

## A PROSPECTIVE COMPARATIVE STUDY TO EVALUATE THE EFFECTIVENESS IN ORAL ANTIFUNGALS: FLUCONAZOLE VERSUS TERBINAFINE IN PATIENTS WITH DERMATOPHYTOSIS

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### ABSTRACT

**Background:** The systemic antifungals such as fluconazole, itraconazole, terbinafine, griseofulvin are widely used for treating dermatophytosis. Here, the aim of the study is to evaluate the effectiveness of two oral antifungals: Terbinafine and Fluconazole. **Methods:** The study was conducted in the outpatient department of dermatology for a period of 6 months. Patients who are clinically diagnosed with dermatophytosis were selected after satisfying inclusion & Exclusion criteria and divided into two groups. Group A received Fluconazole 150mg thrice a week & Group B patients received Terbinafine 250mg daily. The participants were followed up for further evaluation. **Results:** In our study, the effectiveness of two oral antifungals was compared based on the observation of patients TSS (Total Symptom Score) and Extent of lesion score (BSA), which implied that both drugs are effective individually. In reduction of TSS, Group-B patients treated with terbinafine had greater effectiveness, that is a significant mean difference was observed in Group-B patients [7.83(baseline)→2.80(4<sup>th</sup> week)] compared to Group-A patients [7.00(baseline)→4.43(4<sup>th</sup> week)]. Also, Group-B patients who received Terbinafine had significant reduction of lesion score [1.8 (baseline) → 0.43 (4<sup>th</sup> week)] and they achieved more clearance of lesions compared to Group-A patients [1.36(baseline)→0.63(4<sup>th</sup> week)] who received fluconazole. P-value was found to be statistically significant. **Conclusion:** Here we conclude that both oral antifungals, fluconazole and terbinafine are effective in treatment. Nevertheless, Oral Terbinafine was found to be more effective than fluconazole in treating patients with dermatophytosis as it signifies good improvement in the clinical symptoms despite patient age, sex and duration of disease.

**KEYWORDS:** Dermatophytosis, Fluconazole, Terbinafine.

### INTRODUCTION

Superficial fungal infection caused by a dermatophyte is termed as dermatophytosis. It is one of the most common diseases caused by fungi known as dermatophytes.<sup>[1]</sup> Dermatophytes belongs to a group of taxonomically related fungi which has ability to form molecular attachments to keratin and use it as a source of nutrients allows them to colonize keratinized tissues, including stratum corneum of epidermis, hair, nails and the horny tissues of animals. Most of the fungi reside in the soil and are involved in decomposition.<sup>[1]</sup> However, dermatophytes can infect living hosts. In living hosts, dermatophytes usually remain in superficial tissues such as epidermis, hair, and nails, serious consequences are uncommon, and infection can be self-limiting.<sup>[2]</sup>

However, the illness may be uncomfortable as well as disfiguring especially when the skin lesions are widespread. Superficial tinea infection affects 20-25% of world population and is common infective dermatoses in clinical practice.<sup>[3]</sup> Global burden of diseases lists fungal skin diseases as the fourth most prevalent disease globally with significantly impaired quality of life of the patients.<sup>[4]</sup> Moisture and warm conditions are the most encouraged factors for the development of dermatophytosis in tropical conditions. Other factors include increased sweating which may result from outdoor physical activities, hot weather and low degree of hygiene. However, epidemiology of disease has also changed due to lifestyle, migration, socioeconomic conditions.<sup>[3]</sup> Dermatophytosis are clinically classified by

infection site as Tinea corporis(body), Tinea cruris(groin), Tinea manuum (hand), Tinea capitis/favus (Head), Tinea pedis (Foot), Tinea faciei(face), Tinea unguium (Nails).<sup>[5]</sup> Intertriginous areas including groin, axilla, and inter-web spaces are more susceptible to infection due to excess sweating, rubbing and alkaline pH. In limited and solitary lesions, topical lesions are enough but in diffuse and inflammatory lesions, administration of oral antifungal therapy is needed.<sup>[6]</sup> First-line therapy is based on the use of topical agents, typically imidazole antifungals. When such therapy is ineffective, oral therapy with antifungal agents such as terbinafine, itraconazole, fluconazole usually follows. We planned to study the effectiveness of oral antifungals of different category allylamine antifungal and triazole antifungal in patients with dermatophytosis in a government tertiary care hospital using Terbinafine and Fluconazole as the candidate drug, as they are commonly used drugs in the hospital setting for treating tinea infections.

The aim and objective of the study was to compare the effectiveness of Fluconazole and Terbinafine in patients with dermatophytosis.

#### MATERIALS AND METHODS

The study was carried out in the Dermatology outpatient department of government medical college and hospital, Nagapattinam. The study type was a prospective, observational, comparative study with a sample size of sixty patients. The Study was conducted in accordance with all ethical standards of the institutional ethics committee, Written informed consent was obtained from all the patients. The patients who were clinically diagnosed with dermatophytosis and those who were not responding to topical antifungal therapy were included in the study. Both male and female patients were

included in the study with age group of 18-60 years. Patients below age of 18 years and above age of 60 years were not included in the study. Patients who were not willing to give informed consent were excluded from the study and pregnant and lactating women were excluded. Patients with hepatic disease, Diabetes, Thyroid disorders, acute or chronic renal disease and obesity were excluded.

Patients with clinically diagnosed dermatophytosis during the study period were enrolled into the study. Sixty cases were selected, and they were divided into two groups. Group A patients received Tab. Fluconazole 150mg thrice a week and Group B patients received Tab. Terbinafine 250mg daily. Patients were followed up for *Effectiveness evaluation* for that Total symptom score (TSS) was used, it included scoring of pruritus (Itching), Erythema (Redness), Scaling (desquamation) and vesicles along with that Extent of lesion score was calculated based on BSA (body surface area); Each symptom/sign and BSA was scored on 4-point scale (0 to 4) which was recorded at beginning of the study(baseline) and on 4<sup>th</sup> week. (Table I)

The effectiveness was calculated by comparing the scores from baseline and after the follow up for up to 4 weeks (end point). The Data was analyzed using IBM SPSS STATISTICS 29.0.1.0, The Data was gathered using MS excel and it was converted to spreadsheet of SPSS. For conducting statistical analysis, descriptive data was presented as mean and standard deviation. The differences within group A & B at baseline and 4<sup>th</sup> week was analyzed using *Paired t-test*. An *unpaired t-test* was used to compare the differences between Group A & B.

P-value <0.05 was considered to be statistically significant.

**Table I: Scoring system used for clinical evaluation in patients.**

Parameters	Particulars	Score
Total Symptom Score (TSS)	Erythema, Pruritus, Scaling, Vesicles	0- Absent 1- Mild 2- Moderate 3- Severe
Extent of Lesion Score	Body Surface Area (BSA)	0- Absent 1- Mild/BSA 1-2% 2- Moderate/BSA 3-10% 3- Severe/BSA>10%

#### RESULT

##### Demographical data

A total of sixty patients were recruited after satisfying the inclusion and exclusion criteria. Among 60 patients

who were enrolled in the study with dermatophytosis, 36(60%) of patients was found to be female and 24(40%) were male patients. So, here female patients have higher predominance over male patients. (Fig I)

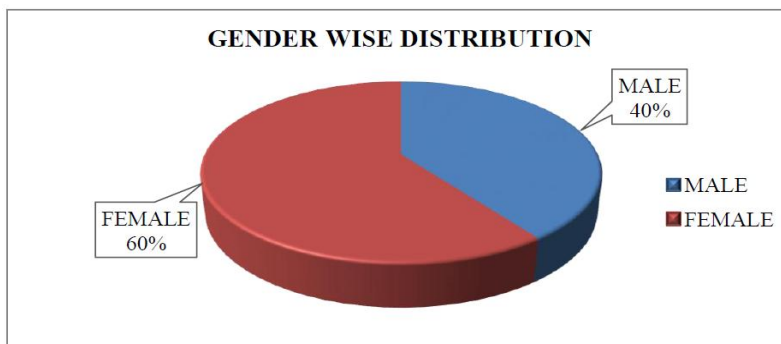


Figure 1: Gender wise distribution of patients.

In age wise distribution, out of 60 patients who were enrolled in the study, the maximum number of subjects 38% (23) belongs to the age group of 18-30 years and

minimum number of subjects 12% (7) was found to be in the age group of 51-60 years. (Table II)

Table II: Age wise distribution.

Age	Group-A (n=30)	Group-B (n=30)	Total (n=60)	Percentage (%)
18-30	11	12	23	38%
31-40	9	6	15	25%
41-50	8	7	15	25%
51-60	2	3	7	12%

In distribution of occupation among study population, out of 60 patients the maximum number of subjects 30%

(18) was found to be homemaker followed by 21.7% (13) subjects was farmers. (Table III)

Table III: Distribution of Occupation among study subjects.

Occupation	Number of participants	Percentage (%)
Homemaker	18	30%
Farmer	13	21.7%
Fisherman	10	16.7%
Salesperson	8	13.3%
Student	5	8.3%
Other	6	10%

Type of dermatophytosis in study subjects

Based on diagnosis the maximum number of cases 31

(50%) was identified as tinea corporis followed by 12 cases (20%) as tinea cruris. (Figure II)

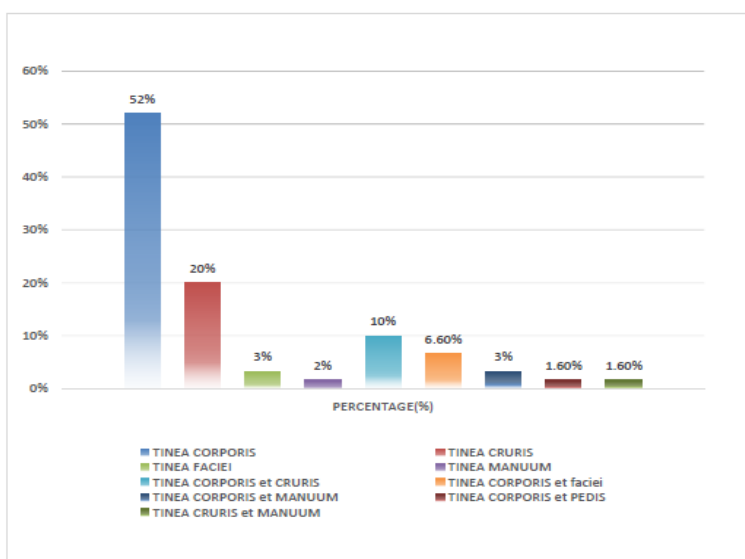


Figure II: Distribution of type of dermatophytosis.

### Evaluation of effectiveness

Based on the observation of patients TSS (total symptoms score) at baseline and end of follow up, the results were tabulated accordingly. Paired t-test was used to analyze the effectiveness of drugs within Group-A and Group-B which shows that both the drugs are effective individually in reduction of TSS and it was statistically significant ( $<0.001$ ). Further, unpaired t-test results were done to find difference between Group-A and B which shows that Group-B patients treated with terbinafine

250mg twice daily had greater effectiveness, that is a significant mean difference was observed in Group-B patients [ $7.83 \pm 0.83$ (baseline)  $\rightarrow 2.80 \pm 1.58$ (4<sup>th</sup> week)] compared to Group-A patients [ $7.00 \pm 1.55$ (baseline)  $\rightarrow 4.43 \pm 1.54$ (4<sup>th</sup> week)]. The p-value was found to be  $0.000159^*$ , it was found to be statistically significant. Therefore, by comparing these two drugs, Terbinafine (Group-B) was found to be more effective than fluconazole (Group-A) in reducing the severity of symptoms. (Table IV)

**Table IV: Statistical analysis of TSS in Group-A and Group-B.**

Parameter			Group-A (n=30)	Group-B (n=30)	P-Value (Unpaired t-test)
TSS	Baseline	Mean $\pm$ SD	7.00 $\pm$ 1.55	7.83 $\pm$ 0.83	0.000159*
	4 <sup>th</sup> Week	Mean $\pm$ SD	4.43 $\pm$ 1.54	2.80 $\pm$ 1.58	
Mean difference			-2.57	-5.03	
P-value (Paired t-test)			$<0.001^{**}$	$<0.001^{**}$	

*n* = number of subjects, \* - Paired t-test \*\* - Unpaired t-test (P-value  $<0.05$  - statistically significant), TSS – Total symptom score, SD – standard deviation.

### Extent of Lesion Score

In our study, the extent of lesion score was analyzed using the body surface area involved in patients with dermatophytosis, Paired t-test was used to compare the extent of lesion score within Group-A and B which showed both groups had reduction of BSA involved and lesion clearance from Baseline to 4<sup>th</sup> week, which reveals both Group-A (Fluconazole) and Group-B (Terbinafine) had proved to reduce the lesion in patients affected with dermatophytosis.

Further, Unpaired t-test was done to find the differences between Group-A and Group- B which shows that Group-B patients treated with terbinafine 250mg daily had greater effectiveness, that is a significant mean difference was observed in Group-B patients [ $1.80 \pm 0.80$  (Baseline)  $\rightarrow 0.43 \pm 0.72$  (4<sup>th</sup> week)] compared to Group-A patients [ $1.36 \pm 0.76$  (Baseline)  $\rightarrow 0.63 \pm 0.76$  (4<sup>th</sup> week)]. The p-value was found to be  $0.023^*$  and it is statistically significant. (Table V)

**Table V: Extent of lesion score.**

Parameter			Group-A (n=30)	Group-B (n=30)	P-Value (Unpaired t-test)
BSA	Baseline	Mean $\pm$ SD	1.36 $\pm$ 0.76	1.8 $\pm$ 0.80	0.023*
	4th Week	Mean $\pm$ SD	0.63 $\pm$ 0.76	0.43 $\pm$ 0.72	
Mean difference			-0.73	-1.37	
P-Value (Paired t-test)			$<0.001^{**}$	$<0.001^{**}$	

*n* = number of subjects

\* - Paired t-test \*\* - Unpaired t-test (P-value  $<0.05$  - statistically significant) BSA- body surface area, SD – standard deviation.

### DISCUSSION

A prospective comparative study was conducted for a period of 6 months to evaluate the effectiveness of fluconazole and Terbinafine which was the most commonly used anti-fungals in our government tertiary care teaching hospital.

In that the female patients 36(60%) was found to have higher predominance over male patients 24(40%). Our findings are in concurrence with Pires CAA et al. Clinical, epidemiological, and therapeutic profile of dermatophytosis who stated that female population affected by dermatophytosis was approximately 1.5 times larger than the male population with this condition.<sup>[7]</sup> Also, our study findings concur with Dr.Prakash, et al. A Randomized open label comparative

study of once-a-week therapy of oral fluconazole with once daily therapy of oral terbinafine in patients with extensive Tinea Corporis.<sup>[8]</sup>

Out of 60 patients who were enrolled in the study, the maximum number of subjects 38% (23) belongs to the age group of 18-30 years and it can be explained with increased sweating associated due to various indoor/outdoor activities are common in this age compared to older age. These findings are comparable with Sivaramakrishnan sangaiah et. al. Study on knowledge, attitude and behavior of patients towards dermatophytosis and importance of maintaining personal hygiene.<sup>[9]</sup>

In our study, among 60 patients with Dermatophytosis,

most number of patients about 18 (30%) were homemakers followed by 13(21.7%) were found to be farmers our study results are concomitant with Sivaramakrishnan sangaiah S et. al. Study on knowledge, attitude and behavior of patients towards dermatophytosis and importance of maintaining personal hygiene.<sup>[9]</sup> The study shows that most of Indian females are being housewives and prefer to clothe themselves completely, enabling a suitable ground of growth for fungal infections. Also, our study results are similar to the studies conducted by Pires CAA et al. Clinical, epidemiological, and therapeutic profile of dermatophytosis as they also reported most of patients were found to be home makers (26.9%) and it was followed by student (23%).<sup>[7]</sup>

Our findings about the most common type of dermatophytosis concur with the study conducted by KAK Surendran et al. A Clinical and Mycological Study of Dermatophytic infections in which the results showed that Tinea corporis was the most common clinical type (44.3%) followed by tinea cruris (38.2%).<sup>[10]</sup>

By evaluating the effectiveness of two oral antifungals, Terbinafine stands out as more effective in treatment for dematophytosis. Our study results are relevant to the findings of Kumar Amit et al. A comparative study of efficacy of Terbinafine and Fluconazole in patients of tinea corporis as they also reported that Group-I-Terbinafine [6.43 (baseline) → 0.79 (4th week)] has slightly more reduction of clinical score than Group- II- fluconazole [6.42 (baseline) → 1.55 (4th week)].<sup>[11]</sup>

The study findings also correspond to the results of Dr.Prakash et al. A randomized open label comparative study of once-a-week therapy of oral fluconazole with once daily therapy of oral terbinafine in patients with extensive tinea corporis, as they concluded that oral terbinafine administered once daily for 2 weeks is more efficacious than fluconazole as observed from rapid improvement in the clinical symptoms and effective mycological cure.<sup>[8]</sup>

Our study results are also similar to the findings of Mustafa A et al. Comparison of Efficacy of Terbinafine and Fluconazole in patients of Tinea corporis as they also reported the frequency of efficacy was significantly higher in patients treated with terbinafine as compared to fluconazole (90.2% vs 64.7%; p-value = 0.002).

## CONCLUSION

Based on the outcome of the study, female patients had high preponderance. Among them, most patients were found to be home makers. Tinea corporis was the most common type of dermatophytosis which is followed by tinea cruris. This study highlights that both oral antifungals, fluconazole and terbinafine are effective in the treatment of dermatophytosis. Even so, oral terbinafine was found to be slightly better effective than fluconazole in treatment as it signifies good

improvement in clinical symptoms of patient despite patients age, sex and the duration of disease. As they are the most used antifungals in our government hospital setting these findings will provide insight for clinicians in the treating patients with tinea infections.

## CONFLICT OF INTEREST

All the authors of this study declare that there is no conflict of interest regarding the publication. The study was conducted with no funding.

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## REFERENCES

1. Katz, Stephen I., Barbara A. Gilchrest, Amy S. Paller, and David J. Leffell. *Fitzpatrick's dermatology in general medicine*. Edited by Klaus Wolff, and Lowell A. Goldsmith. New York: McGraw-Hill, 2008; 1807-1809.
2. Microsporum, Trichophyton. "Ringworm, Tinea." (2004).
3. Verma SB, Panda S, Nenoff P, Singal A, Rudramurthy SM, Uhrlass S, Das A, Bisharwal K, Shaw D, Vasani R. The unprecedented epidemic-like scenario of dermatophytosis in India: III. Antifungal resistance and treatment options. *Indian Journal of Dermatology, Venereology and Leprology*, 2021 Jun 30; 87(4): 468-82.
4. Hay RJ, Johns NE, Williams HC, Bolliger IW, Dellavalle RP, Margolis DJ, Marks R, Naldi L, Weinstock MA, Wulf SK, Michaud C. The global burden of skin disease in 2010: an analysis of the prevalence and impact of skin conditions. *Journal of investigative dermatology*, 2014 Jun 1; 134(6): 1527-34.
5. Jartarkar SR, Patil A, Goldust Y, Cockerell CJ, Schwartz RA, Grabbe S, Goldust M. Pathogenesis, immunology and management of dermatophytosis. *Journal of Fungi*, 2021 Dec 31; 8(1): 39.
6. Yazdanpanah MJ, Shamsian AA, Shafiee M, Hedayati-Moghadam MR, Ghazvini K, Moghaddas E. Comparison between Fluconazole and Terbinafine in the treatment of Tinea corporis and Tinea cruris. *Journal of Mycology Research*, 2015 Jul 1; 2(2): 105-10.
7. Pires CA, Cruz NF, Lobato AM, Sousa PO, Carneiro FR, Mendes AM. Clinical, epidemiological, and therapeutic profile of dermatophytosis. *Anais brasileiros de dermatologia*, 2014 Mar; 89: 259-64.
8. Dr.prakash, Dr.Hemavathy. "A Randomized Open Label Comparative Study of Once-a-Week Therapy of Oral Fluconazole with Once Daily Therapy of Oral Terbinafine in Patients with Extensive Tinea Corporis. Volume 14, Issue 10 Ver.III (Oct. 2015)

PP 97-104.

9. Sivaramakrishnan SA, Kumar AN, Sukanya G. Study on knowledge, attitude and behaviour of patient towards dermatophytosis and importance of maintaining personal hygiene. *International journal of advances in medicine*, 2021; 8(6).
10. Surendran KA, Bhat RM, Bolor R, Nandakishore B, Sukumar D. A clinical and mycological study of dermatophytic infections. *Indian journal of dermatology*, 2014 May 1; 59(3): 262-7.
11. Amit K, Navin B, Priyamvada S, Monika S. A comparative study of efficacy of terbinafine and fluconazole in patients of tinea corporis. *International Journal of Biomedical Research*, 2013; 4: 11.
12. Mustafa A, Hussain S, Shaheen G. Comparison of Efficacy of Terbinafine and Fluconazole in Patients of Tinea Corporis. *Annals of Punjab Medical College*, 2021 Mar 31; 15(1): 21-4.