

Treatment Approach for Superficial Dermatophytosis Infections and Factors Contributing for Noncompliance to Antifungal Therapy in India: An Epidemiological Survey

Abstract

Background: The prevalence of superficial dermatophytosis has ascended in India over the past 6–7 years. Chronic, recurrent, and steroid-modified tinea with nonresponse to the conventional treatment regimens are being commonly reported. This can be attributed to a complex interplay of factors related to environment, host, and virulence of the organism and a rampant use of topical corticosteroid, antifungal, antibacterial, and irrational combination creams. Host factors such as living conditions, immunity, poor adherence to general measures, and non-compliance to treatment may affect the spread of infection and clinical presentation. **Objective:** The objective of this study was to understand the prevailing treatment approach for superficial dermatophytosis in India and the host factors contributing to noncompliance to antifungal therapy. **Materials and Methods:** This was a cross-sectional qualitative knowledge, attitude, and practice study conducted with 220 dermatologists who participated in DERMACON national conference held at Kochi in 2018. **Results:** Of the 220 dermatologists, 87.3% stated that there was a rise of tinea fungal infection clinical cases in India. About, 42.3% reported that recalcitrant tinea infection attributed to 10%–30% of increase in the number of clinical cases per week. The treatment of choice for superficial dermatophytosis, as per majority of the surveyed dermatologists is a combination of oral azole and topical azole. For recalcitrant fungal infections, 37.3% of the dermatologists stated that at least 4 weeks of antifungal therapy would be the optimal duration for new tinea cases. Overall, 30%–50% of the patients were noncompliant to the prescribed treatment as per 35.5% of the dermatologists. Almost all (97.7%) dermatologists agreed that there is a need for treatment consensus on treating superficial fungal infection. **Conclusion:** Majority of the dermatologists agreed that there is an increase in the prevalence of superficial dermatophytosis in India. Appropriate use of oral (optimal dosage) and topical antifungals are considered vital for the successful management of this infection. Appropriate use of topical and systemic antifungal agents for the right duration along with proper counseling is considered vital for the successful management of this infection.

Keywords: Antifungal, attitude, compliance, dermatophytosis, epidemiology, tinea

Introduction

Superficial fungal infections account for nearly 25% of the global skin mycoses.^[1] Worldwide, dermatophytes are the leading cause for superficial dermatophytosis and even more widespread in developing countries such as India, where there is high temperature and relative humidity.^[2] Recent Indian epidemiologic studies on dermatophytosis from various states also reported an increasing prevalence with spectrum change and isolation of rare species.^[2] *Trichophyton rubrum* remains the most common isolate. The most common clinical presentations are tinea corporis and

tinea cruris reported from studies conducted in Chennai and Rajasthan. However, Lucknow and New Delhi-based studies reported *Trichophyton mentagrophytes* and *Microsporum audouinii* to be the leading isolates. Rare species such as *Microsporum gypseum* were isolated in non-endemic regions globally.^[2] Superficial dermatophytosis infections lead to a significant distress to the patients affecting them socially, physically, and financially.

A complex interplay between host, fungus, drug, and environment catalyzed by hot and humid climate, rampant use of topical corticosteroid-based combinations, an increased use of broad-spectrum antibiotics,

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How to cite this article: Inamadar A, Rengasamy M, Charugulla SN. Treatment approach for superficial dermatophytosis infections and factors contributing for noncompliance to antifungal therapy in India: An epidemiological survey. *Clin Dermatol Rev* 2022;6:15-21.

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Submitted: 15-09-2020

Accepted: 27-05-2021

Published: 25-02-2022

Access this article online

Website: www.cdriadvlkn.org

DOI: 10.4103/cdr.cdr_122_20

Quick Response Code:



antifungal resistance may be attributed to an escalation of superficial dermatophytosis infections in India.^[3,4]

Allylamines and azoles (imidazoles and triazoles) are the common drug categories used for the treatment of dermatophytosis. An Indian expert group recommended the use of topical therapy in the management of naïve cases of tinea cruris and corporis (localized lesion) and combination therapy for recalcitrant tinea cruris.^[5] However, there is a lack of pertinent treatment guidelines or algorithm that addresses dermatophytosis concisely and thoroughly. The choice of treatment generally varies according to the region and personal experience of the individuals. Nonadherence to the prescribed treatment is another important issue that has a long-term impact on the patient outcomes. A previous study noted that 48% of patients did not follow the prescribed therapy schedule and one-quarter of patients tend to stop the treatment as soon as the disappearance of the symptoms (particularly older patients, who did not view superficial fungal infections as a serious concern).^[6]

Changing pattern of infection, an unprecedented rise in prevalence, inadequate treatment, and noncompliance to therapy are some of the challenges confronting the dermatologists across India. The current knowledge, attitude, and practice (KAP) study conducted among dermatologists in India used a structured questionnaire to identify the factors that contribute toward increased burden of tinea infections, treatment of choice for each of the categories of tinea infections, duration of antifungal therapy prescribed, patients who are noncompliant to the antifungal treatment and interventions to be addressed in order to obtain better clinical outcomes.

Materials and Methods

The dermatologists who participated at the DERMACON held at Kochi in 2018 were enrolled to participate in this questionnaire-based KAP survey. Prior to KAP study participation, formal introduction was given to participants regarding the purpose of seeking information, and informed verbal consent was obtained. Specific instructions were provided for filling up the questionnaire to avoid ambiguity. The questionnaire consisted of 22 multiple-choice questions and was divided into five parts addressing burden of tinea infection, treatment of choice for each of the tinea conditions, duration of antifungal therapy, noncompliance to treatment, and treatment gaps. The data were collected and analyzed descriptively using SPSS version 16 (SPSS Inc. Released 2007. SPSS for Windows, Version 16.0. Chicago, USA, SPSS Inc.). The study protocol was approved by IEC.

Results

Of 232 dermatologists who were briefed about the study, 220 consented and participated in the KAP study. All the participants had either a master's degree or diploma in

dermatology and minimum 1 year of clinical experience thereafter.

Burden of Infection

An overwhelming majority of participants agreed that there has been an increase in the prevalence of tinea infection in their practice. The likely reason for this increase as responded by the participants was increased steroid usage (5.9%), patient's nonadherence to therapy (2.7%), change in pattern of dermatophytes (2.3%), and environmental and lifestyle factors (1.8%), but most notably, 87.3% of them responded that all these factors were responsible for an increase in tinea infections. Overall, 42.3% of dermatologists felt that 10%–30% of burden attributed to recalcitrant dermatophytosis.

Treatment of choice for each of the categories of tinea infections

Superficial Dermatophytic Infections

The preferred treatment of choice for superficial dermatophytosis was a combination of oral azole and topical azole (31.4%) followed by combination of oral allylamine and topical azole (30.5%), combination of oral azole and topical allylamine (25.5%), combination of oral allylamine and topical allylamine (8.2%), and other treatment options (4.5%) respectively [Figure 1].

Localized

For 50.9% of dermatologists, a combination of topical and oral antifungal therapy was the treatment of choice to treat localized tinea lesions followed by topical antifungal application alone (46.8%) and combination of topical antifungal and topical steroid therapy (2.3%), respectively.

Extensive

For larger tinea lesions, a combination of topical antifungal and oral antifungal therapy was the preferred choice (93.2%). Only 6.8% favored a topical steroid initially with an oral antifungal and then shifting to topical antifungals alone.

Inflammatory

In patients with increased redness and itching, the preferred therapy was a combination of topical antifungal application with antihistaminics (40.9%) and topical antifungal with better anti-inflammatory activity (40.9%) followed by a combination of topical antifungal and topical steroid (12.7%) and others (5.5%), respectively [Table 1].

Recalcitrant

The preferred treatment of choice for recalcitrant dermatophytosis was a combination of oral azole and topical allylamine (37.7%) followed by combination of oral allylamine and topical azole (28.2%), combination of oral azole and topical azole (24.1%), other treatment

Table 1: Treatment of choice for fungal infections (n=220)

	n (%)
Treatment of choice for tinea infection with increased redness and itching	
Topical antifungal + antihistaminic	90 (40.9)
Topical antifungal with better anti-inflammatory effect	90 (40.9)
Topical antifungal + steroid	28 (12.7)
Other specific option	12 (5.5)
Factors to be considered while addressing recalcitrant cases	
With wide spectrum of coverage	11 (5)
With anti-inflammatory properties	9 (4.1)
A molecule with established clinical success rates	11 (5)
Formulation advantage with better penetration	11 (5)
Faster itch relief	10 (4.5)
Faster clearance of lesions	5 (2.3)
All of the above	163 (74.1)
Type of topical formulation that would help in better clinical outcomes and patient adherence in widespread lesions	
Clear solution	26 (11.8)
Cream	76 (34.5)
Ointment	48 (21.8)
Creamy lotion	70 (31.8)

options (5.5%), and combination of oral allylamine and topical allylamine (4.5%), respectively [Figure 2].

Majority of the dermatologists stated that the treatment of choice for onychomycosis was the combination of oral azole and topical allylamine (31.8%) followed by a combination of oral azole and topical azole (28.2%), oral allylamine and topical azole (22.3%), combination of oral allylamine, and topical allylamine and others (6.4%), respectively [Figure 3].

Duration of antifungal therapy

Majority of the dermatologists opined that for new cases, the optimal duration of topical (37.3%) and systemic antifungal therapy (38.2%) was at least 4 weeks. For recalcitrant cases, the optimal duration of therapy for topical (65.5%) and systemic (45.5%) antifungal therapy duration was 8–12 weeks.

Non-compliance to antifungal treatment

Overall, 70.5% of the participants responded that about that 20%–50% of their patients were noncompliant to the prescribed treatment. Lack of counseling to patient (5.5%), cost of therapy (5.5%), initial symptomatic relief (4.5%), drugs and duration of therapy (3.2%), and not following hygiene recommendations (3.2%) were acknowledged as individual factors responsible for noncompliance [Table 2]. However, a vast majority (78.2%) of dermatologist considered all these factors to be responsible for noncompliance.

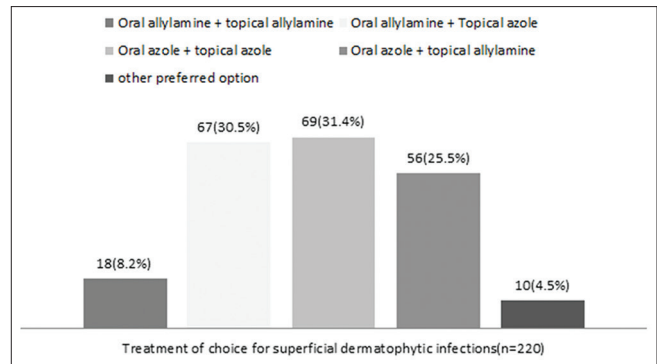


Figure 1: Treatment of Choice for Superficial Dermatophytic Infections

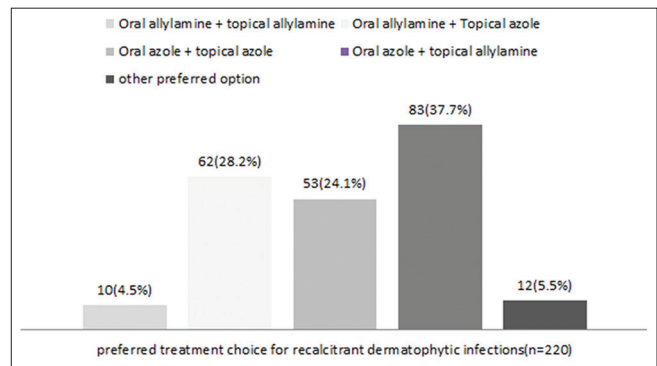


Figure 2: Preferred Treatment Choice for Recalcitrant Dermatophytic Infections

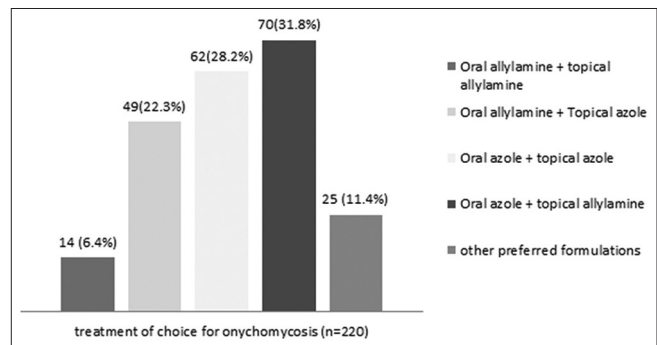


Figure 3: Treatment of Choice for Onychomycosis

About 92.3% of dermatologists stated that there is certainly a therapy gap in the management of dermatophytosis. Majority (80.9%) of the dermatologists identified all the following factors contributing for therapy gaps: Self-medication (5%), improper diagnosis at the initial stage of infection (2.3%), erratic usage of steroid combination (2.7%), over usage of current antifungal (5.5%), change of dermatophytic patterns (0.9%), lack of newer antifungal drugs (1.8%), cost of therapy (0.5%), and lack of patient compliance (0.5%).

Majority (97.7%) of these dermatologists agreed that there is a need for a national level treatment consensus on managing dermatophytosis in current Indian scenario and medical education activities such as patient awareness

Table 2: Noncompliance to antifungal treatment and treatment gaps (n=220)

	n (%)
Factors leading to noncompliance of treatment	
Initial symptomatic relief	10 (4.5)
Drug dosage and duration of therapy	7 (3.2)
Cost of therapy	12 (5.5)
Lack of counseling to patient	12 (5.5)
Not following hygiene parameters	7 (3.2)
All of the above	172 (78.2)
Factors contributing to treatment gap	
Self-medication	11 (5)
Improper diagnosis at initial stages of infection	5 (2.3)
Erratic usage of steroid combinations	6 (2.7)
Over usage of current antifungal	12 (5.5)
Change of dermatophytic patterns	2 (0.9)
Lack of newer antifungal molecules	4 (1.8)
Cost of therapy	1 (0.5)
Duration of therapy	0 (0)
Lack of patient compliance	1 (0.5)
All of the above	178 (80.9)

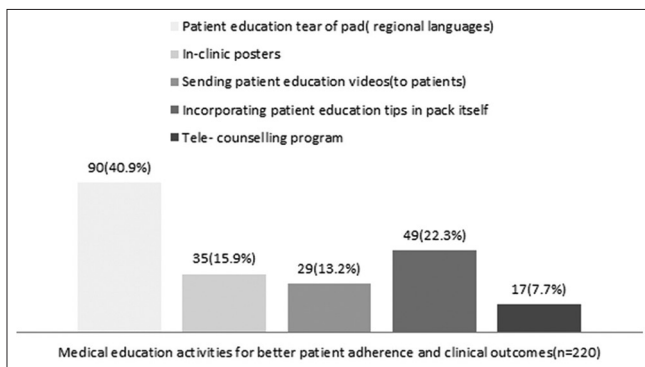


Figure 4: Medical Education Activities for Better Patient Adherence and Clinical Outcomes

programs (54.1%), continuous medical education (19.1%), focus group discussions (11.8%), advisory board meetings (8.6%), and case reports (6.4%) are required on a regular basis.

To improve patient adherence and clinical outcomes, educating the patient in regional language (40.9%), incorporating patient education tips in the drug package (22.3%), in-clinic posters (15.9%), sending patient education videos (22.3%), and tele-counseling program (7.7%) were suggested [Figure 4].

Discussion

From numerous studies conducted, it is an indisputable fact that there is an increase in the prevalence of dermatophytosis across the Indian continent in the recent past. The present KAP Study was conducted with a core objective to understand the factors contributing in this sudden rise of superficial dermatophytic cases in routine

clinical practice in India and treatment approaches being preferred in the management of dermatophytic infections, and to better understand the unmet needs from a dermatologist's point of view.

Reasons for the increase in the prevalence of Tinea infections

The number of infections reported in our survey was slightly higher than the previously conducted E-mail questionnaire survey, wherein, 1041 dermatologists registered with Northern chapter of the Indian Association of Dermatologists, Venereologists and Leprologists responded that 36.9% encountered 50–100 cases of dermatophytosis per week; 68.4% observed recurrent/chronic disease in 10%–30% cases.^[7]

A combination of factors such as increased steroid usage, patient's nonadherence to treatment, change in the pattern of the dermatophytes, and environmental and lifestyle factors were reported as the key factors contributing for the increase of tinea infections. Role of modifiable factors has been deemed important in tinea infections in previous studies. A study by Sharma and Tendolkar^[8] observed that apart from climatic factors and demographic factors such as age and gender which are nonmodifiable; environmental factors such as ill-ventilated houses (75.9%), tight clothing (33.6%), and unhygienic practices such as sharing of towels among other family members (51.8%) are some of the modifiable risk factors associated with an increased prevalence of tinea infections. A positive family history has been accounted as a major factor; close family members tend to share towels and wash clothes in the same lot that might be a reason for an increased risk of prevalence of dermatophytosis in the family contacts. In a survey-based study of 113 families of affected patients, it was observed that the spouse was always affected and overall 55.4% of family members were affected by dermatophytosis. Washing all the family's clothing together was a common factor. Further, all these families reported a history of using OTC drugs.^[9]

Jamuna *et al.* in a study of 72 clinically diagnosed cases of chronic dermatophytosis reported that 72% of the patients had an intrafamilial contact, 60% had shared fomites, and 77% of the patients wore occlusive and synthetic clothing.^[10] In yet another study of patients with dermatophytic superficial fungal infections, Lakhani *et al.* observed that 46% of patients had a positive family history while 37% had a history of fomite, overall, 65% of the patients had a history of use of OTC preparations.^[11] In children, a positive family history and/or close contact affection has been accounted for over 83% of cases of dermatophytic infections.^[12,13]

Some other studies also had similar observations such as exhausting physical activity in an open environment leading to excess sweating and the use of tightly worn

synthetic clothes resulting in increased humidity and temperature of the body which makes skin as a suitable growth environment for dermatophytes.^[5,13] Zacharia and Kunjukunju noted that 64% of patients with chronic dermatophytosis had a history of exposure to hot sun for >3 h and 68% of patients had a history of increased sweating.^[14]

Indiscriminate use of OTC drugs is an important risk factor that contributes toward gap in the successful management of dermatophytosis. In the present study, about 80.8% of the dermatologists responded that gaps in successful management included factors such as self-medication, improper diagnosis at initial stages of infection, improper usage of steroid combinations, over usage of current antifungals, change of dermatophytic patterns, lack of newer antifungal drugs, cost of therapy, improper duration of prescribed therapy, and lack of patient compliance. In a previous survey, rampant topical corticosteroid usage was accounted for nonresponse/chronicity in dermatophytosis by 72.5% of the dermatologists.^[7] In a previous study from eastern India, about 21.7% of patients had a history of application of OTC medications containing steroids and 3.85% agreed to application of indigenous preparations and “preparations containing coal tar, anthralin, salicylic acid.”^[15] Duration of topical steroid application was significantly correlated with the body surface area ($P = 0.000$) in a study of 235 children, of which 221 (94%) had applied topical steroid/steroid antifungal combination.^[16] It is pertinent to note here that mostly the patients are unaware of the adverse events that could be caused by the overuse of these steroid applications. In a study of 100 patients with dermatophytosis, though 77.94% of the patients had used steroid-based preparations, 89% of the patients had never heard of steroids and were not aware of the adverse effects of steroids.^[17]

Treatment choices for fungal infections

We observed that combination of topical and oral antifungal agents is the most preferred option to treat smaller localized tinea lesions followed by topical antifungal application alone and combination of topical antifungal and topical steroid therapy. For addressing symptomatic inflammatory tinea lesions with itching and redness, majority of the dermatologists preferred a combination of topical antifungal with systemic antihistaminics followed by topical antifungal agents with anti-inflammatory activity. Localized lesions that covered smaller body surface area may respond well to the topical therapies alone provided patients are adhering to the prescribed treatment regimens. However, lesions covering larger body surface area may not respond to topical therapies alone and combination with systemic antifungals should be considered.^[17] Data on combination therapies of topical and systemic therapies are still lacking. Sahoo and Mahajan^[2] on the management

of cutaneous dermatophytosis opined that among various options, topical allylamine for 4 weeks as treatment of choice for limited disease. For more extensive disease, both allylamine and azoles are effective management options. A meta-analysis by Rotta *et al.*^[18] evaluated the efficacy in the form of mycological cure at the end of treatment and sustained cure of antifungal treatment involving 14 different topical antifungals. No statistically significant differences among the topical antifungals concerning the outcome of mycological cure at the end of treatment were observed. For sustained cure, butenafine and terbinafine each were found to be superior to clotrimazole. Mahajan *et al.* conducted a sensitivity testing on 50 isolates of *T. mentagrophytes* isolated from 256 patients of suspected dermatophytosis observed that itraconazole was the most effective drug, followed by ketoconazole, terbinafine, fluconazole, and griseofulvin.^[19] In the present KAP Study, dermatologists opined that the preferred treatment of choice for recalcitrant dermatophytic infections is combination of oral azole and topical allylamine followed by combination of oral allylamine and topical azole, combination of oral azole and topical azole, other treatment options, and combination of oral allylamine and topical allylamine. Kaul *et al.*^[20] observed that in recalcitrant/recurrent dermatophytosis, a longer duration with or without an increase in the dose of terbinafine may be tried. However, if antifungal drug susceptibility pattern is supportive, itraconazole may be preferred as a systemic agent.

In general, an effective antifungal therapy should have a wide spectrum of activity, negligible toxicity, good penetration, and reservoir effect.^[21] Drug resistance is another issue while considering any antifungal therapy. A combination therapy using complementary drugs with synergistic mechanism action might be able to achieve these goals. Cyclosporine and D-octapeptides have been found to counteract drug resistance due to efflux pumps.^[22]

Duration of antifungal therapy

In the present KAP Study, more than one-third of the dermatologists opined that duration of treatment for new cases should be 4 weeks. For recalcitrant infections, two-thirds stated that the duration should be for 8–12 weeks. Similar views were expressed by Verma and Madhu^[3] on commonly employed treatment measures for superficial dermatophytosis. In a previous survey-based study, 38.9% of dermatologists agreed that for the management of chronic dermatophytosis, a longer duration of itraconazole (6–8 weeks) and higher doses of itraconazole (200 mg BD) should be used.^[7]

Non-compliance to antifungal treatment and treatment gaps

Poor compliance to prescribed medications and the duration is a major cause of treatment failure and re-infections.

Zacharia and Kunjukunju previously reported that a whopping 94% of their patients were non-compliant.^[14] In the present KAP Study, majority of dermatologists opined that noncompliance to prescribed antifungal therapy was about 30%–50% of their patients. Zhou *et al.*^[23] found that the overall compliance rate of the total antifungal treatment was 23.9%. Factors responsible for the noncompliance were adverse effects of drug, number of lesions, site of the disease, too busy in daily life, lack of related knowledge, personal income, and inconvenience in access to the treatment, keep forgetting in taking the medicine regularly as advised, being impatient and few others. Multiple possible causes for patient's nonadherence have been postulated in the literature. They include problems with the therapy, such as adverse events, poor instructions given to the patient by the prescriber, poor physician-patient relationship, poor memory on the part of patients, and patients' inability to pay for medications.^[20] To improve the adherence to medication, dermatologists in this KAP study stated that using local regional language to educate patients, posters, videos, and telecounseling programs can help to remove most barriers to successful therapy. Similar opinions were expressed by Osterberg and Blaschke^[24] where strategies to improve adherence involve practical actions such as frequent and better communication with patients on the part of healthcare personnel, better patient education, and easier dosing schedules. Weinberg JM^[25] suggested one daily dosing treatment to be effective in both cure and compliance.

Although KAP surveys permit rapid assessment, yield quantitative data that helps in assessing the knowledge of the participants, this study had certain limitations as well. First, dermatologists were not categorized based on place of practice (Rural/Urban/Metro) and facility (Private/Institution/Both). The difference in their knowledge/attitude/practice may be due to these factors. Second, the dermatologists who had at least 1 year of clinical experience after their PG were included in this study and this may not help in a comparative perspective of change in prevalence over the long term. Third, in KAP surveys it is difficult to get a standard reference to classify knowledge and practice levels of participants. This KAP study yielded important information about treatment approaches of superficial dermatophytosis that could help understand the needs, problems, and barriers to help plan and implement interventions for dermatophytosis.

Conclusion

Increased topical steroid usage, nonadherence to antifungal treatment, environmental factors, and lifestyle factors are some key factors that may have been responsible for the sudden rise of tinea infections in Indian settings. Combination of topical and oral antifungal therapy for a minimum of 4 weeks should be followed in addressing tinea lesions. Preferred treatment of choice for recalcitrant

dermatophytic infections is combination of oral azole and topical allylamine for 8–12 weeks. Poor compliance to prescribed medications and duration of therapy and poor personal hygiene are believed to be crucial factors to be considered for treatment failure and reinfections. Using local regional language would be more beneficial in educating the patient and posters, videos, and telecounseling programs would help in removing the barriers and to provide better clinical outcomes.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Acknowledgment

The authors acknowledge all the participating doctors in this survey-based study.

Financial support and sponsorship

The medical writing support for this manuscript was provided by Shivali Arora, medical writer for Knowledge Isotopes (<http://www.knowledgeisotopes.com>) and was funded by Dr Reddy's Laboratories Limited, India.

Conflicts of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest. Dr. Arun Inamadar and Dr. Madhu Rengasamy have not received any honoraria or grant for this project. Dr. Sujeet NC is an employee of Dr. Reddy's Laboratories India. The authors declare conflict of interest.

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