

Factors responsible for difficult to treat superficial fungal infections: A study from a tertiary healthcare centre in India

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Abstract

Background: Recurrent and clinically unresponsive dermatophytosis is being increasingly observed in India. However, there is little information regarding the extent of the problem and the factors responsible for these difficult to treat superficial fungal infections.

Aim: To identify factors contributing to difficult to treat recurrent superficial fungal infections.

Materials and methods: This prospective cross-sectional study enrolled 105 patients of all age groups presenting with either recurrent or long-standing dermatophyte infection attending the outpatient department of Dermatology, Venerology and Leprosy of Bharati Hospital, Pune, India, between September 2018 and March 2020. Patients were clinically examined, clinical history was taken and questions were asked regarding their current complaints and recorded in a proforma. Data were analysed using the SPSS software package.

Results: The males outnumbered females (74.3% vs 25.7%). A strong association was observed between the presence of past history and duration of disease ($p = .007$). The association of use of topical steroids or keratolytic agents with the duration of disease was statistically significant ($p = .022$). There was a statistically significant inverse association of duration of disease with dermatologist consultation ($p < .001$). The association between consultation with non-dermatologist and the duration of disease was statistically significant ($p = .035$).

Conclusion: Hyperhidrosis, obesity, positive family history, tight clothing and chronic diseases may be considered important factors in acquiring dermatophytic infection. However, when it comes to difficult to treat tinea infections, irrational usage of topical steroids, treatment from non-dermatologists and a past history of tinea appear to be more critical causative factors. Treatment of dermatophytosis by dermatologists/trained physicians and increasing general awareness of the public regarding the current situation about tinea in the country would help to alleviate the current crisis.

KEYWORDS

chronic dermatophytosis, recurrent dermatophytosis, superficial fungal infections

1 | INTRODUCTION

Dermatophytes are fungi that can utilise keratin and are responsible for superficial infections of skin, nail and hair known as dermatophytosis.¹ In common parlance, it is called a 'ringworm' infection due to the circular, itchy and inflammatory patches seen in the standard form of the disease. Occasionally, the patches may become widespread and may significantly impact social, psychological and occupational health, thereby compromising the quality of life.²

Dermatophytosis is a communicable disease that spreads by direct or indirect contact. Until recently, it was easily treatable using antifungal agents. In recent years, there has been an alteration in the disease characteristics, seriousness, response to treatment and relapse rate with conventional therapy.^{3,4} Currently, there is a considerable increase in dermatophytosis prevalence across India, reaching epidemic proportions.⁴ This has also given rise to difficult to treat fungal infections. Difficult to treat fungal infections are those that are unresponsive to treatment and exhibit multiple site lesions, recurrence or chronicity.^{5,6}

Numerous factors have been observed to be responsible for the development of recurrent and chronic dermatophytosis. These include the usage of irrational fixed drug combinations of steroid-antibiotic- antifungal drugs, the increasing use of broad-spectrum antibiotics, the growing numbers of immune-compromised people, increased prevalence of Trichophyton mentagrophytes infections causing inflammatory lesions and the extensive use of antifungals in the agricultural industry and antifungal drug resistance.⁴ However, the exact interplay of various above factors leading to the current situation remains speculative.

The purpose of the current study is to identify the factors contributing to difficult to treat superficial fungal infections and examine their interrelationship in developing difficult to treat fungal infection.

2 | MATERIALS AND METHODS

The current study was conducted at a tertiary care centre in western India. Ours was an observational, cross-sectional and descriptive study.

Institutional ethics committee approval was secured before conducting the study.

Patients visiting the dermatology outpatient department for management of dermatophytosis were screened and included in the study after obtaining informed consent.

Following inclusion criteria were utilised.

(1) Patients clinically diagnosed with recurrent dermatophyte infection (dermatophytosis in which the infection reoccurred within 6 weeks of stopping the adequate antifungal treatment with at least two such episodes in the last 6 months).

And / Or

(2) The patients having a long-standing fungal infection (disease continuing for more than 6 months to 1 year with or without recurrence despite being treated).

(3) Patients of all age group were included.

Participants who were unwilling were excluded.

2.1 | Collection of data

Participant age, sex, occupation and rest of the demographic details were noted.

Clinical history like the site, type and duration of the lesion along with any predisposing factors like exposure to an animal source (farmers, veterinary personnel and pet keepers) or family contact was noted in the Proforma. History of hyperhidrosis and type of clothing used regularly were enquired for. Any history of similar past complaints (which was significantly separated from the current prolonged episode) was noted. History of treatment taken, if any, was asked in detail. Details of past treatment were noted carefully as to sources of treatment, duration, regularity and medications. BMI of all patients was calculated.

2.2 | Plan of statistical analysis

Data were entered into Microsoft Excel, and statistical analysis was carried out in SPSS software version 17.0. Qualitative variables were presented as frequency and percentages. Quantitative variables were presented as mean (standard deviation) or median (range) depending upon data distribution. Bar diagram and pie charts were used for graphical representation of data.

Categorical variables between the two groups (presence or absence of side effects) were compared using Chi-Square test. Similarly, categories based on the duration of disease were compared in subgroups using the Chi-Square test. A 'P' value of less than .05 was considered as statistically significant.

3 | RESULTS

The current study was conducted in the intervening period of September 2018 to March 2020. 130 patients were studied during this period. Out of these, data of 105 patients were complete and could be included in the final study. The following observations were noted during the study.

The males (74.3%) outnumbered females (25.7%). The male: female ratio was 1:0.35.

A majority of cases (59.1%) were in the age group of 21 to 40 years, 24.8% were in the age group 41 to 60 years, 13.3% were aged less than 20 years, and 2.8% of cases were above 60 years of age.

The mean age was 33 years \pm 13 years, with the range being nine months to 81 years.

In most cases (52.4%), the duration of disease was between 1 to 3 years, in 41.9% of cases, the duration of disease was \leq 1 year while in 5.7% of cases, the duration of disease was more than three years.

Among the cases with the disease for ≤ 1 year, 61.4% of cases had hyperhidrosis while 38.6% did not. Among the cases with the disease for 1 to 3 years, 69.1% had hyperhidrosis, while 30.9% did not have history. Among the 6 cases with the disease > 3 years, 33.3% of cases reported hyperhidrosis while 66.7% of cases did not.

Among the cases with the disease for ≤ 1 year, 59.1% wore tight-fitting clothes while 40.9% did not. Among the cases with the disease for 1 to 3 years, 58.2% wore tight-fitting clothes, while 41.8% did not. Among the 6 cases with the disease for > 3 years, the number of cases who wore tight-fitting clothes equalled those who did not.

When the occupation was considered, we noted that 63.8% of cases were in occupations which were more prone to sweating, while 36.2% of cases were from occupations which were less prone to sweat.

14.28 % of subjects had co-morbidities. Diabetes mellitus (DM) was the most common co-morbidity in 7.6%, while 6.7% of cases had co-morbidities other than DM.

In the cases of ≤ 1 year, 11.4% had diabetes mellitus, while 88.6% did not. In the cases who had the disease for 1 to 3 years, 1.8% reported diabetes mellitus, while 98.2% did not. In the 6 cases with the disease > 3 years, 16.7% had diabetes mellitus, while 83.3% did not.

In the cases with the disease for ≤ 1 year, 4.5% had immunosuppressive disorders while 95.5% did not. In the cases who had the disease for 1 to 3 years, 1.8% reported immunosuppressive disorders, while 98.2% did not. In the 6 cases with the disease > 3 years, none of the cases had immunosuppressive disorders.

76.2% of subjects had a history of dermatophytosis before a prolonged current episode. In the cases with the disease for ≤ 1 year, 61.4% had a past history of the disease while 38.6% did not. In the cases with the disease for 1 to 3 years, 85.5% reported a past history, while 14.5% did not. In the six cases with the disease > 3 years, all the cases reported a disease's past history.

In total, 82.9% of cases had a family history of dermatophytosis. 79.6% of patients with disease duration ≤ 1 year had a family history, 83.6% of patients with disease for 1 to 3 years had a family history, while 100% patients with disease duration of > 3 years had a positive family history.

87.6 % ($n = 92$) of cases had taken at least some form of prior treatment, while 12.4% ($n = 13$) had not taken any treatment.

Out of 92 patients who took treatment, 87% had taken medications directly from chemists, 69.5% had non-dermatologist consultations including practitioners of the traditional system of medicine (TSM) who prescribed them modern medicines, 68.5% had taken self-medication based on advice from relations, advertisements and/or internet.

On enquiring the treatment history in detail from subjects, it was found that 54.3% of patients had never visited a dermatologist for the treatment of dermatophytosis. 45.7% ($n = 42$) patients had consulted a dermatologist at least once for treatment either as a sole or as one of the sources of treatment.

Of the 34 cases whose duration of disease ≤ 1 year, 88.2% had consulted a dermatologist. Of the 52 cases who had a duration of

TABLE 1 Various factors suspected of contributing to the prolonged duration of the superficial dermatophytic infections and their statistical significance

Sr No	Causative factor	'P' value	Remark
1	Hyperhidrosis	.203	NS
2	Tight clothing	.914	NS
3	Immunosuppressive disorders	.656	NS
4	Diabetes mellitus	.100	NS
5	Past history	.007	Significant
6	Family history	.448	NS
7	Dermatologist consultation	$<.001$	Significant
8	Topical steroids or keratolytic agents	.022	Significant
9	BMI categories	.648	NS

Note: Abbreviations: NS, Not significant.

disease between 1 to 3 years, only 21.2% of cases had consulted a dermatologist, while of the 6 cases who had a duration of disease more than 3 years, only 16.7% had consulted a dermatologist.

Out of patients who took treatment from dermatologists ($n = 42$), only 19.1% of cases were regular and had taken a reasonable course of treatment. In comparison, 80.9% of cases were not regular in pursuing their treatment and had a history of inadequate treatment.

In the cases with the disease for ≤ 1 year, 77.3% had applied topical steroids or keratolytic agents while 22.7% had not. In the cases with the disease for 1 to 3 years, 94.6% reported the use of topical steroids or keratolytic agents, while 5.4% did not. In the 6 cases having the disease > 3 years, all had used topical steroids or keratolytic agents.

62.0 % of cases showed signs of topical steroid use during the first visit to our OPD, while 38% did not.

A majority of cases (53.3%) experienced atrophy, 25.0% of cases reported side effects of striae and hypopigmentation and 23.9% reported adverse effects of acneiform eruption.

The majority of cases had normal BMI (58.1%), 28.6% of cases were overweight, 9.5% of cases were obese and 3.8% of cases were underweight. Among the cases who had the disease for ≤ 1 year, 6.8% of cases were underweight, 52.3% of cases had normal BMI while 40.9% of cases were overweight or obese. Among the cases who had the disease for 1 to 3 years, 1.8% of cases were underweight, 61.8% had normal BMI and 36.4% cases were obese. Among the 6 cases having the disease for > 3 years, 66.7% of cases had normal BMI while 33.3% of cases were obese or overweight.

3.1 | Statistical analysis

Chi-square test was used to check statistical significance between various factors mentioned in the Table 1 and duration of infection.

As seen in Table 1, past history of dermatophytic infection, consultation with dermatologist and usage of topical steroid/keratolytic

were found to be significant, while rest of the factors were found to be non-significant.

4 | DISCUSSION

This prospective cross-sectional exercise studied 105 patients of all age groups presenting with either recurrent or long-standing dermatophyte infection attending the outpatient department of Dermatology, Venerology and Leprosy of Bharati Hospital, Pune between September 2018 and March 2020.

This study has considered two types of difficult to treat fungal infections: recurrent infections and chronic infections. Dermatophytosis in which the infection reoccurred within 6 weeks of stopping the adequate antifungal treatment with at least two such episodes in last 6 months was considered as 'recurrent dermatophyte infection', whereas disease continuing for more than 6 months to 1 year with or without recurrence despite being treated was regarded as 'chronic dermatophytosis'.

In our study, the males outnumbered females (74.3% vs 25.7%). The male: female ratio was 2.89:1.

As shown in Table 2, several other studies also reported male preponderance similar to our study, the only exception being a study by Sivaprakasam and Govindam,¹² which reported a female preponderance.

The variation in the incidence of superficial infections between the sexes probably reflects the differing sebum production rates. Higher incidence in men may reflect their increased likeliness to engage in more outdoor and physical activities making them more prone to sweating and trauma.^{1,11,13,14}

In our study, a majority (59.1%) of cases were in the age group 21 to 40 years, reflecting that the most commonly younger population bore the brunt of difficult to treat infection. Across various studies, we noticed a similar trend of the young people being the most common affected.

The differences in the occurrence of superficial infections between the age groups reflect differing rates of immunity fluctuations with ageing.¹⁵ Generally, across various studies, it has been observed that chronic dermatophytosis tends to affect a relatively younger population. This may be probably because younger people are more likely to be engaged in activities that may provide the fungus with a conducive atmosphere for growth. Also, during our study, we noted that younger, professionally active people tend to miss regular follow-ups, which may hamper mycological cure and result in chronic infection.

In our study, in a majority of cases (52.4%), the duration of disease was between 1 to 3 years. In 41.9% of cases, the duration of disease was between six months to one year. In 5.7% of cases, the duration of disease was more than three years.

In a study by Vineetha *et al.*⁹ the duration of illness was 1–6 months in 47% and more than 6 months in 53%.

The association of wearing tight-fitting clothes with the duration of disease was not statistically significant ($p = .914$) in the current study.

Like our observation, a study in Varanasi by Singh *et al.*⁷ also reported that wearing jeans did not increase the risk of chronic or relapsing tinea.

However, a recent consensus statement formulated by the IADVL Taskforce Against Recalcitrant Tinea (ITART) advises against the use of synthetic and tight clothing. The statement also discourages wearing bands, threads, drawstrings and rings as they could carry fungus and add to persistence and recurrence of infection.¹⁶

The association of hyperhidrosis with the duration of disease was found to be statistically insignificant ($p = .203$) in our study.

Similar to our findings, Singh *et al.*⁷ also reported that a history of excessive sweating did not increase the risk of chronic or relapsing tinea.

In our study, 76.2% cases had past history of similar infections. By past history, we mean dermatophytosis which occurred before the current and prolonged episode.

A statistically significant association was observed between duration of disease and presence of past history.

If a person is infected with dermatophytosis and gets cured still he/she continues to be exposed to the factors that probably caused the dermatophytosis in the first place. For example, hot and humid climate, excessive sweating, tight-fitting clothes, improper washing and drying of clothes, sharing of bathing soap and bath towel, continued contact with infected community members etc There is a greater chance of re-contracting dermatophytosis. No study has examined the association of duration of disease with presence of past history.

Re-infection from the contacts or through fomites is a significant contributing factor for the increasing prevalence of chronic and recurrent forms of superficial dermatophytosis.¹⁷

Pathania *et al.*⁸ reported that family members of 72% of patients had dermatophytosis, the spouse being frequently affected.

Family history of dermatophytosis was found in 21% of cases in the first episode of dermatophytosis and 28% in chronic cases in a study by Vineetha *et al.*⁹ The studies, however, did not comment on the statistical significance of the association between family history and duration of disease.

TABLE 2 Distribution of disease among the genders in various studies

	Current study	Singh <i>et al.</i> ⁷	Pathania <i>et al.</i> ⁸	Vineetha <i>et al.</i> ⁹	Ghosh <i>et al.</i> ¹⁰	Janardhan and Vani ¹¹	Sivaprakasam and Govindam ¹²
Male	74.3%	67.3%	63%	72%	52.5%	65%	40%
Female	25.7%	32.7%	37%	48%	47.5%	35%	60%
M:F ratio	2.89:1	2.08:1	1.7:1	1.5:1	1.1:1	1.86:1	1:1.5

Singh *et al*⁷ reported a positive association between family history of tinea and chronic or relapsing tinea. They opined that early treatment of a family member with tinea is likely to reduce the chances of an individual getting chronic and relapsing tinea.

Sultan *et al*⁵ have also reported the presence of dermatophyte infection among family members to be a major risk factor with a significant association with chronic/ recurrent infections.

A recent consensus statement formulated by ITART recommends that since infection among other family members is very common, the treatment of all infected members simultaneously is essential to prevent recurrences or persistence of infection.¹⁶ In our study, like other authors, we frequently noticed the presence of family history in patients; however, the association of family history with disease duration was not statistically significant ($p = .448$).

Comorbid conditions such as diabetes can predispose an individual to immunosuppression, thereby promoting recurrence or persistence of infection.¹⁸

In our study, there were 7.6% known cases of diabetes mellitus, and 6.7% of cases had other associated diseases. However, when it comes to difficult to treat dermatophytosis infection, our study did not find any statistically significant correlation between the presence of diabetes mellitus and duration of tinea infection. In a study by Singh *et al*⁷ 5.3% of cases had pre-existing diabetes. The authors found a positive association between diabetes mellitus and the risk of chronic or relapsing dermatophytosis. A study by Vineetha *et al*⁹ reported that diabetes and thyroid disorders were present in 2.6% of cases each in the first episode of dermatophytosis and diabetes was present in 11% of chronic cases ($p > .5$). Bindu *et al*¹⁹ noted diabetes in 11% cases in the first episode of dermatophytosis. Diabetes mellitus (30%) and bronchial asthma (16.6%) were the most frequent systemic associations observed in a study by Sivaprakasan and Govindan.¹² When the association between duration of disease and dermatologist consultation was assessed, it was seen that there was a statistically significant inverse association of duration of disease with dermatologist consultation ($p < .001$). This highlights that treatment for dermatophytosis from non-dermatologists had higher chances of failure.

During our study, when we examined patients' past prescriptions by non-dermatologists, we came across many instances of improper management. Many prescriptions included systemic antibiotics without any valid indication. Simultaneous usage of proton pump inhibitors and itraconazole was widespread, reducing the absorption and effectiveness of itraconazole. Use of topical steroids either alone or in combination with antibiotics and antifungals was frequent.

During the study, we noted that pharmacists directly dispensed the irrational combination of topical steroid-antifungal-antibiotic agents and oral antifungals (often in wrong doses and manner) without a physician prescription.

Due to the skewed ratio of dermatologists in the rural areas, patients often visit a general practitioner or practitioner of the traditional system of medicine (TSM) for their complaints. As a result, the

patient is treated for dermatoses by a doctor who is inadequately trained for the purpose, consequently prescribing steroids injudiciously.²⁰ This has led to a veritable epidemic of steroid modified tinea in India. Even in urban settings like in current study, the general population's awareness about proper management from dermatologist remains low.

The association of use of topical steroids or keratolytic agents with chronicity of disease was found statistically significant ($p = .022$).

Like our study, Sultan *et al*⁵ in Srinagar also reported that injudicious use of topical steroids was a major risk factor with a significant association with chronic/ recurrent infections. In a study by Vineetha *et al*,⁹ the drug history of chronic dermatophytosis revealed the use of topical steroid- antifungal combination in 42%, topical steroid in 21%, azoles in 28% and allylamines in 19% cases.

Topical corticosteroid prescription, whether alone or in combination with other components, was strongly discouraged by all the experts of the Indian Association of Dermatologists, Venereologists and Leprologists (IADVL) Taskforce Against Recalcitrant Tinea (ITART).¹⁶

Obesity is a host-related risk factor for dermatophytosis.²¹ In our study, the majority of cases had a normal BMI (58.1%). A study by Singh *et al*⁷ reported a mean BMI to be 23.12 ± 4.69 . Mean BMI in our study was 24.14 ± 4.15 . In our study, the association of BMI categories with the duration of disease was not statistically significant ($p = .648$). In line with our observation, Singh *et al*⁷ also reported that BMI did not increase chronic or relapsing tinea risk. As per the consensus statement formulated by IADVL Taskforce Against Recalcitrant Tinea (ITART) on dermatophytosis management in India, obese patients should be advised to lose weight to avoid recurrence of infection, particularly in intertriginous regions like the groin.¹⁶

5 | CONCLUSION

Hyperhidrosis, obesity, positive family history, tight clothing and chronic diseases may be considered important factors in acquiring dermatophytic infection.

However, when it comes to difficult to treat tinea infections, irrational usage of topical steroids, treatment from non-dermatologists and a past history of tinea appear to be more critical causative factors.

Treatment of dermatophytosis by dermatologists/ trained physicians, increasing general awareness of the public regarding the current situation about tinea in the country would help to alleviate the current crisis.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

AUTHOR CONTRIBUTION

Amit Jain: Conceptualization, Data Curation, Formal Analysis, Investigation, Methodology, Project Administration, Resources, Visualisation, Writing—Original, Draft, Writing—review and editing; Suyog Dhamale: Suyog Dhamale: Conceptualization, Data Curation, Formal Analysis, Investigation, Project Administration, Validation, Writing—review and editing; Vidyadhar Sardesai: Conceptualization, Methodology, Project Administration, Supervision, Writing—review and editing.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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