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Letter to Editor

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Trichophyton indotineae, an emerging species of *Trichophyton mentagrophytes* complex, causing aggravating antifungal-resistant epidemic

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Letter to editor

Superficial Dermatophyte infections are also known as tinea or ringworm and have been known to have existed since prehistoric times. Superficial dermatophytosis are considered among the most frequent forms of human infections, affecting more than 20–25% of the world's population.[1] Earlier *Trichophyton indotineae* was called *Trichophyton mentagrophytes* ITS (Internal Transcribed spacer) genotype VIII by Nenoff et al, 2019.[2] Later, in 2020, Kano et al. renamed this dermatophyte species as *Trichophyton indotineae* (*T. indotineae*), which is categorized by its high resistance to terbinafine.[3]

In the past, the dermatophyte infections used to be mild and easy to treat. For the past decade and a half, the treatment has become very challenging and it is spreading in overwhelming extent, which is considered primarily due to antifungal resistance.

Common dermatophyte infections in India are caused by *Trichophyton rubrum* (*T. rubrum*), *Trichophyton mentagrophytes* (*T. Mentagrophytes*), *Trichophyton violaceum* (*T. violaceum*), *Trichophyton interdigitale* (*T. interdigitale*) and *Microsporum canis* (*M. canis*). Prevalence of different dermatophytes vary in different geographical regions and keep on changing from time to time.

Identification of dermatophytes requires adequate experience to confidently report the dermatophytes. My first experience with identification and processing of dermatophyte samples was from 1998 to 2011 in sub-Sharan Africa, while working at National Health Laboratory in Botswana, where the predominant species was found to be *T. violaceum* and never came across *T. rubrum* except in External Quality Assurance samples.[4] I always preferred to examine the patient and collected samples myself and also, further processing. Contrary to the common belief that *T. rubrum* was the most common species, does not hold true for all the countries.

On my arrival to India in 2012, I found *T. interdigitale* as the most common species, which was later confirmed as *Trichophyton indotineae* (*T. indotineae*). Here in Western Uttar Pradesh (U.P.), during my tenure at Muzaffarnagar Medical College, Muzaffarnagar, it was noted that, *T. rubrum* is rare. We wanted to publish an outbreak due to *T. interdigitale*, which had spread in the epidemic proportions. But, our paper was not accepted in the official journal of dermatology because no other researchers had yet reported *T. interdigitale* in such a huge percentage, e.g. 95-100%. It is not possible to differentiate *Trichophyton mentagrophytes*, *T. interdigitale* and the new emerging species, e.g. *T. indotineae* on phenotypical characteristics. It requires molecular typing.[5] The facility of molecular typing is currently available at very few mycology laboratories in India. Lesions caused by *T. indotineae* are usually multiple, itchy, may be inflammatory, with no central clearing and are commonly found over gluteal, abdominal, groin regions, genital area (Figure 1) and back (Figure 2). Involvement of nails and scalp are rare. There are three case reports of onychomycosis and one of tinea capitis till date.[6–9]

Figure 1 A 45-year-old female. Multiple erythematous scaly highly pruritic lesions involving different anatomical sites: Tinea cruris et corporis, tinea genitalis, scaly erythematous lesions under and over breast and scattered over abdomen. There is no central clearing.

Figure 2 A 40-year-old female. Extensive tinea corporis with pruritic multiple scaly plaques spreading over back, nape of the neck and both upper arms also known as Tinea corporis generalisata. There is no central clearing and borders are slightly raised.

Clinical lesions caused *by T. interdigitale* are usually tinea pedis, tinea unguium or tinea corporis. But, in our case, the lesions were extensive, multiple, mildly inflammatory, no central clearing, no involvement of lymph nodes. Also got some cases of tinea genitalis.[10] There can be lesions at other sites due to auto-inoculation.

Rippon JW, cited in one of his papers "The Changing Epidemiology and Emerging Patterns of Dermatophyte Species" There is active evolution in *Trichophytom mentagtrophytes* complex (T/M complex). Furthermore, host- specific strains have and possibly separate as species."[11] This has actually happened.

Currently available molecular techniques have made exceptional distinction within the complex, which has made the recognition of distinct species such as *Trichophyton erinacei, Trichophyton quinckeanum*, *T. interdigitale*, *T. indotineae* and *T. mentagrophytes*. Within *Trichophyton Mentagrophytes* complex, numerous genotypes have been established. It ranges from Type I to XII in *T. interdigitale* and Type I to XXVIII in *T. mentagrophytes*.[12–14]

Patients with dermatophytosis due to *Trichophyton indotineae* usually present with extensive lesions of tinea corporis, tinea cruris, tinea faciei, tinea corporis et cruris, and tinea genitalis. Involvement of nails and scalp is rare, but recently, there have been case reports of three cases of onychomycosis, and one of tinea capitis.[6–9] We also published a case repot of tinea universalis.[15] In 2019, we shipped 49 skin scraping from patients suffering from superficial dermatophytosis to G. Sybren de Hoogs' laboratory in Netherlands for ITS molecular typing. *T. ind*otineae was identified in 97% of the skin scrapings and 3% were identified as *T. rubrum*.[16] So, the inference can be drawn that the outbreak reported in 2016 could have been due to *T. indotineae*.[17]

Researchers are concerned about the infection due to transmission of *T. indotineae* between humans and animals. Recently, ITS based sequencing confirmed etiologic agent as *T. indotineae* in two calves from Egypt and one dog from India.[18] Also, multi-drug resistant *Trichophyton indotineae* was isolated from a stray dog in Iran, which was found resistant to terbinafine, itraconazole, ketoconazole miconazole, griseofulvin, tolnaftate and butenafine.[19] The scenario has become quite alarming as animals are also getting involved in this epidemic. Timely diagnosis is highly crucial for the treatment and prevention of the spread of this global infection. The resistance to the commonly used drugs like terbinafine and Itraconazole is worrisome. *T. indotineae* is predominantly anthropophilic, but transmission between humans and animals is possible.[18]

Molecular typing is available at few mycology laboratories in India. Poor people cannot even procure medicine. The fungus has been isolated from a dog in India and the population of stray dogs in India is huge. There is possibility of rodents like rats and mice could harbor the organism. Wild life and veterinary staff should be the part of research. If dogs like in Iran are infected with multiple-resistant *T. indotineae* in India,[16] there can be disaster in preventing the infection.

Conclusion

The dual characteristics of the organism being anthropophilic primarily and also possibly possessing some zoonotic potentials and rapid development of multi-drug resistance, further make it very difficult to treat and prevent the infection. We should create awareness amongst the people and dermatologist must visit rural area from time to time.

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Conflict of interests

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