Drugs Standard Control Organisation (CDSCO) have proposed restrictions on fixed-dose combination topical preparations containing high-potency corticosteroids with antifungals, but enforcement at the pharmacy level has been inconsistent [17]. Dermatological societies in India, such as the Indian Association of Dermatologists, Venereologists and Leprologists (IADVL) and Indian Society for Dermatology Research (ISDR) have urged for a blanket ban of all combinations sold over the counter nationwide due to the harm done to patients by such products [18].

5. CONCLUSION

T. mentagrophytes complex (including terbinafine-resistant T. indotineae) is highly prevalent in paediatric dermatophytosis in India, topical steroid combination misuse is prevalent and the recalcitrant infection rates are 36%. Three modifiable risk factors for treatment failure were determined: topical steroid combination misuse, lack of treatment of family contacts, and short duration of antifungal therapy. The study highlights the need for a strict prescription-only regimen for all combination preparations containing topical corticosteroids, culture and antifungal susceptibility testing before initiating empirical terbinafine therapy in areas of high prevalence, and for itraconazole to be the first-line oral therapy in areas with proven T. indotineae prevalence.

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