Section: DVL

Original Research Article

COMPARATIVE EVALUATION OF ITRACONAZOLE, TERBINAFINE, AND FLUCONAZOLE IN THE MANAGEMENT OF SUPERFICIAL DERMATOPHYTOSIS: A PROSPECTIVE OBSERVATIONAL STUDY

Indira Pavan[1], *Veda Shruthi Valluru*[2]

[1]*Assistant Professor, Department of DVL, Malla Reddy Medical College for Women, Suraram Hyderabad, Telangana, India.*
[2]*Associate Professor, Department of DVL, TRR Institute of Medical Sciences, Patancheru, Hyderabad, Telangana, India.*

Received *: 29/09/2025*
Received in revised form *: 11/11/2025*
Accepted *: 30/11/2025*

Corresponding Author:
Dr. Indira Pavan,
Assistant Professor, Department of DVL, Malla Reddy Medical College for Women, Suraram Hyderabad, Telangana, India.
Email: drindirapavan@gmail.com

DOI: 10.70034/ijmedph.2025.4.391

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2025; 15 (4); 2181-2186

ABSTRACT

Background: Superficial dermatophytosis has re-emerged as a major public health concern, particularly in India, with increasing reports of chronic, relapsing, and treatment-resistant infections. Systemic antifungal therapy is often required for moderate-to-severe disease. This study compares the effectiveness of itraconazole pulse therapy, terbinafine intermittent dosing, and fluconazole intermittent therapy in patients with dermatophytosis.

Material and Methods: A total of 135 patients with superficial dermatophytosis attending the DVL outpatient department were enrolled and randomized into three treatment groups (45 each): Group 1 received itraconazole 200 mg twice daily for one week/month; Group 2 received terbinafine 250 mg once every three days; and Group 3 received fluconazole 150 mg every three days. Baseline assessment included BSA involvement, erythema, scaling, vesiculation, itching, and KOH microscopy. Clinical and mycological responses were assessed at 4 and 8 weeks, with recurrence monitored over 12 months. Statistical analysis was performed using Chi-square and ANOVA tests, with $p < 0.05$ considered significant.

Results: Itraconazole achieved the highest complete clearance (69.6%) at 4 weeks and the highest mycological cure rate (80.4%) at 8 weeks. Terbinafine showed moderate response (63.6% clinical cure; 77.3% mycological cure), while fluconazole exhibited the lowest cure rates (40.9% clinical; 47.7% mycological). Recurrence at 12 months was lowest with itraconazole (15.6%), followed by terbinafine (21.4%), and highest with fluconazole (55.6%). Adverse events were mild and manageable across groups.

Conclusion: Itraconazole pulse therapy demonstrated superior clinical and mycological efficacy with the lowest recurrence, making it the most effective systemic option for dermatophytosis. Terbinafine remains moderately effective, while intermittent fluconazole is less reliable and associated with higher relapse.

Keywords: Dermatophytosis; Itraconazole; Terbinafine; Fluconazole; Antifungal therapy.

INTRODUCTION

Superficial dermatophytosis represents a highly prevalent fungal infection globally, primarily induced by species of Trichophyton, Microsporum, and Epidermophyton, which target keratinized tissues in the skin, hair, and nails.[1] Traditionally viewed as a benign and easily treatable condition, recent years have witnessed significant changes in its epidemiology, clinical behavior, and therapeutic response, especially in tropical countries like India. Numerous studies have indicated a concerning increase in chronic, relapsing, and recalcitrant dermatophytosis, frequently necessitating extended

or combination systemic treatment.[2] The evolving landscape is linked to the misuse of over-the-counter steroid-antifungal combinations, inadequate treatment adherence, and the rise of antifungal resistance.[3]

Dermatophytosis represents a considerable public health challenge due to its high transmissibility, effects on quality of life, and economic consequences. The clinical presentation may range from mild erythematous plaques to extensive inflammatory lesions affecting large body surface areas, with pruritus as a prominent symptom. Topical antifungals may prove insufficient for extensive disease, thereby requiring systemic therapy.[4] Terbinafine and itraconazole are the most commonly utilized oral antifungal agents, whereas fluconazole is typically reserved for specific cases due to its fungistatic properties and delayed response.[5]

Recent comparative studies indicate that itraconazole is a more effective option for managing extensive dermatophytosis. Singh et al. found that itraconazole yielded significantly higher clinical and mycological cure rates than terbinafine,[6] while Bhatia et al. also showed greater efficacy and more rapid improvement with itraconazole.[2] Fluconazole, while historically utilized, has demonstrated lower cure rates and higher relapse rates in multiple studies, particularly with intermittent administration.[3,7] Variations in pharmacokinetics, tissue deposition, and emerging species-specific antifungal resistance patterns have been associated with these differences.[8]

The rising prevalence of Trichophyton indotineae, a species linked to diminished sensitivity to terbinafine and other treatments, has complicated the selection of therapeutic options. Research conducted in India has indicated instances of multidrug failure with terbinafine, itraconazole, and fluconazole, highlighting the necessity for optimized treatment regimens and evidence-based therapeutic decisions.[10] This highlights the significance of comparative clinical evaluations of existing systemic therapies, especially in areas facing resistant or recurrent dermatophytosis.

This study compares the clinical effectiveness, mycological cure rates, recurrence rates, and safety profiles of pulse itraconazole, intermittent terbinafine, and intermittent fluconazole in patients with superficial dermatophytosis. This study enhances therapeutic outcomes in dermatophytosis by aligning with published evidence and addressing regional epidemiologic trends.

MATERIALS AND METHODS

This observational study was conducted within the Department of DVL at Malla Reddy Medical College in Hyderabad, covering the period from January 2024 to June 2025. A total of one hundred and thirty-five participants, encompassing both genders and aged over 12 years, diagnosed with superficial dermatophytosis, were recruited from the outpatient department of DVL.

Inclusion Criteria: Four cases presented with plaques in one of two distinct anatomical sites, with no prior antifungal treatment in the preceding three months. All showed positive KOH direct microscopy for fungal elements and provided written informed consent.

Exclusion Criteria: Patients with hepatic or renal disease, cardiovascular disorders, pregnancy or lactation, allergies to azoles or allylamines, non-dermatophytosis tinea infections, immunosuppression, current use of immunosuppressive drugs, or unwillingness to participate were excluded.

An informed consent in writing was secured from the participants of the study, and the study protocol received approval from the institutional ethics committee.

Each participant underwent comprehensive physical and clinical examination to document lesion dimensions, distribution, erythema, peripheral vesicles, scaling, and signs of inflammation. The extent of lesions was assessed using Body Surface Area (BSA), with 1% equivalent to the palmar surface (wrist to fingertips). Lesions covering <3% of BSA were classified as mild, 3-10% as moderate, and >10% as severe.

Treatment Protocol

Participants were randomized into three groups. Group 1: Itraconazole pulse regimen - Tab. Itraconazole 200 mg twice daily for one week, followed by a three-week drug-free interval; total duration: 1 month. Group 2: Terbinafine intermittent pulse therapy - Tab. Terbinafine 250 mg once daily every three days; total of eight doses over 1 month. Group 3: Fluconazole - Tab. Fluconazole 150 mg once every three days for six weeks; total duration: 1.5 months.

Follow-up and Outcome Measures

Participants were monitored for 4 weeks during therapy, with a further 8 weeks of post-treatment assessment. Recurrence cases were followed up for 12 months. Both subjective and objective measures were documented at each visit, including:

- Emergence of new lesions
- Changes in lesion size and extent
- Erythema, scaling, vesiculation/postulation
- Absence of central clearing
- Warmth
- Patient-reported itching

The area encompassed by an outstretched palm, extending from the wrist to the fingertips, can be approximated to constitute about 1% of the total body surface area. Fewer than 3% may be classified as mild, 3-10% as moderate, and exceeding 10% as severe. Even a finding of less than 3% was regarded as a favourable indication of the lesion's extent in our study, which may elucidate the advancement of the disease state.

The gathered data underwent analysis utilizing SPSS version 26.0. Calculations were performed for frequencies, percentages, means, and standard deviations concerning demographic variables and clinical findings. The relationships among categorical variables were examined through the application of the Chi-square test. Continuous variables were articulated as the mean accompanied by the standard deviation. A p-value below 0.05 was considered to be statistically significant.

RESULTS

Table 1: Sociodemographic profile of study participants

Parameters	Group 1 (n=45) Frequency (%)	Group 2 (n=45) Frequency (%)	Group 3 (n=45) Frequency (%)	Chi-square value	p-value
Age (In years)					
11-20	03	05	05	2.134	0.844
21-30	19	17	15		
31-40	10	11	15		
41-50	07	06	06		
Above 50	06	06	04		
Gender					
Male	19	21	23	6.329	0.072
Female	26	24	22		
Marital status					
Married	31	33	29	2.208	1.563
Unmarried	14	12	16		
Family history					
Present	13	10	06	4.873	0.632
Absent	32	35	39		

Table 2: History treatment profile in study participants

Parameters	Group 1 (n=45) Frequency (%)	Group 2 (n=45) Frequency (%)	Group 3 (n=45) Frequency (%)	Chi-square value	p-value
Contact history					
Present	26	29	25	2.517	1.093
Absent	19	22	20		
Details of topical medication					
Steroid +Ve	23	25	22	3.922	0.982
Steroid -Ve	22	20	23		
KOH before treatment					
Yes	37	35	35	1.384	0.252
No	12	10	10		
Duration of disease	3.2±1.89	3.9±2.62	4.1±2.99	0.610	0.725

Table 3: Details of treatment follow up in study participants

Parameters	Group 1 Frequency (%)	Group 2 Frequency (%)	Group 3 Frequency (%)	Chi-square value	p-value
Itching					
Baseline	45 (100%)	45 (100%)	45 (100%)	7.93	0.001
At 4 weeks	45 (100%)	45 (100%)	45 (100%)		
At 8 weeks	45 (100%)	27 (60%)	45 (100%)		
Erythema					
Baseline	45 (100%)	45 (100%)	45 (100%)	10.30	0.001
At 4 weeks	38 (84.4%)	41 (91.1%)	43(95.5%)		
At 8 weeks	39 (86.7%)	39 (86.7%)	41 (91.1%)		
Scaling					
Baseline	34 (75.6%)	36 (80%)	34 (75.6%)	5.127	0.604
At 4 weeks	29 (64.4%)	31 (68.9%)	34 (75.6%)		
At 8 weeks	33 (73.3%)	36 (80%)	35 (77.8%)		
Vesiculation					
Baseline	28 (62.2%)	29 (64.4%)	30 (66.7%)	**6.368**	**0.001**
At 4 weeks	17 (37.8%)	20 (44.4%)	22 (48.9%)		
At 8 weeks	09 (20%)	01 (2.22%)	01 (2.22%)		

Table 4: Comparison of grading during follow up period in study participants

Parameters	Group 1 Frequency (%)	Group 2 Frequency (%)	Group 3 Frequency (%)	Chi-square value	p-value
At baseline					
Mild	-	-	-	2.652	0.738
Moderate	23 (51.1%)	21 (46.7%)	17 (37.8%)		
Severe	22 (48.9%)	24 (53.3%)	28 (62.2%)		

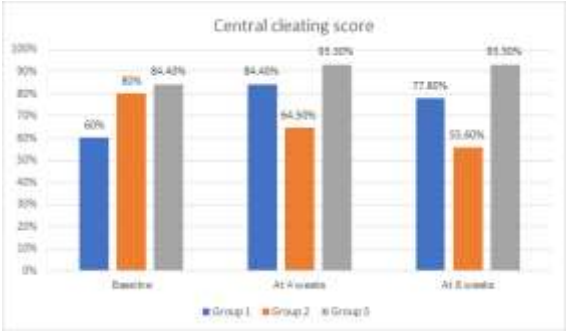
At 4 weeks					
Mild	-	-	-	7.995	0.001
Moderate	28 (62.2%)	30 (66.7%)	28 (62.2%)		
Severe	17 (37.8%)	15 (33.3%)	17 (37.8%)		
At 8 weeks					
Mild	-	36 (80%)	-	12.472	0.001
Moderate	36 (80%)	09 (20%)	38 (84.4%)		
Severe	09 (20%)	-	07 (15.5%)		

Table 5: Adverse reactions to treatment in study participants

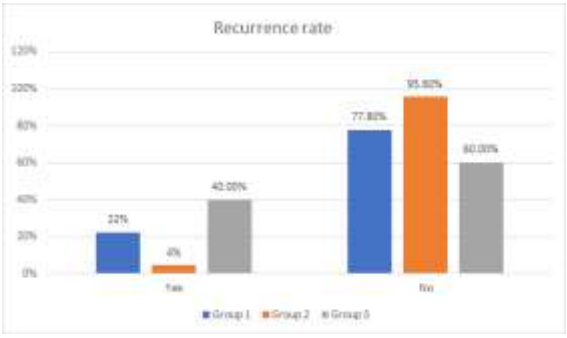
Adverse Events	Group 1	Group 2	Group 3
	Frequency (%)	Frequency (%)	Frequency (%)
Gastritis	5 (11.1%)	2 (4.4%)	4 (8.8%)
Headache	1 (2.2%)	1 (2.2%)	3 (6.7%)
Nausea/Vomiting	2 (4.4%)	1 (2.2%)	2 (4.4%)
Elevated LFTs	1 (2.2%)	-	2 (4.4%)
Pruritus Worsening	-	1 (2.2%)	1 (2.2%)

Table 6: Comparison of key outcomes across groups

Outcome Measure	Group 1	Group 2	Group 3
Clinical Response (4 weeks)	Highest	Moderate	Lowest
Mycological Cure (8 weeks)	Highest	High	Low
Recurrence (12 months)	Lowest	Moderate	Highest
Adverse Events	Mild	Minimal	Mild to Moderate



Graph 1: Details of central clearing score during follow up



Graph 2: Recurrence rate in study participants

DISCUSSION

The present study evaluated and compared the therapeutic effectiveness of three systemic antifungal regimens pulse itraconazole, intermittent terbinafine, and intermittent fluconazole in 135 patients with superficial dermatophytosis. Our findings demonstrate that itraconazole produced the highest clinical and mycological cure rates, lowest recurrence over 12 months, and acceptable safety profile. Terbinafine showed moderate cure rates and slightly higher recurrence than itraconazole, while fluconazole showed the lowest cure rates and the highest recurrence. These findings closely reflect existing published evidence from various Indian and international studies.

Several studies conducted in the last decade have documented the superior efficacy of itraconazole compared with terbinafine, particularly in the Indian subcontinent where dermatophytosis has become increasingly chronic, relapsing, and difficult to treat. In a comparative study by Singh et al., itraconazole consistently achieved significantly higher cure rates than terbinafine at both four and eight weeks ($p<0.001$), with an overall clinical improvement that was more marked in the itraconazole arm.[11] Similarly, Bhatia et al. reported mycological cure rates of 91.8% for itraconazole and 74.3% for terbinafine at four weeks, confirming itraconazole's superior performance in clinical practice.[2]

Our study demonstrated comparable findings, with itraconazole yielding approximately 70% complete clearance at four weeks and over 80% mycological cure at eight weeks. These values parallel the high cure rates reported by previous Indian cohorts and reinforce itraconazole's position as a first-line systemic agent, especially in extensive or recurrent dermatophytosis.

Comparative studies involving fluconazole have consistently shown lower efficacy. In a randomized trial directly comparing itraconazole, terbinafine, and fluconazole, itraconazole demonstrated superior outcomes, while fluconazole lagged in both clinical and mycological response.[7] This aligns closely with our results, where fluconazole demonstrated the slowest response, lowest cure rate, and highest recurrence (over 50% at 12 months). A 2024 study evaluating efficacy of itraconazole versus fluconazole similarly concluded that itraconazole provided faster and more complete resolution, whereas fluconazole required prolonged therapy and still resulted in inferior cure rates.[12]

A review by De Doncker et al. also emphasized that itraconazole's broader antifungal spectrum and favorable pharmacokinetics especially extensive deposition in keratinized tissues contribute to its prolonged clinical effect and superior outcomes when compared with terbinafine and fluconazole.[14] This pharmacologic advantage likely explains the lower relapse rates seen in our itraconazole group.

One of the major concerns in India today is the increasing trend of recurrent and chronic dermatophytosis. Recent literature indicates emergence of strains such as Trichophyton indotineae, associated with decreased sensitivity and treatment failure to commonly used agents including terbinafine, itraconazole, and fluconazole.[13] Our findings of recurrence rates being lowest with itraconazole (15.6%), moderate with terbinafine (21.4%), and highest with fluconazole (55.6%) are consistent with emerging resistance patterns and align with studies that highlight fluconazole's poor relapse-prevention capacity. An Indian study investigating multidrug failure in dermatophytosis reported lack of sustained response to terbinafine, itraconazole, and fluconazole in a subset of patients.[10] While our cohort did not encounter true treatment failure of this extent, the markedly higher recurrence seen with fluconazole strongly supports restricting its use, especially in endemic regions with known resistance challenges.

Our study demonstrated significant reductions in erythema, scaling, itching, and vesiculation across the groups, with itraconazole showing the most rapid symptom improvement. This correlates well with findings by Swaroopa and Kumar, who reported superior early symptomatic relief in itraconazole-treated patients[3]. Similarly, Sharma et al. found that itraconazole in combination regimens produced faster improvement in erythema and scaling compared to monotherapy with terbinafine or fluconazole.[12] The differences observed in our study were statistically significant for itching, erythema, and vesiculation at various follow-ups, indicating that itraconazole may lead to earlier suppression of inflammatory signs, possibly due to higher tissue concentrations and stronger fungistatic action.

In our cohort, adverse events were mild across all groups. Gastritis was the most common side effect in the itraconazole group, while headache and mild liver enzyme elevation were noted occasionally in the fluconazole group. These findings mirror the safety data reported in earlier studies, where gastrointestinal symptoms and transient LFT elevations were the most frequent events with itraconazole and fluconazole, while terbinafine was generally well tolerated.[2,14] Bhatia et al. observed similar patterns, with both itraconazole and terbinafine being well tolerated, and only mild adverse effects reported.[2] De Doncker et al. also emphasized the overall safety of itraconazole and terbinafine in superficial mycoses, especially when administered in pulse regimens that reduce cumulative hepatotoxicity.[14] Our findings confirm that all three drugs remain safe when prescribed appropriately, with no severe or irreversible adverse events noted.

This study did not perform fungal culture or molecular identification, which could provide insight into species-specific drug response particularly relevant given emerging resistance trends in T. indotineae. However, we use of both clinical and mycological parameters to assess outcomes and twelve-month follow-up, allowing assessment of recurrence, rarely reported in existing literature

CONCLUSION

This comparative study of three systemic antifungal regimens for superficial dermatophytosis, itraconazole pulse therapy demonstrated the highest clinical and mycological cure rates, faster symptom resolution, and the lowest recurrence over 12 months. Terbinafine intermittent therapy showed moderate efficacy with acceptable tolerability, while fluconazole exhibited the least favourable outcomes, including slower clinical improvement and the highest relapse rates. All three treatments were generally safe, with only mild and manageable adverse events. Overall, itraconazole emerged as the most effective and reliable systemic option in the current clinical setting, particularly for moderate-to-severe or recurrent dermatophytosis. The findings emphasize the need for rational antifungal use, avoidance of inappropriate topical steroid–antifungal combinations, and further research incorporating species identification and resistance profiling to optimize treatment strategies for dermatophytosis.

REFERENCES

1. Havlickova B, Czaika VA, Friedrich M. Epidemiological trends in skin mycoses worldwide. Mycoses. 2008;51 Suppl 4:2-15.
2. Bhatia A, Kanish B, Badyal DK, Kate P, Choudhary S. Efficacy of oral terbinafine versus itraconazole in treatment of dermatophytic infection of skin - A prospective, randomized comparative study. Indian J Pharmacol. 2019;51(2):116-119.
3. Panda S, Verma S. The menace of dermatophytosis in India: The evidence that we need. Indian J Dermatol Venereol Leprol. 2017; 83:281-284
4. Gupta AK, Cooper EA. Update in antifungal therapy of dermatophytosis. Mycopathologia. 2008;166(5-6):353-367.
5. Ely JW, Rosenfeld S, Seabury Stone M. Diagnosis and management of tinea infections. Am Fam Physician. 2014;90(10):702-710.
6. Singh SK, Subba N, Tilak R. Efficacy of Terbinafine and Itraconazole in Different Doses and in Combination in the Treatment of Tinea Infection: A Randomized Controlled Parallel Group Open Labeled Trial with Clinico-Mycological Correlation. Indian J Dermatol. 2020;65(4):284-289.
7. Swaroopa K, Kumar AV. Terbinafine Vs Itraconazole Vs Fluconazole in the Management of Superficial Dermatophytosis – A Randomized Comparative Study. Int J Curr Pharm Rev Res. 2022;14(4):170-175.
8. Rudramurthy SM, Shankarnarayan SA, Dogra S, Shaw D, Mushtaq K, Paul RA, et al. Mutation in the squalene epoxidase gene of trichophyton interdigitale and trichophyton rubrum associated with allylamine resistance. Antimicrob Agents Chemother. 2018; 62:59.
9. Nenoff P, Verma SB, Vasani R, Burmester A, Hipler UC, Wittig F, et al. The current Indian epidemic of superficial

dermatophytosis due to Trichophyton mentagrophytes-A molecular study. Mycoses. 2019;62:336–356
10. Sharath S, Sardana K, Khurana A. Multi drug failure of tinea corporis to terbinafine, itraconazole and fluconazole; translating extensive Indian microbiological and resistance data to a trial of ketoconazole with remarkable efficacy. Indian J Dermatol Venereol Leprol. 2025; 91:807-9.
11. Singh SK, Chandra U, Anchan VN, Verma P, Tilak R. Efficacy of Terbinafine and Itraconazole in Different Doses and in Combination in the Treatment of Tinea Infection: A Randomized Controlled Parallel Group Open Labeled Trial with Clinico-Mycological Correlation. Indian J Dermatol. 2020;65(4):284-289.
12. Sharma P, Bhalla M, Thami GP, Chander J. Evaluation of efficacy and safety of oral terbinafine and itraconazole combination therapy in the management of dermatophytosis. J Dermatolog Treat. 2020;31(7):749-753
13. Ramzi SHT, Arif SA, Majid A, et al. Efficacy of Terbinafine and Itraconazole Combination Therapy Versus Terbinafine or Itraconazole Monotherapy in the Management of Fungal Diseases: A Systematic Review and Meta-Analysis. Cureus. 2023;15(11):e48819.
14. De Doncker P. Itraconazole and terbinafine in perspective: from petri dish to patient. J Eur Acad Dermatol Venereol. 1999;12 Suppl 1:S10-S17.