



Prevalence of Dermatophytes in Egypt & Mycological Assessment Before and After Itraconazole Therapy in Patient with Recalcitrant Dermatophytosis

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ABSTRACT

Background: A common superficial illness called dermatophytosis brought on by dermatophytes, a genus of keratinophilic, pathogenic fungi. In addition to invading the epidermal barrier, host immunological reactions to dermatophytes may partially cause tissue injury and pathologic inflammation. Understanding the pathophysiology of dermatophytosis, including fungal virulence factors and immune responses against pathogens, is therefore very beneficial. Dermatophytes are classified into nine genera based on the characteristics of their asexual spores, or macroconidiae. This study aimed to detect the prevalence of dermatophytes in Egypt with mycological assessment before and after oral itraconazole therapy for chronic, recurrent, and recalcitrant dermatophytosis.

Patients and methods: This study included 75 patients with different clinical types of chronic, recurrent, and/or recalcitrant dermatophytosis. All patients were subjected to adequate dermatological examination as regarding site and size of the lesions, the presence of associated papules, vesicles and/or pustules, lesion distribution, morphological variants, duration, and the presence of inflammation and scaling at each follow-up visit. All patients received oral itraconazole at a dose of 200mg/day for 6 weeks.

Results: *T. mentagrophytes* was the most common isolated dermatophyte in patient with recalcitrant dermatophytosis (28%), followed by *T. rubrum* which represents (20%) of the recalcitrant tinea cases. as regarding Therapeutic response after end of itraconazole therapy, complete mycological cure was observed in (66.7%) of cases and complete clinical cure (69.3%) of cases. Recurrence after end of itraconazole therapy was detected in 13 cases (17%).

Conclusion: *T. mentagrophytes* the most common fungal isolates in patients with recalcitrant dermatophytosis.

Key words: Dermatophytosis; Dermatophytes; Itraconazole; Mycological; Prevalence.

INTRODUCTION

Dermatophytosis regarded as a common skin condition globally. Approximately 20% to 25% of the global population is affected by it. In tropical nations, two of the

most significant risk factors for dermatophytosis are moisture and warmth. The frequency of dermatophytosis also linked to other variables, such as excessive sweating

and poor cleanliness. Migration, lifestyle, immunosuppressive status, immunosuppressive therapy, and socioeconomic circumstances can all affect this epidemiological distribution [1].

With the wide range of antifungal medications on the market, treating superficial fungal infections has always been straight forward. But during the past few years, a worrisome trend in dermatophytosis has been noted, with a significant shift in patient clinical profiles linked to a rise in the incidence of chronic, recurrent, and resistant cases [2].

The increase in the incidence of resistance, particularly in *T. mentagrophytes* and *T. rubrum* species, is currently reported especially from India and South-East Asia. The problem with dermatomycoses treatment in this region began as early as 2010 and has significantly worsened in subsequent years.³ Resistant isolates often have reduced affinity for terbinafine due to identify point mutations that cause one or more amino acids to be substituted in the squalene epoxidase enzyme (SQLE) gene, altering the conformation of the substrate binding site and significantly reducing the affinity of the drug for the enzyme. This results in a resistant phenotype of the strains and the antifungal agent's minimum inhibitory concentration (MIC) rises [3].

In a study conducted in Egypt by **Khattabet al.** [4] in patients with chronic recurrent dermatophytosis. They were equally divided into three groups: itraconazole monotherapy, combined itraconazole/isotretinoin therapy, and voriconazole monotherapy, and the most common isolated fungi was *T. rubrum* followed by *T. mentagrophytes* and *T. violaceum*.

AIM OF THE WORK

This study aimed to detect the prevalence of dermatophytes in Egypt with mycological assessment before and after oral itraconazole therapy for chronic, recurrent, and recalcitrant dermatophytosis.

PATIENTS AND METHODS

75 patients with various clinical forms of resistant severe dermatophytosis were included

in this investigation. Patients with cardiac conditions, those with impaired liver or kidney function, women who were pregnant or lactating, or those who had received topical or systemic antifungal medication within two weeks of the study's start were not allowed to participate. Recalcitrant dermatophytosis refers to recurrences, relapses, reinfection, persistence or chronic infections, and possibly microbiological resistance. Recurrent tinea is defined by the reoccurrence of the disease within a few weeks (4 weeks) of the completion of approved systemic therapy.

Study design: Every patient underwent a comprehensive history taking and a comprehensive questionnaire that included information on their socio demographics (age, sex, place of residence, occupation), its course, duration, recurrence, and the medications they had previously received. Enough clinical dermatologic examinations for tinea should be performed at baseline and at every follow-up appointment to determine the location, size, distribution, morphological variations, presence of inflammation, and scaling of the lesion, along with any associated papules, vesicles, and pustules. During the research time, patients were advised not to utilize any other fungal-directed medication.

Inclusion criteria were adult patients of both sexes having chronic, recurrent, recalcitrant dermatophytosis (Including atypical forms of tinea corporis, tinea cruris, tinea pedis, tineafaciei). With laboratory confirmation by direct microscopy and fungal culture.

Exclusion criteria were pregnancy and lactation, Previous systemic treatment within 1 month or topical within 2 weeks prior to the study, Immunosuppressive states, Hepatic&Renalimpairment.

Ethical considerations:

The Institutional Review Board (IRB) of Zagazig University approved the protocols (approval number is 10690/26/4/2023) and informed consent forms utilized in this investigation. Each participant completed a written survey including personal and medical information and signed a written consent form.

Itraconazole therapy:

All patients received oral itraconazole at a dose of 200mg/day for 6 weeks. Every visit involved photographic assessment and comparison using baseline photos. At every appointment, the unfavorable effects both immediate and delayed were noted. Following the end of treatment, all patients were monitored for six months in order to look for any recurrences. At the conclusion of the six-month follow-up period, the culture was performed again for cases that were clinically recurrent.

Statistical analysis:

Data were analyzed using IBM SPSS 23.0 for windows (SPSS Inc., Chicago, IL, USA) and NCSS 11for windows (NCSS LCC., Kaysville, UT, USA). Quantitative data were expressed as mean ± standard deviation (SD). Qualitative data were expressed as frequency and percentage. Data were tested for normality using Kolmogorov Smir.

RESULTS

The majority of patients were females (66.6%). The age of the patients ranged from 13 to 73 years. The most affected site was lower limb (40%), then trunk (37.3%), and upper limb (17.3%), and lastly the face (16%). History of recurrent tinea (50.6%), As regards the type of tinea according to the site (8%) had tinea faciei, while (9%) had tinea barbae, and (10%) had tinea mannum, (15%) had tinea corporis, (24%) had tinea cruris, (6%) had tinea pedis, (5%) had onchomycosis(**Table 1**).

Fungal isolates of the culture:

The most prevalent isolated dermatophyte found in the patient was *T. mentagrophytes*.

with recalcitrant dermatophytosis (number=21, 28%), followed by *T.rubrum*(number=15) which represents 20% of the recalcitrant tinea cases. *T. verrucosum*(number=8, 10.7%), *T.interdigitale* (number= 6, 8%), *T.soudanense*(number=5, 6.7%), *T. concentricum*(number=5, 6.7%), *T. erniacea* (number=4, 5.3%), *T.tonsurous* (number=6, 8%) and *E.follucosum*(number=5, 6.7%) **Table (2)**.

Figure 1: A 26 years-old female patient with recalcitrant and recurrent tinea manuum (A), (B) demonstrating full lesion healing six weeks following itraconazole therapy.

Figure 2; A 60 years-old female with recalcitrant and recurrent tinea corporis (A),(B) demonstrating full lesion healing six weeks following itraconazole therapy.

Therapeutic response after end of itraconazole therapy:

Mycological cure

Mycological cure occurred in 50 cases (66.7%) while 25 cases (33.3%) were still positive at the end of therapy, clinical cure was complete in 52 cases (69.3%), while incomplete cure occurred in 23 cases (30.6%) of incompletely cured 8 cases attained partial response (10.7%) **Table (3)**.

Recurrence after end of itraconazole therapy:

Recurrence was detected in 13 cases (17%).

This table shows that the most common factors affecting therapeutic response was female gender that gave high percent of complete response (33.3%) and short disease duration where tinea of the least duration (from 3 to 6 months) gave higher response (33.3%) (**Table 4**).

Table (1): Baseline characteristics in patients with recalcitrant dermatophytosis:

	N=75	Percentage %
Age		
Mean ±SD	45.6 ± 11.7	
Range	13-73	
Sex		
Male	25	33.3%
Female	50	66.6%
Type of tinea		

Tinea faciei	8	10%
Tinea barbae	9	12%
Tinea manuum	10	13.3%
Tinea corporis	15	20%
Tinea cruris	24	32%
Tinea pedis	6	8%
Onchomycosis	5	6.6%
Duration of disease		
3- 6 months	30	40%
6m - 1 year	18	24%
>1 year	27	36%
Previous treatment		
Ultrariseofulvin	4	5.3%
Terbinafine	8	10.6%
Itraconazole	5	66.6%
Fluconazole	3	4%
Voriconazole	4	5.33%
Lamisil		
Tinea distribution		
Face	12	16%
Upper limb	13	17.3%
Lower limb	30	40%
Trunk	28	37.3%
History of recurrent tinea	38	50.6%

Table (2): Fungal isolates of the culture in patients with recalcitrant dermatophytosis:

Fungal isolates	N=75	Percentage %
<i>T. rubrum</i>	15	20%
<i>T. mentagrophytes</i>	21	28%
<i>T. verrucosum</i>	8	10.7%
<i>T. interdigitale</i>	6	8%
<i>T. soudanense</i>	5	6.7%
<i>T. concentricum</i>	5	6.7%
<i>T. erniacea</i>	4	5.3%
<i>T. tonsurous</i>	6	8%
<i>E. follicosum</i>	5	6.7%

Table (3):Therapeutic response after completion of itraconazole therapy:

	Itraconazole	
	N=75	%
Mycological cure		
Positive	25	33.3%
Negative	50	66.7%
Clinical cure	52	69.3%
Complete	23	30.6%
Incomplete:		
Partial response	8	10.7%
No response	15	20%

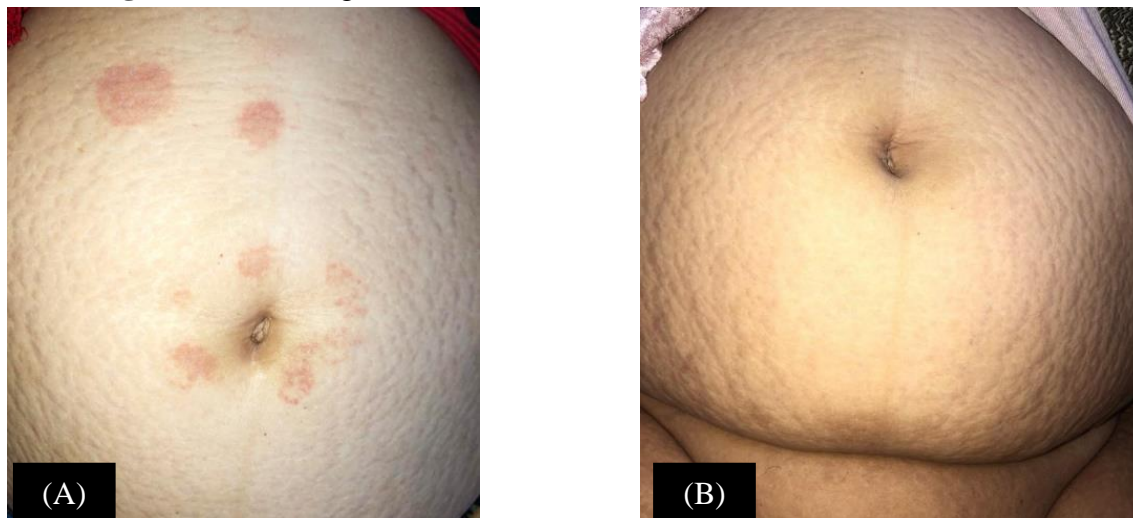
Table (4) Relation between therapeutic response and baseline characteristics:

Tinea characteristics	Therapeutic response	N= 75	
		N	%
Age Range	Complete Partial No	33.5 (13-73) 27 (26-53) 46 (44-52)	
Male gender	Complete Partial No	20 5 0	26.6% 6.6% 0.0%
Female gender	Complete Partial No	25 20 5	33.3% 26.7% 6.6%
Duration: 3-6 months	Complete Partial No	25 0 5	33.3% 0.0% 6.6%
6 months-1 years	Complete Partial No	15 1 2	20% 1.3% 2.6%
>1 years	Complete Partial No	19 6 2	25.3% 8% 2.6%
Tinea distribution: Face	Complete Partial No	10 1 1	10% 6.7% 1.3%
Upper limb	Complete Partial No	20 0 8	26.7% 0.0% 10.6%
Lower limb	Complete Partial No	25 4 1	33.3% 5.3% 1.3%
Trunk	Complete Partial No	12 1 0	16% 1.3% 0%
History of recurrent tinea	Complete Partial No	30 6 2	40% 8% 2.7%

Figure (1): Showing recalcitrant tinea in one hand before and after treatment.



Figure (2): showing recalcitrant tinea in the abdomen before and after treatment



DISCUSSION

The most prevalent superficial fungal infection, dermatophytosis, is brought on by keratinophilic fungi that can cause a variety of pathologic clinical presentations, such as tinea corporis, tinea cruris, tinea pedis, etc. *Trichophyton*, *Microsporum*, and *Epidermophyton* are the three genera of dermatophytes that cause it [5].

The prevalence of atypical clinical varieties of dermatophytosis, as well as chronic, recurrent, and difficult-to-treat forms, is on the rise. Many antifungals are employed in the hopes of providing a full recovery, but these rarely work [6].

Triazoleantimycotic drug itraconazole has potent keratophilic and lipophilic characteristics. It works by inhibiting 14- α -demethylase, which impairs sterol production in the fungal cell membrane[7].

In this work, we assessed the effectiveness of itraconazole medication before and after treatment of dermatophytosis that is persistent, recurring, and resistant to treatment.

The current study's cure rate and mycological cure using oral itraconazole were 69.3% and 66.7% higher, respectively, than those reported by **Khattab et al** [4]. Who demonstrated mycological cure of 56.7% and lower cure rates, including complete cure in 53.3% of patient. Given that *T. Mentagrophytes* was the most common organism in our study (28%), whereas *T.rubrum* was the most common fungus in the

other study (56.7%), this discrepancy may be explained by variations in the causative fungi. There have been reports linking *T. rubrum* to more persistent and resistant dermatophytosis[8].

Nenoff et al. [9]. reported that mentagrophytes might be disseminated Indian-wide due to wide spread topical steroid abuse (now called the T. indotinea). In our study as well, we found a predominance of *T. mentagrophytes*, However, due to limited resources, molecular research was unable to be performed. The epidemiological transition from *T. rubrum* to *T.mentagrophytes* has therapeuticimplications. Zoophilic *T. mentagrophytes* has acclimatized and anthropized, with quicker transmissibility, increased virulence, and improved survival on fomites.

The present study is also higher than that done by **Sharma et al.** [8], who showed complete resolution in 50% of their patients. But similar to cure rates reported by **Singh et al.**[10] showed complete cure in 66% of patients. On the contrary, the cure rate with oral itraconazole in the present study was lower than that reported by **Bhatia et al**[11], who showed mycological cure of 91.8%. Additionally, **Shah et al.** [12], have shown 76.31% complete cure in response to itraconazole. This difference may be due to short duration of treatment 3 weeks in Sharma study, and the number of patients enrolled in the study of Bhatia 130 patients makes it

higher in mycological cure rate and the study treated dermatophytic infection not recalcitrant one as this study, but in **Shah** study they used additional ciclopiroxolamine cream for 6 weeks along with antihistamines and also the study didn't treat recalcitrant tinea.

In this study, 13 out of 75 patients who were totally cured (17%) had recurrence after using itraconazole. This rate of recurrence is more than the 12% reported by Singh et al. This discrepancy might result from the fact that our study had a longer follow-up period (6 months) than their study did (8 weeks only). The high rate of recurrence seen with standard itraconazole therapy may be related to the difficult problem of recalcitrant dermatophytosis, which is becoming more resistant to the array of traditional antifungal drugs that were once useful against naive tinea. Furthermore, a number of the itraconazole patients included in this trial had previously received oral itraconazole therapy but had relapsed after stopping treatment [13].

CONCLUSION

In conclusion, *T. mentagrophytes* the most common fungal isolates in patients with recalcitrant dermatophytosis

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