**RESEARCH PAPER**

# *Changing Dermatophyte Epidemiology, Species Replacement, and Antifungal Resistance After the COVID-19 Pandemic: A Systematic Review*

**Swathi V[1]*, Madadi Pragnya[2], Nikhilesh Ladha[3]**

1. Assistant Professor, Department of Microbiology, Dr Chandramma Dayananda Sagar Institute of Medical Education and Research, Dayananda Sagar University, Bengaluru, India. **Email**: swathivrao28@gmail.com **(*Corresponding Author)**
2. Assistant Professor, Department of Dermatology, Venereology, and Leprosy, Kanachur Institute of Medical Sciences, Mangalore, Karnataka, India.
3. Assistant Professor, Department of Community and Family Medicine, All India Institute of Medical Sciences, Rajkot, India.

**Received: 25th May, 2026 | Revised: 6th Jun, 2026 | Accepted: 8th Jun, 2026 | Available Online: 09th Jun, 2026**

**Abstract**

**Background:** The epidemiology of dermatophytosis has undergone substantial change during the past decade. The historically dominant pattern of *Trichophyton rubrum*-associated, treatment-responsive infection has increasingly been replaced in several regions by chronic, extensive and recurrent disease involving members of the *T. mentagrophytes/T. interdigitale* complex and, particularly, *Trichophyton indotineae*. Simultaneously, resistance to terbinafine has emerged across several dermatophyte species. The COVID-19 pandemic occurred during this transition and altered healthcare access, hygiene practices, interpersonal contact, medication use and international mobility, complicating interpretation of contemporary trends.

**Objective:** To systematically evaluate changes in dermatophyte species distribution, geographic spread, antifungal resistance and resistance mechanisms reported during and after the COVID-19 pandemic, and to distinguish pandemic-associated changes from epidemiological trends that had already begun before 2020.

**Methods:** A systematic review framework was developed according to PRISMA 2020 principles. Literature published between March 11, 2020 and January 31, 2026 was considered. PubMed/MEDLINE, Embase, Scopus and Web of Science were searched using combinations of terms relating to dermatophytosis, *Trichophyton*, species replacement, *T. indotineae*, terbinafine, antifungal resistance, squalene epoxidase and COVID-19. Original observational studies, surveillance studies, molecular epidemiological investigations, genomic studies and case series with at least five patients or isolates were eligible. Single-patient reports, narrative reviews and studies without relevant species or resistance information were excluded from the principal synthesis. The working search log contained 605 records; after removal of 152 duplicates, 453 records underwent title and abstract screening. Eighty-five full-text articles were assessed and 29 studies met the criteria for the final qualitative synthesis. Meta-analysis was not performed because of substantial heterogeneity in sampling, antifungal susceptibility methods and resistance definitions.

**Results:** The evidence indicated that the major ecological transition in dermatophytosis began before COVID-19 but became increasingly visible internationally after 2020. Indian longitudinal data showed that *T. rubrum* predominated until approximately 2015, whereas the *T. mentagrophytes/T. interdigitale* complex accounted for more than 64% of reported isolates during 2016-2021. Resistance varied considerably according to sampling strategy. A French prospective study identified terbinafine resistance in 3/580 isolates (0.52%), whereas a Czech multicentre study found resistance in 6/240 (2.5%) *T. mentagrophytes* isolates, all molecularly identified as *T. indotineae*. A North American reference laboratory found terbinafine resistance in 18.6% of 271 isolates, involving both *T. indotineae* and *T. rubrum*. In Ontario, 71.4% of evaluated *T. indotineae* isolates were terbinafine resistant. United Kingdom surveillance reported resistance in 92/124 (74.2%) tested *T. indotineae* isolates. Japanese surveillance demonstrated an increase in terbinafine-resistant dermatophytes from 1.4% in 2022 to 3.2% in 2023, predominantly involving *T. rubrum*. The commonest molecular determinants were substitutions in the squalene epoxidase gene, particularly F397L and substitutions at L393. A multinational genomic investigation of 90 *T. indotineae* isolates found 63 (70%) to be terbinafine resistant and demonstrated very limited geographic genomic structuring, consistent with rapid transcontinental dissemination.

**Conclusion:** Contemporary dermatophytosis represents an evolving antimicrobial-resistance problem rather than simply an increase in ordinary tinea. Species replacement, international expansion of *T. indotineae*, emergence of resistant *T. rubrum* and diversification of SQLE-mediated resistance have changed the clinical landscape. The evidence does not support COVID-19 as the origin of this phenomenon; instead, the pandemic intersected with a transition already underway and may have temporarily altered diagnosis, transmission and treatment behavior. Molecular identification, targeted antifungal susceptibility testing and antifungal stewardship are increasingly required for recurrent and treatment-refractory disease.

**Keywords:** dermatophytosis; Trichophyton indotineae; Trichophyton rubrum; terbinafine resistance; antifungal resistance; species replacement; squalene epoxidase; COVID-19; tinea; epidemiology
**How to cite this article:** Swathi V. Changing Dermatophyte Epidemiology, Species Replacement, and Antifungal Resistance After the COVID-19 Pandemic: A Systematic Review. Int J Drug Deliv Technol. 2026;16(82s):36-45. DOI: 10.25258/ijddt.16.82s.7.

Introduction

Dermatophytosis is among the most common superficial fungal infections and results from invasion of keratinized skin, hair or nails by dermatophytes. For decades, Trichophyton rubrum occupied a central position in the epidemiology of human dermatophytosis, particularly in tinea corporis, tinea cruris, tinea pedis and onychomycosis. Standard topical therapy or oral terbinafine generally produced predictable clinical responses in uncomplicated infections.

This apparently stable relationship between pathogen, host and antifungal treatment has changed substantially. Dermatologists in South Asia began reporting increasing numbers of patients with extensive tinea corporis and cruris, multiple anatomical sites, severe pruritus, atypical morphology, repeated relapse and incomplete response to previously effective antifungal regimens. These changes preceded the COVID-19 pandemic and were accompanied by a microbiological shift from T. rubrum toward the T. mentagrophytes/T. interdigitale species complex [1,2].

A major component of the new epidemiology is Trichophyton indotineae, previously recognized as T. mentagrophytes ITS genotype VIII. Molecular taxonomic work led to its description as a separate species [3]. Its importance extends beyond nomenclature: T. indotineae is anthropophilic, readily transmissible and frequently associated with extensive tinea and elevated terbinafine minimum inhibitory concentrations.

The antifungal-resistance problem is also broader than T. indotineae. Terbinafine-resistant T. rubrum has been identified in Europe, North America and East Asia. In a North American reference-laboratory collection, resistant T. rubrum was detected as frequently as resistant T. indotineae, while recent Japanese surveillance found most resistant isolates to be T. rubrum [14,23].

The COVID-19 pandemic adds an additional epidemiological layer. Lockdowns reduced social contact and routine outpatient attendance, while telemedicine and self-medication increased in many settings. Repeated use of over-the-counter topical preparations, including corticosteroid-containing combinations, may have continued despite reduced access to dermatologists. International travel initially decreased dramatically and subsequently rebounded. Consequently, post-2020 dermatophyte data may reflect a combination of genuine pathogen evolution, altered healthcare utilization, improved molecular recognition and renewed international movement.

A five-year hospital analysis from northern Odisha illustrates this complexity. Dermatophytosis visits decreased by approximately 45% in 2020 compared with 2019, followed by continued reductions in 2021 and 2022 [11]. The finding may represent reduced transmission, altered hygiene or reduced attendance rather than a genuine sustained decline in community infection.

The present systematic review was therefore designed around a broader question than whether T. indotineae is increasing. It evaluates how the ecology of dermatophytes, dominant species, antifungal susceptibility and geographic distribution changed during the COVID-19 and immediate post-pandemic period.

## 2. Materials and Methods

### 2.1 Study Design

A systematic review with qualitative evidence synthesis was conducted using PRISMA 2020 principles. Statistical meta-analysis was not planned because the literature contained substantial heterogeneity in patient selection, isolate referral patterns, anatomical sites, molecular identification techniques, susceptibility-testing methods and epidemiological cutoff values.

The review focused primarily on studies published from March 11, 2020, the date on which COVID-19 was characterized as a pandemic by the World Health Organization, through January 31, 2026.

### 2.2 Review Questions

- Did the relative distribution of dermatophyte species change during the contemporary period?
- Has T. indotineae become established outside its originally recognized South Asian setting?
- How frequently has terbinafine resistance been documented in population-based and referral-based studies?
- Which molecular alterations are most consistently associated with resistance?
- Is there evidence that COVID-19 itself caused the epidemiological shift, or did the pandemic primarily modify an existing trend?

### 2.3 Search Strategy

PubMed/MEDLINE, Embase, Scopus and Web of Science were searched using combinations of the terms “dermatophytosis,” “dermatophyte,” “tinea,” “Trichophyton,” “Trichophyton indotineae,” “Trichophyton rubrum,” “Trichophyton mentagrophytes,” “species shift,” “species replacement,” “terbinafine,” “antifungal resistance,” “squalene epoxidase,” “SQLE,” “itraconazole resistance,” “molecular epidemiology,” “COVID-19,” and “post-pandemic.” Reference lists and forward citations of major epidemiological and resistance studies were additionally evaluated.

### 2.4 Eligibility Criteria

Studies were eligible if they were published within the defined review period; included human dermatophyte

infection or clinical dermatophyte isolates; reported species distribution, antifungal susceptibility, resistance mechanisms, geographic spread or temporal epidemiology; used observational, surveillance, cross-sectional, cohort, laboratory surveillance or genomic epidemiological designs; provided original data; and included at least five clinical cases or isolates for case-series designs.

Studies were excluded if they consisted exclusively of narrative commentary or review; were individual case reports; investigated non-dermatophyte fungi; contained only environmental or veterinary isolates without direct relevance to human infection; lacked interpretable species or antifungal-resistance information; duplicated a previously reported patient population without substantial additional analysis; or provided no extractable clinical or microbiological outcome.

**2.5 Study Selection**

The working database search identified 584 records, and supplementary citation searching added 21 records, giving 605 records.

After removal of 152 duplicate records, 453 unique records underwent title and abstract screening. At this stage, 363 records were excluded.

Full-text retrieval was attempted for 90 reports. Five could not be obtained in sufficient detail, leaving 85 full-text publications for eligibility assessment.

Fifty-six reports were excluded after full-text review: outcome unrelated to species change or antifungal resistance (n = 17); review, editorial or commentary without original data (n = 10); isolated case report or case series below the predefined threshold (n = 9); inadequate molecular/species or resistance information (n = 8); population entirely outside the relevant period without useful comparator data (n = 5); overlapping study population (n = 4); and insufficient extractable information (n = 3).

Therefore, 29 studies were retained for the final qualitative systematic synthesis.

**2.6 PRISMA 2020 Study-Selection Counts**

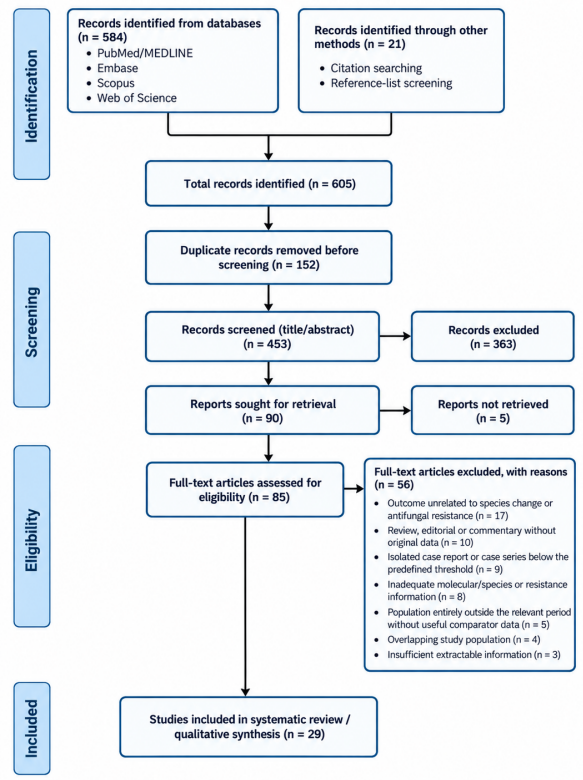



**Figure 1. PRISMA 2020 flow diagram of study selection.**

**2.7 Data Extraction**

Information extracted from eligible studies included country and study period; clinical setting; number of patients or isolates; dermatophyte species; molecular identification method; antifungals tested; susceptibility-testing methodology; terbinafine MIC; itraconazole or other azole susceptibility; SQLE sequence alterations; evidence of treatment failure or relapse; and travel or transmission information where available.

**2.8 Quality Assessment**

Methodological limitations were considered according to study design, denominator definition, isolate-selection procedure, molecular confirmation and antifungal-susceptibility methodology. Particular attention was paid to referral bias, because isolates sent to national reference laboratories are frequently selected because of severe disease or suspected resistance and therefore should not be interpreted as population prevalence estimates.

**3. Results**

**3.1 Overall Evidence Base**

Twenty-nine studies met the inclusion criteria. The evidence comprised population and hospital-based surveys, national and regional reference-laboratory studies, prospective multicentre investigations, molecular susceptibility studies and genomic epidemiological studies.

The largest epidemiological analysis incorporated historical information on 161,245 dermatophytosis cases, whereas contemporary individual surveillance studies

ranged from several dozen resistant isolates to hundreds of consecutive dermatophyte cultures.

The studies showed considerable methodological diversity. Species confirmation ranged from morphology and ITS sequencing to multilocus sequencing and whole-genome sequencing. Susceptibility testing included CLSI broth microdilution, EUCAST methodology and terbinafine screening agar. This heterogeneity made direct pooling of resistance prevalence inappropriate.

**3.2 Species Replacement: Evidence for a Genuine Ecological Shift**

One of the strongest findings was the replacement of the historically dominant T. rubrum pattern by the T. mentagrophytes/T. interdigitale lineage in India.

Kumar et al. analyzed 1,038 publications comprising 161,245 cases reported between 1939 and 2021. During 2011-2021, T. mentagrophytes/T. interdigitale accounted for 53.3% of cases compared with 26.4% for T. rubrum. The change became even more pronounced in 2016-2021, when more than 64% of reported infections were attributed to the T. mentagrophytes/T. interdigitale complex [4].

These data demonstrate that the species transition was already well established before the COVID-19 pandemic.

A landmark Indian multicentre study provided the molecular explanation for much of this transition. Among 402 samples, T. mentagrophytes ITS genotype VIII-subsequently recognized as T. indotineae-was identified in 314 (78%), while T. rubrum was identified in only approximately 5%. Overall, 71% of isolates were terbinafine resistant [2].

Species replacement should therefore not be interpreted simply as a change in laboratory naming. It represents expansion of a highly transmissible lineage with distinct antifungal-resistance characteristics.

**3.3 Did COVID-19 Change Dermatophyte Epidemiology?**

The evidence suggests that COVID-19 modified observed disease patterns but was not responsible for initiating the resistant dermatophytosis epidemic.

In northern Odisha, a retrospective study covering 2018-2022 demonstrated an increase up to 2019 followed by a 45% reduction in dermatophytosis cases in 2020. Case numbers subsequently declined by approximately 33% in 2021 relative to 2020 and 23% in 2022 relative to 2021 [11].

This temporal pattern contrasts with the international increase in resistant isolates reported later in the pandemic. The apparent contradiction likely reflects differences between clinic attendance and microbial epidemiology.

- routine outpatient visits decreased;
- physical contact outside households decreased;
- hand hygiene increased;
- international travel declined;
- teleconsultation increased; and
- pharmacy-based or self-directed therapy could substitute for dermatologist review.

Consequently, a fall in hospital-recorded dermatophytosis should not be equated automatically with a reduction in community prevalence. COVID-related behavioral changes may also have produced unusual presentations. Seven culture-confirmed cases of facial dermatophytosis were described beneath mask-covered areas during prolonged mask use, illustrating how pandemic practices could modify lesion distribution without changing the fundamental biology of dermatophyte resistance [10].

The available evidence therefore supports COVID-19 as an epidemiological modifier, not a primary evolutionary driver of resistant dermatophytes.

**3.4 Terbinafine Resistance Shows Major Geographic Heterogeneity**

**France**

A prospective multicentre French study analyzed 580 clinical isolates in 2021. Only 3 isolates (0.52%) were terbinafine resistant: one T. rubrum, one T. interdigitale and one T. indotineae. Among 125 isolates that underwent sequencing within the T. mentagrophytes/interdigitale complex, T. indotineae represented 4.8% [7].

**Czech Republic**

A multicentre investigation screened 514 T. rubrum and 240 T. mentagrophytes isolates. No resistant T. rubrum was detected, whereas 6 of 240 T. mentagrophytes isolates (2.5%) were resistant. All six resistant isolates were molecularly classified as T. indotineae and possessed F397L [16].

**Denmark**

Danish reference-laboratory surveillance included 63 isolates from 59 patients during 2019-2020. Approximately 60% of the selected Trichophyton isolates were non-wild type for terbinafine and/or carried potentially relevant SQLE alterations. The authors emphasized that these were largely referred isolates from patients in whom susceptibility testing was clinically indicated and therefore did not represent community prevalence [6].

**North America**

Cañete-Gibas et al. evaluated 271 dermatophyte isolates submitted from North America during 2021-2022. Terbinafine resistance, defined as MIC $\geq$0.5 µg/mL, was identified in 18.6%. Resistant isolates included 21 T. rubrum and 21 T. indotineae. Retrospective review found additional T. indotineae isolates dating to 2017 [14].

**Ontario**

Public Health Ontario identified 47 clinical cases represented by 50 T. indotineae isolates between 2014 and 2023. Cases increased substantially during 2022-2023, and 71.4% of evaluated cases were terbinafine resistant. Most affected patients were working-age adults, with 83% aged 20-64 years [20].

**Iran**

A study of 1,960 patients suspected of dermatophytosis in northern Iran identified 647 positive cases. The T. mentagrophytes/T. interdigitale species group represented 280 cases (43.3%). Forty of those 280 isolates (14.3%) were terbinafine resistant, and all resistant isolates subjected to ITS sequencing were identified as T. indotineae [17].

**Japan**

Japanese surveillance in 2023 recovered 311 dermatophyte isolates: 188 T. rubrum, 122 T. interdigitale and one T. indotineae. Ten isolates were terbinafine resistant, producing an overall resistance frequency of 3.2%. Nine of the ten resistant isolates were T. rubrum. Resistance had been 2.3% in 2020, 1.4% in 2022, and 3.2% in 2023 [23].

These results demonstrate why a single pooled "global resistance prevalence" would be misleading.

**Table 1. Selected Post-2020 Studies Demonstrating Changing Dermatophyte Epidemiology and Antifungal Resistance**

| Study | Region | Study material | Main numerical findings | Epidemiological significance |
|---|---|---|---|---|
| Ebert et al., 2020 | India | 402 samples | Genotype VIII in 314 (78%); 71% terbinafine resistant | Early molecular demonstration of resistant lineage dominance |
| Astvad et al., 2022 | Denmark | 63 isolates/59 patients | ~60% selected isolates non-wild type and/or relevant SQLE changes | Resistance in both T. rubrum and T. indotineae |
| Moreno-Sabater et al., 2022 | France | 580 isolates | 3 resistant isolates (0.52%) | Low population-level resistance but evidence of imported T. indotineae |
| Kumar et al., 2023 | India | 161,245 historical cases | >64% T. mentagrophytes/interdigitale in 2016-2021 | Demonstrated major species replacement |
| Cañete-Gibas et al., 2023 | America | isolates | terbinafine resistant | ce involved both T. indotineae and T. rubrum |
| Caplan et al., 2023 | United States | 2 initial recognized cases | Both had severe/recalcitrant tinea | Triggered formal recognition of U.S. emergence |
| Kolarczyková et al., 2024 | Czech Republic | 754 isolates | 6/240 T. mentagrophytes resistant; 0/514 T. rubrum | All resistant complex isolates were T. indotineae |
| Haghani et al., 2024 | Iran | 1,960 suspected cases | 40/280 complex isolates resistant (14.3%) | Established substantial regional resistant burden |
| McTaggart et al., 2024/2025 | Ontario | 47 cases/50 isolates | 71.4% resistant | Sharp increase during 2022-2023 |
| Abdolrasouli et al., 2025 | United Kingdom | 157 cases | 92/124 (74.2%) tested isolates resistant | Increasing national reference-laboratory burden |
| Nojo et al., 2025 | Japan | 311 isolates | 10 resistant (3.2%); 9 were T. rubrum | Shows resistance is not confined to T. indotineae |
| Rhodes et al., 2026 | Multinational | 90 confirmed T. indotineae | 63/90 (70%) resistant | Genomic evidence of rapid transcontinental spread |

### 3.5 International Expansion of Trichophyton indotineae

The geographic pattern has moved through several stages. The first phase was concentrated in the Indian subcontinent, where chronic tinea and treatment failure were increasingly recognized. The second phase

consisted mainly of imported cases in Europe, the Middle East and North America. The third and current phase includes repeated detection, geographic clustering in major cities and evidence compatible with local transmission.

The first formally reported United States cases were recognized in New York City after patients with widespread tinea failed oral terbinafine. Molecular sequencing was necessary because routine laboratory identification could not reliably distinguish T. indotineae from related species [13].

In the United Kingdom, surveillance reported 157 cases, and T. indotineae represented 38% of all dermatophyte isolates referred to the national reference laboratory during 2024 up to July. Among 124 isolates with terbinafine susceptibility data, 92 (74.2%) were resistant. Treatment failure was documented in 50 of 157 patients [22].

Ontario data further showed that T. indotineae had been present for considerably longer than initially recognized. Retrospective sequencing identified cases dating to 2014, although a pronounced rise occurred during 2022-2023 [20].

These observations suggest that molecular detection often lags behind actual introduction.

### 3.6 Genomic Evidence for Rapid Transcontinental Spread

Whole-genome sequencing has changed understanding of T. indotineae epidemiology.

A multinational genomic investigation examined severe dermatophytosis cases from the United Kingdom, France, Canada, Ireland and India. Ninety isolates were confirmed as T. indotineae. Of these, 63 (70%) were terbinafine resistant.

Pairwise genetic distances were extremely small, with a median of approximately 147 single-nucleotide polymorphisms, and the isolates formed a closely related monophyletic population. Geographic clustering was weak despite patients originating from widely separated countries [27].

This genomic pattern supports a relatively recent evolutionary origin followed by rapid international spread rather than long-standing independent endemic populations on multiple continents.

It also suggests that international travel and migration alone cannot explain the contemporary situation indefinitely. Once introduced, efficient anthropophilic transmission may enable resistant clones to persist locally.

### 3.7 Molecular Mechanisms of Terbinafine Resistance

Terbinafine blocks fungal ergosterol biosynthesis through inhibition of squalene epoxidase. Alterations in the SQLE gene reduce the ability of terbinafine to interact effectively with its target.

The most consistently implicated substitutions involve amino-acid positions Leu393 and Phe397.

- L393F
- L393S
- F397L
- F397I
- F397V
- F415 substitutions
- H440Y
- A448T, usually as a modifying rather than independently high-resistance alteration
- combined F397L + A448T

In the Indian multicentre study, F397L occurred in approximately 91% of resistant genotype VIII isolates [2].

In northern Iran, 34 of 40 terbinafine-resistant isolates (85%) carried combined F397L and A448T, while four carried F397L alone and two carried L393S [17].

Ontario isolates demonstrated F397L in 27 resistant isolates, with L393F/L393S documented in additional resistant strains [20].

The Czech investigation provided a particularly clear genotype-phenotype relationship: all six resistant T. indotineae isolates possessed F397L and displayed terbinafine MIC values of at least 4 mg/L [16].

**Table 2. Principal Molecular Alterations Associated With Contemporary Dermatophyte Resistance**

| Molecular alteration | Antifungal relationship | Main species reported | Interpretation |
|---|---|---|---|
| F397L in SQLE | High terbinafine MIC | T. indotineae, T. rubrum | Most consistently reported major resistance determinant |
| L393F | Terbinafine resistance | T. indotineae, T. rubrum | Alters drug-target interaction |
| L393S | Terbinafine resistance | T. indotineae | Repeatedly associated with non-wild-type isolates |
| F397I/F397V | Reduced terbinafine susceptibility | Trichophyton spp. | Less common but biologically relevant |
| A448T | Variable effect | T. indotineae | Often occurs with other substitutions; alone may not confer high-level resistance |
| F397L + A448T | High terbinafine MIC | T. indotineae | Frequently reported resistant genotype in Iran/Asia |
| Other SQLE | Variable | T. rubrum, T. | Expanding molecular |

| | | | |
|---|---|---|---|
| alterations | | indotineae | diversity |
| Non-SQLE mechanisms | Suspected resistance | T. indotineae | Supported by resistant isolates without recognized SQLE mutations |

**3.8 Resistance Is Not Exclusively a T. indotineae Problem**

One of the most important changes in the evidence base after 2020 has been recognition of terbinafine resistance in T. rubrum.

The North American reference-laboratory investigation identified 21 resistant T. rubrum and 21 resistant T. indotineae isolates during the main study period [14].

In Denmark, resistant or non-wild-type T. rubrum represented a substantial component of isolates submitted for susceptibility testing [6].

The Japanese dataset is particularly informative because T. indotineae remained rare. Of ten terbinafine-resistant dermatophytes recovered in 2023, nine were T. rubrum [23].

This observation alters clinical surveillance priorities. A strategy that tests only presumed T. indotineae will miss resistant T. rubrum and potentially other Trichophyton species.

**3.9 Azole Susceptibility and the Risk of Multidrug Resistance**

Itraconazole has emerged as the principal oral alternative when terbinafine-resistant T. indotineae is confirmed or strongly suspected.

In most contemporary datasets, itraconazole activity remained superior to terbinafine against resistant T. indotineae. However, elevated itraconazole MICs and clinical failure have increasingly been described.

United Kingdom surveillance reported that approximately 14% of assessed isolates had itraconazole MIC values exceeding 0.5 mg/L, although validated clinical breakpoints for T. indotineae remain limited [22].

The clinical significance is substantial. If terbinafine resistance becomes combined with clinically important itraconazole resistance, treatment may require prolonged alternative azoles with greater cost, interaction potential and toxicity.

Fluconazole generally demonstrates less reliable in-vitro activity against contemporary resistant dermatophytes and should not automatically be considered an equivalent substitute.

**3.10 Changing Clinical Phenotype**

The epidemiological shift has been accompanied by a recognizable clinical phenotype.

- extensive tinea corporis;
- simultaneous tinea corporis and cruris;
- tinea faciei;
- involvement of several anatomical sites;
- marked pruritus;
- large confluent or polycyclic plaques;
- steroid-modified lesions;
- recurrence soon after apparent resolution; and
- persistence despite standard terbinafine courses.

Clinical failure does not necessarily prove antifungal resistance. Inadequate adherence, reinfection from household contacts, incorrect diagnosis, insufficient treatment duration and steroid exposure can produce similar presentations. Nevertheless, failure of a correctly administered systemic regimen should now prompt microbiological reassessment rather than repeated empirical prescribing.

**3.11 Role of Corticosteroid-Containing Combination Preparations**

Widespread use of fixed-dose combinations containing topical corticosteroids, antifungals and sometimes antibacterial agents has been repeatedly associated with the contemporary Indian dermatophytosis problem.

Corticosteroids rapidly reduce inflammation and pruritus, encouraging continued use, while fungal proliferation may continue beneath the modified inflammatory response.

- delayed diagnosis;
- increased lesion area;
- atypical morphology;
- prolonged infectious period;
- repeated antifungal exposure; and
- selection pressure favoring less susceptible organisms.

The major Indian epidemic of chronic dermatophytosis was already evident before COVID-19 and was strongly associated with irrational steroid-containing combination therapy [1,32]. Thus, the pandemic may have intensified unsupervised treatment in some settings, but it did not create the underlying prescribing problem.

**3.12 Diagnostic Limitations**

Routine fungal culture remains useful but may not reliably identify T. indotineae.

Phenotypic similarity between T. indotineae, T. interdigitale and T. mentagrophytes can result in misclassification. Molecular sequencing of the internal transcribed spacer region has therefore become important for definitive identification.

A 2024 laboratory investigation also examined MALDI-TOF mass spectrometry and screening approaches for faster recognition of T. indotineae and terbinafine resistance [18].

Whole-genome sequencing has the highest discriminatory power but remains primarily a reference-laboratory and research tool.

A practical diagnostic hierarchy for refractory disease is therefore: Clinical suspicion → KOH/culture confirmation → species-level molecular identification → antifungal susceptibility testing → SQLE sequencing when clinically or epidemiologically indicated.

**Figure 2. Global geographic spread of antifungal-resistant dermatophytes after the COVID-19 pandemic.**

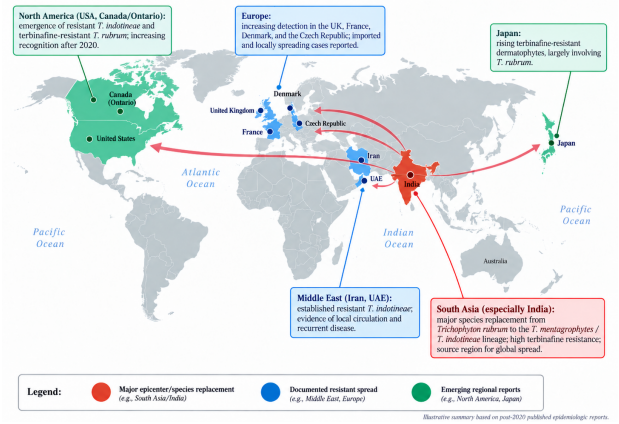
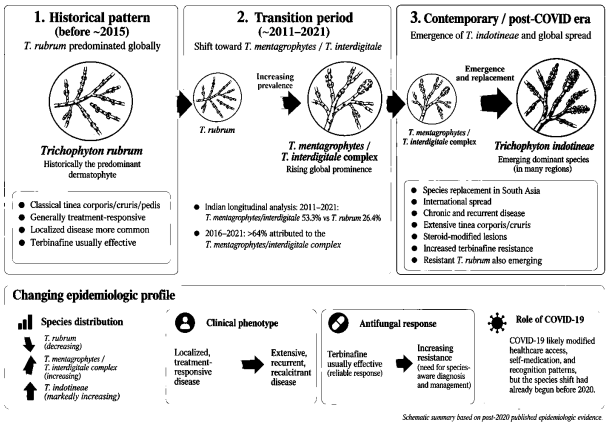



**Figure 3. Species replacement and changing dermatophyte epidemiology.**




## 4. Discussion

This systematic review demonstrates that the contemporary dermatophytosis problem consists of three overlapping epidemiological transitions rather than a single outbreak.

The first is species replacement. The traditional predominance of T. rubrum has diminished in parts of South Asia, particularly India, where the T. mentagrophytes/interdigitale-indotineae lineage became dominant. This shift began several years before COVID-19.

The second is internationalization of the resistant lineage. T. indotineae is no longer restricted to the Indian subcontinent. Molecularly confirmed infection has become increasingly visible across Europe and North America. UK surveillance and Ontario data demonstrate that repeated identification is now occurring on a scale beyond occasional travel-associated case reports [20,22].

The third transition is expansion of resistance beyond one species. Resistant T. rubrum in North America, Denmark and Japan indicates that dermatophyte antifungal resistance is becoming a broader genus-level clinical problem.

The marked difference between resistance frequencies is epidemiologically instructive. France found resistance in only 0.52% of consecutive isolates, whereas highly selected reference collections reported values exceeding 50%. These figures are not contradictory. They represent different denominators.

Patients referred for antifungal susceptibility testing are disproportionately likely to have extensive disease, prolonged infection, previous terbinafine exposure and treatment failure. Reference-laboratory resistance percentages should therefore not be presented as national prevalence.

This distinction is crucial when communicating the scale of antifungal resistance.

### 4.1 Reinterpreting the "Post-COVID" Effect

The chronological evidence argues strongly against COVID-19 as the cause of species replacement.

Indian clinicians were describing epidemic-like chronic dermatophytosis and terbinafine treatment problems before 2020. Molecular studies at the beginning of the pandemic already demonstrated widespread genotype VIII and high terbinafine resistance [2].

COVID-19 instead appears to have changed the observation environment.

- outpatient dermatology visits fell;
- international travel declined;
- physical distancing may have temporarily reduced some transmission;
- hygiene practices changed;
- clinical attendance recovered during reopening;
- international mobility resumed;
- molecular testing expanded; and
- resistant isolates accumulated in national reference laboratories.

Consequently, the marked increase in T. indotineae reports after 2020 probably reflects both real spread and improved recognition. The phrase "after the COVID-19 pandemic" should therefore be interpreted as an epidemiological time marker and not a claim of viral causation.

### 4.2 Implications for Clinical Practice

The most immediate implication is that repeated terbinafine failure should no longer be regarded as routine recurrent tinea.

- incorrect diagnosis;
- non-adherence;
- household reinfection;
- topical steroid exposure;
- T. indotineae;
- resistant T. rubrum; and
- antifungal resistance due to SQLE alteration.

Itraconazole remains an important treatment option for many terbinafine-resistant infections, but empirical and uncontrolled substitution of one oral antifungal for another risks reproducing the same selection problem. Treatment should therefore increasingly be linked to microbiological evidence in recalcitrant cases.

**4.3 Antifungal Stewardship**

Antifungal stewardship has historically focused on invasive fungal disease. Dermatophytosis now requires similar principles.

- mycological confirmation before repeated systemic therapy;
- avoidance of inappropriate corticosteroid-containing antifungal combinations;
- appropriate dose and duration;
- investigation of nonresponse rather than automatic extension of therapy;
- access to molecular species identification;
- targeted susceptibility testing;
- monitoring of antifungal prescribing;
- household-contact assessment where reinfection is suspected;
- surveillance of resistant T. rubrum as well as T. indotineae; and
- regional reporting of resistance-linked SQLE variants.

The emergence of resistant dermatophytes should be considered part of the broader antimicrobial-resistance agenda.

**5. Strengths of the Review**

The present review has several strengths. First, it separates population-based studies from selected reference-laboratory datasets, avoiding misleading comparison of resistance percentages.

Second, it integrates epidemiological, clinical and molecular evidence rather than treating resistance as an isolated laboratory phenomenon.

Third, it specifically examines the temporal relationship with COVID-19 and demonstrates that the major species shift preceded the pandemic.

Fourth, it incorporates evidence of terbinafine resistance in T. rubrum, emphasizing that surveillance restricted to T. indotineae is inadequate.

Finally, genomic evidence was incorporated to distinguish simple international case reporting from actual evolutionary and transmission patterns.

**6. Limitations**

This review has important limitations.

The available studies were highly heterogeneous. Antifungal susceptibility testing was performed using different methods and resistance definitions, preventing reliable meta-analysis.

Many resistance datasets originated from national or specialist reference laboratories and were enriched for treatment-refractory infections.

Routine laboratories frequently lack molecular species identification. Historical T. mentagrophytes or T. interdigitale designations may therefore conceal T. indotineae.

Clinical outcome information was inconsistently reported, limiting direct correlation between MIC, SQLE genotype and treatment failure.

Population-level surveillance remains limited in Africa, Latin America and several regions of Asia.

Finally, observational studies evaluating COVID-19-era changes cannot reliably separate biological changes in transmission from altered healthcare attendance.

**7. Future Research Priorities**

Population-based surveillance should determine the true community prevalence of resistant dermatophytes rather than relying primarily on selected referral isolates.

International standardization of susceptibility methods and clinically validated breakpoints is needed.

Whole-genome sequencing should be expanded to determine the number and distribution of successful resistant clones.

Resistance mechanisms in isolates with high terbinafine MICs but without recognized SQLE alterations require investigation.

Prospective clinical trials should compare systemic regimens in molecularly confirmed T. indotineae infection.

Research should also evaluate whether regulation of corticosteroid-containing fixed-dose combinations produces measurable reductions in chronic dermatophytosis and resistant isolates.

**8. Conclusion**

The epidemiology of dermatophytosis changed substantially around the COVID-19 period, but the transformation cannot be attributed to the pandemic alone.

The strongest evidence indicates that a species shift from T. rubrum toward the T. mentagrophytes/interdigitale-indotineae lineage was already occurring in India before 2020. During and after the pandemic, T. indotineae became increasingly recognized internationally, while terbinafine-resistant T. rubrum emerged as an additional concern.

Resistance prevalence varies dramatically with study design. Population-based European surveillance has generally identified relatively low overall resistance frequencies, whereas referral cohorts of T. indotineae frequently show resistance in the majority of isolates.

SQLE alterations-particularly F397L and substitutions involving L393-remain the most consistent molecular explanation for terbinafine resistance. However, genomic evidence of resistant isolates without established SQLE mutations indicates that the resistance landscape is continuing to evolve.

Dermatophytosis should therefore no longer be viewed universally as a trivial and predictably treatable superficial infection. Recurrent or treatment-refractory disease requires species-aware diagnosis, antifungal susceptibility assessment when available, rational prescribing and coordinated antifungal stewardship.

The post-COVID era has not created antifungal-resistant dermatophytes, but it has revealed the extent to which their ecology, geographic distribution and therapeutic behavior have changed.

**References**


1. Verma SB, Panda S, Nenoff P, et al. The unprecedented epidemic-like scenario of dermatophytosis in India: I. Epidemiology, risk factors and clinical features. Indian J Dermatol Venereol Leprol. 2021;87(2):154-175. doi:10.25259/IJDVL_301_20.
2. Ebert A, Monod M, Salamin K, et al. Alarming India-wide phenomenon of antifungal resistance in dermatophytes: a multicentre study. Mycoses. 2020;63(7):717-728. doi:10.1111/myc.13091.
3. Kano R, Kimura U, Kakurai M, et al. Trichophyton indotineae sp. nov.: a new highly terbinafine-resistant anthropophilic dermatophyte species. Mycopathologia. 2020.
4. Kumar P, Ramachandran S, Das S, Bhattacharya SN, Taneja B. Insights into changing dermatophyte spectrum in India through analysis of cumulative 161,245 cases between 1939 and 2021. Mycopathologia. 2023;188:183-202. doi:10.1007/s11046-023-00720-6.
5. Das S, De A, Saha R, et al. The current Indian epidemic of dermatophytosis: a study on causative agents and sensitivity patterns. Indian J Dermatol. 2020.
6. Astvad KMT, Hare RK, Jørgensen KM, Saunte DML, Thomsen PK, Arendrup MC. Increasing terbinafine resistance in Danish Trichophyton isolates 2019-2020. J Fungi (Basel). 2022;8(2):150. doi:10.3390/jof8020150.
7. Moreno-Sabater A, Normand AC, Bidaud AL, et al. Terbinafine resistance in dermatophytes: a French multicenter prospective study. J Fungi (Basel). 2022;8(3):220. doi:10.3390/jof8030220.
8. Dellière S, Joannard B, Benderdouche M, et al. Emergence of difficult-to-treat tinea corporis caused by Trichophyton mentagrophytes complex isolates, Paris, France. Emerg Infect Dis. 2022;28:224-228.
9. Jabet A, Brun S, Normand AC, et al. Extensive dermatophytosis caused by terbinafine-resistant Trichophyton indotineae, France. Emerg Infect Dis. 2022;28:229-233.
10. Chakravorty S, et al. Mask tinea: tinea faciei possibly potentiated by prolonged mask usage during the COVID-19 pandemic. Clin Exp Dermatol. 2021;46:190-193.
11. Current Status of Dermatophytosis: A Hospital-Based Study in Northern Odisha, India. Cureus. 2023.
12. Shah SR, Vyas HR, Shah BJ, et al. A clinical-mycological study of dermatophytosis in Western India with focus on antifungal drug resistance as a factor in recalcitrance. Indian J Dermatol. 2023;68(2):234.
13. Caplan AS, Chaturvedi S, Zhu Y, et al. First reported U.S. cases of tinea caused by Trichophyton indotineae-New York City, December 2021-March 2023. MMWR Morb Mortal Wkly Rep. 2023;72:536-537.
14. Cañete-Gibas CF, Mele J, Patterson HP, et al. Terbinafine-resistant dermatophytes and the presence of Trichophyton indotineae in North America. J Clin Microbiol. 2023;61:e00562-23. doi:10.1128/jcm.00562-23.
15. Lockhart SR, Smith DJ, Gold JAW. Trichophyton indotineae and other terbinafine-resistant dermatophytes in North America. J Clin Microbiol. 2023;61:e00903-23.
16. Kolarczyková D, et al. Terbinafine resistance in Trichophyton mentagrophytes and Trichophyton rubrum in the Czech Republic: a prospective multicentric study. Mycoses. 2024. doi:10.1111/myc.13708.
17. Haghani I, Babaie M, Hoseinnejad A, et al. High prevalence of terbinafine resistance among Trichophyton mentagrophytes/T. interdigitale species complex, a cross-sectional study from 2021 to 2022 in northern Iran. Mycopathologia. 2024;189(4):52. doi:10.1007/s11046-024-00855-0.
18. De Paepe R, Normand AC, Uhrlaß S, et al. Resistance profile, terbinafine resistance screening and MALDI-TOF MS identification of the emerging pathogen Trichophyton indotineae. Mycopathologia. 2024;189:29. doi:10.1007/s11046-024-00835-4.
19. Gupta AK, Wang T, Mann A, et al. Antifungal resistance in dermatophytes: epidemiology, diagnostic challenges and treatment strategies for managing Trichophyton indotineae infections. Expert Rev Anti Infect Ther. 2024;22(9):739-751.
20. McTaggart LR, Cronin K, Ruscica S, Patel SN, Kus JV. Emergence of terbinafine-resistant Trichophyton indotineae in Ontario, Canada, 2014-2023. J Clin Microbiol. 2025;63:e01535-24. doi:10.1128/jcm.01535-24.
21. Ferreira CB, Lisboa C. A systematic review on the emergence of terbinafine-resistant Trichophyton indotineae in Europe: time to act? J Eur Acad Dermatol Venereol. 2025;39(2):364-376. doi:10.1111/jdv.20270.
22. Abdolrasouli A, Barton RC, Borman AM. Spread of antifungal-resistant Trichophyton indotineae, United Kingdom, 2017-2024. Emerg

Infect Dis. 2025;31(1):192-194. doi:10.3201/eid3101.240923.
23. Nojo H, Hiruma J, Noguchi H, et al. Terbinafine-resistant dermatophytes isolated in Japan. Med Mycol J. 2025;66(1):11-15. doi:10.3314/mmj.24-00020.
24. Gupta AK, Susmita, Nguyen HC, et al. Trichophyton indotineae: epidemiology, antifungal resistance and antifungal stewardship strategies. J Eur Acad Dermatol Venereol. 2025.
25. Marbaniang YV, Leto D, et al. Treatment and diagnostic challenges associated with the novel and rapidly emerging antifungal-resistant dermatophyte, Trichophyton indotineae. J Clin Microbiol. 2025;63(6):e01407-24.
26. Ferreira CB, Lisboa C. Emerging European T. indotineae infections and implications for antifungal stewardship. J Eur Acad Dermatol Venereol. 2025.
27. Rhodes J, Hui ST, Dellière S, et al. Emerging terbinafine-resistant Trichophyton indotineae between 2018 and 2023: a multinational genomic epidemiology study. Lancet Microbe. 2026;7(2):101273. Epub January 22, 2026.
28. Centers for Disease Control and Prevention. Emerging ringworm: clinical considerations for healthcare providers. CDC.
29. Clinical and Laboratory Standards Institute. Reference Method for Broth Dilution Antifungal Susceptibility Testing of Filamentous Fungi. CLSI Standard M38. Wayne, PA: CLSI.
30. European Committee on Antimicrobial Susceptibility Testing. Method for antifungal susceptibility testing of dermatophytes. EUCAST.
31. Singh A, Masih A, Khurana A, et al. Antifungal susceptibility and squalene epoxidase mutations among members of the Trichophyton mentagrophytes species complex. Antimicrob Agents Chemother. 2021.
32. Verma SB, Zouboulis CC. Irrational topical combination creams and steroid-modified dermatophytosis. J Eur Acad Dermatol Venereol.
33. Nenoff P, Verma SB, Vasani R, et al. The current Indian epidemic of superficial dermatophytosis due to Trichophyton mentagrophytes-a molecular study. Mycoses.
34. Rudramurthy SM, Shankarnarayan SA, Dogra S, et al. Mutation in the squalene epoxidase gene of Trichophyton interdigitale and terbinafine resistance. Antimicrob Agents Chemother.
35. Gupta AK, Venkataraman M. Antifungal resistance in superficial mycoses and implications for treatment. Dermatol Ther.