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A COMPARATIVE COST-EFFECTIVE STUDY BETWEEN TOPICAL AND ORAL ANTIFUNGAL DRUGS IN TINEA INFECTIONS

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ABSTRACT

Objective: This study evaluates the relative cost-effectiveness of oral and topical antifungal drugs used to treat tinea infections.

Methods: Data was collected over six months by reviewing prescriptions in the Dermatology Department at Tertiary Care Hospital in Kemari, Karachi. The average cost of antifungal drugs per prescription was calculated. However, we only considered oral and topical antifungal medications. All drug prices were calculated in Pakistani rupees. Each drug's cost was calculated per milligram and w/w, w/v.

Results: Among 402 prescriptions reviewed for tinea infections, topical antifungals were more commonly prescribed than oral formulations, with clotrimazole and terbinafine being the most cost-effective. Significant cost variations were noted, especially for fluconazole and griseofulvin, highlighting the need for rational prescribing and price regulation.

Conclusion: This study compares and highlights the advantages of using antifungal drugs topically and orally. It also enhances the practice of prescribing generic medications and makes treatment more affordable for patients.

Keywords: Cost-effectiveness, Tinea infections, Topical antifungals, Oral antifungals, Prescription analysis, Rational prescribing.

1. INTRODUCTION

Dermatophytosis is one of the most common fungal infections, especially Tinea, which involves hair, nails, and skin with keratinized tissues (Reddy, 2017; AL-Khikani, 2020; Arenas et al., 2017). About 25% of people worldwide are estimated by the WHO to be affected by tinea (Chen and Yu, 2023; Sahoo, and Mahajan, 2016). There are several types of tinea infections, that affect different parts of the body. Here are some of the most common types of tinea infections (Shemer and Babaev, 2018; Sahoo and Mahajan, 2016, Ilkit and Durdu, 2015):

1. Tinea Pedis (Athlete's Foot): affects the feet
2. Tinea Corporis (Ringworm): affects the body, especially the arms, legs, and trunk
3. Tinea Cruris (Jock Itch): affects the groin area
4. Tinea Capitis (Ringworm of the Scalp): affects the scalp
5. Tinea Barbae (Ringworm of the Beard): affects the beard area
6. Tinea Faciei (Ringworm of the Face): affects the face
7. Tinea Manuum (Ringworm of the Hand): affects the hand
8. Tinea Unguium (Onychomycosis): affects the fingernails or toenails.

Different commercial antifungal medications are used to control these pathogens. Terbinafine from the allylamines class of drug, is the most successful oral treatment, with a 50–70% cure rate (Hammoudi et al., 2022; Hay, 2023). Because of its unique mechanism of squalene epoxidase inhibition, it predominantly acts as a fungicidal agent against a wide variety of fungi, including ringworm, athlete's foot, and jock itch (Wal et al., 2022; Borah et al., 2023). Both oral and topical dosage form is available to treat pityriasis (Tinea versicolor), a fungal infection that causes skin to lighten or darken in the neck, chest, arms, and legs (Mittal and Sarkar, 2021; Usatine, 2024). Another drug which is used in Tinea infection is griseofulvin (Saleh et al., 2024; Bonifaz et al., 2024; Houglum et al., 2024). The primary source of the antifungal polyketide metabolite griseofulvin is ascomycetes. Since its commercial introduction in 1959, dermatophyte infections have been treated with griseofulvin. It blocks the production of nuclear acid and the mitosis of fungal cells (Aris, 2024; Yu et al., 2024). Ketoconazole and clotrimazole belong to the imidazole antifungal class of drugs, increase membrane fluidity, and stop the fungus from growing by blocking the formation of ergosterol, the fungal version of cholesterol (Hameed, 2024; Ivanov et al., 2022). It is available in both oral and topical dosage forms. Clotrimazole is very effective against Tinea infection, especially athlete’s foot and joke itch, by breaking down the fungal cytoplasmic membrane's permeability barrier (Houglum et al., 2024).

Fluconazole, voriconazole, and itraconazole belong to the triazole class of antifungal drugs (Ferreira et al., 2024; Chai, et al., 2022). It hinders the formation of fungal cell walls by blocking the enzyme 14-α lanosterol demethylase, and voriconazole primary mode of action is to inhibit fungal cytochrome P-450-mediated 14 alpha-lanosterol demethylation, which is an important step in fungal ergosterol biosynthesis (Pasi et al., 2024). Fluconazole is given in various dosage forms to the patients, like IV, oral, and topical; voriconazole is available in IV and oral forms only (Akinosoglou et al., 2024; Thompson and Lewis, 2010). Voriconazole, a broad-spectrum triazole antifungal agent, is currently available in oral and intravenous formulations. However, its topical application is not commercially available, necessitating the development of a topical formulation to prevent systemic side effects and drug interactions associated with oral and intravenous administration. Voriconazole also has significant drug-drug interactions because it is metabolized by and inhibits cytochrome P450 enzymes (CYP2C19, CYP2C9, and CYP3A4). The availability of a topical voriconazole formulation would provide a targeted and localized treatment approach, reducing the risk of systemic adverse effects, such as hepatotoxicity, visual disturbances, and skin reactions. Furthermore, a topical formulation would minimize the potential for drug interactions, which are a concern with oral and intravenous voriconazole administration.

Voriconazole is significantly more expensive compared to most other antifungal drugs listed (like terbinafine, fluconazole, and clotrimazole). Even though there is no cost variation (because only one brand seems to be available), its price is very high 400 Rs for 40 mg and 1100 Rs for 200 mg

tablets. A topical voriconazole formulation is urgently needed to provide a safer and more targeted treatment option for fungal infections, while minimizing systemic side effects and drug interactions. Infections of skin require long-term therapy, which increases the cost of medication. The patient has a significant financial burden as a result of the treatment (Yousefian et al., 2024; Cîrstea et al., 2024). Therefore, the patient's financial situation occasionally influences the therapy they receive. Drug resistance occurs occasionally in these superficial fungal infections (Cosio et al., 2024; Roy et al., 2024; Sharma et al., 2024). Assessing the comparative cost-effectiveness of both topical and oral antifungal drugs for the treatment of tinea infections is the aim of this investigation.

Understanding the changing patterns of superficial fungal infection allows governments and social agencies to better allocate health resources for the benefit of humanity. Medical practitioners typically prescribe more effective and safer antifungals. It's worth investigating the impact of drug prices on prescription patterns. For this study, we emphasized only oral and topical dosage forms. The study aimed to assess participants' perceptions of antifungal efficacy, safety, and cost, as well as their correlation with prescribed volume.

2. METHOD

The study was conducted in the Dermatology Department at Tertiary Care Hospital in Kemari, Karachi, Pakistan. Prescriptions were taken from patients who visited the outpatient dermatology department for six months, from December 2023 to May 2024. The prescription served as a means of collecting patient information regarding oral and topical antifungal drugs used in Tinea infections. Prescriptions were evaluated and discussed with a Dermatologist and Pharmacists to determine the per-prescription costs of oral and topical antifungal drugs. The collected prescriptions were analyzed for drug choice, dose/strength, duration, frequency of administration, and dosage form. Tinea infection patterns were analyzed for all dermatology OPD patients and classified based on their condition. The average per-prescription cost analysis of antifungal drugs was conducted. However, we only looked at topical and oral antifungal drug costs. All drug costs were estimated in Pakistani rupees. Each drug's cost was calculated as per milligram in oral formulation and w/w, w/v in topical formulations.

3. RESULT

A total of 402 patient prescriptions were reviewed during the study period. The demographic characteristics and age distribution of the patients are summarized in **Table 1**. Among the reviewed prescriptions, 245 (60.95%) were for female patients and 157 (39.05%) for male patients, resulting in a male-to-female ratio of approximately 1:1.56. In terms of age distribution, adult patients (18–65 years) accounted for the majority of visits to the outpatient department (OPD), representing 55.72% (n=224) of the total prescriptions. Adolescents (12–18 years) comprised 23.63% (n=95), children (1–12 years) represented 13.68% (n=55), and geriatric patients (>65 years) constituted the smallest group, with only 6.96% (n=28) of total prescriptions.

Table 1: Age Distribution of Patients

Age	No of Patients' Prescriptions (n= 402)	Percentage (%)
Children's (1-12 years)	55	13.68 %
Adolescents (12-18 years)	95	23.63 %
Adults (18-65 years)	224	55.72 %
Geriatrics (> 65years)	28	6.96 %

Regarding antifungal therapy, out of 402 prescriptions, 115 (28.61%) prescriptions were for oral antifungal medications, 127 (31.59%) were for topical antifungal agents, and 160 (39.80%) were combination therapies involving both oral and topical antifungal drugs. Topical antifungal drugs

were prescribed more frequently than oral agents, primarily due to their lower cost and localized site of action, which minimizes systemic exposure and potential adverse effects.

Table 2 presents the commonly prescribed topical antifungal medications for the treatment of tinea infections, along with dosing regimens, available strengths, and price ranges. Terbinafine, ketoconazole, and clotrimazole were the most frequently used topical agents. Among these, ketoconazole and clotrimazole were available in multiple formulations, including creams, solutions, and lotions, allowing flexibility in treatment based on lesion location and severity. Several systemic antifungal agents (e.g., fluconazole, griseofulvin, itraconazole, and voriconazole) were not available in topical formulations during the study period.

Table 3 summarizes the oral antifungal drugs prescribed during the study. Terbinafine, fluconazole, and itraconazole were the most frequently used oral antifungal agents. Doses varied depending on the drug and clinical indication, with some therapies extending up to 12 weeks. Voriconazole, while effective, was among the most expensive agents, potentially limiting its use.

According to **Table 4**, the allylamine antifungal terbinafine works by inhibiting squalene epoxidase, which prevents ergosterol synthesis. Although it was accessible topically and orally, its higher systemic action led to its more widespread usage in oral form. It also showed excellent efficacy against dermatophytes. It was also discovered to be quite economical. However, fluconazole and itraconazole inhibit lanosterol 14α-demethylase but differ in their spectrum among triazoles. Fluconazole showed excellent activity against yeast and moderate efficacy against dermatophytes, whereas itraconazole displayed a broader antifungal spectrum, including efficacy against molds. Fluconazole is generally more affordable, while itraconazole is moderately cost-effective but valuable for treating diverse infections. Voriconazole, another triazole, is notable for its broad- spectrum efficacy, particularly against invasive fungal pathogens like Aspergillus spp., although its high cost limits its use primarily to life-threatening conditions. Griseofulvin, which disrupts fungal mitosis via interference with microtubule function, demonstrated limited efficacy restricted to dermatophytes and was associated with lower cost-effectiveness due to narrower utility. Ketoconazole and clotrimazole, both imidazoles, also act by inhibiting lanosterol 14α-demethylase. Clotrimazole was highly effective for superficial infections and was primarily used topically, making it highly cost-effective. In contrast, oral ketoconazole possesses a higher risk profile, leading to a preference for topical use.

Table 5 presents a detailed analysis of the price range and variation for different oral antifungal drugs across various formulations and dosages. Fluconazole exhibited the highest cost variation, with the price of 50 mg capsules ranging from Rs. 98 to Rs. 967, resulting in a staggering 886.7% variation. Similarly, the 150 mg formulation ranged from Rs. 79 to Rs. 731, showing an 825.3% variation. Griseofulvin also demonstrated significant cost variability, particularly for the 125 mg tablet, with a variation of 565.5%. Itraconazole showed a moderate cost difference of Rs. 207 (147.9% variation). Terbinafine's 250 mg tablet presented a 63.5% cost variation, although its 125 mg form remained relatively stable. Ketoconazole had a 259.7% variation, while clotrimazole remained consistently priced with minimal variation (1.6% to 8.3%), suggesting market price stability. Voriconazole, despite being the most expensive, exhibited zero cost variation in the formulations assessed, indicating a fixed pricing structure possibly due to its limited and critical clinical use.

The cost analysis of topical antifungal preparations is outlined in **Table 6**. Clotrimazole cream (1% w/w) showed the highest cost variation at 366.7%, followed by its lotion form (260.0%). Ketoconazole topical preparations also displayed substantial price differences, with its cream (2% w/w) exhibiting a 136.8% variation and lotion (2% w/v) 64.5%. However, terbinafine cream (1% w/w) exhibited a 92.3% variation, while other formulations, including terbinafine lotion and all topical forms of fluconazole, griseofulvin, itraconazole, and voriconazole, were not widely available or showed no price variation, possibly due to limited or specialized use.

From a clinical and economic standpoint, clotrimazole and terbinafine were found to be the most cost-effective treatment for superficial and dermatophytic infections, respectively. Fluconazole,

despite of the high-cost variation, remained widely accessible due to the availability of low-cost generic versions. Itraconazole provided good value in managing broad fungal infections but was moderately priced. Voriconazole, while effective against resistant and invasive fungi, posed a significant financial burden and was reserved for severe infections.

Table 2: Topical Antifungal Drugs Used in Tinea Infection

S. No	Drug of Choice	Frequency	Dose/ strength	Price
1	Terbinafine	1-2 times daily for 7-14 days	Cream:1 %w/w, 4 % w/w Lotion: 1 %w/v	104-200 Rs 80 Rs
2	Fluconazole	Not available	-	-
3	Griseofulvin	Not available	-	-
4	Itraconazole	Not available	-	-
5	Ketoconazole	Apply once daily to the affected area and the surrounding area	Cream 2 %w/w Solution 2 %w/v Lotion 2 %w/v	38-95 Rs 217-308 Rs 150-255 Rs
6	Clotrimazole	Apply every 12 hours to the affected area	Cream 1 %w/w 2 %w/w 10 %w/w Lotion 1 %w/v	21-56 Rs 60-70 Rs 110 Rs 30-108 Rs
7	Voriconazole	Not available	-	-

Table 3 Oral Antifungal Drugs Used in Tinea Infection

S. No	Drug of Choice	Frequency	Dose/ strength	Price
1	Terbinafine	250 milligrams (mg) once a day for 12 weeks.	Tab:125mg, 250 mg	250-340 Rs
2	Fluconazole	150 mg once weekly for 2-4 weeks	Tabs:150 mg Caps: 50 mg,150 mg, 200 mg	90-490 Rs
3	Griseofulvin	375 milligrams (mg) per day	Tabs: 125 mg, 500 mg	58-386 Rs
4	Itraconazole	200 mg 2 times a day for 1 week.	Caps:100 mg	140-347 Rs
5	Ketoconazole	200-400 mg per day for four weeks	Tabs:200 mg	77-277 Rs
6	Clotrimazole	Once daily at bedtime for 6 days	Tabs: 100mg,200mg	60-65 Rs
7	Voriconazole	200 mg 2 hourly	Tabs: 40 mg, 200 mg	400-1100 Rs

Table. 4: Pharmacological Profile and Efficacy Comparison

Drug	Class	Mechanism of Action	Efficacy	Oral/Topical Use	Cost-Effectiveness
Terbinafine	Allylamine	Inhibits squalene	Highly effective vs	Both (more oral)	High

		epoxidase → disrupts ergosterol	dermatophytes		
Fluconazole	Triazole	Inhibits lanosterol 14α-demethylase	Excellent vs yeast; moderate vs dermatophytes	Oral only (rare topical)	Good (varies)
Itraconazole	Triazole	Inhibits lanosterol 14α-demethylase	Broad-spectrum, highly effective	Oral only	Moderate (valuable for broad infections)
Griseofulvin	Griseofulvin class	Disrupts fungal microtubules	Limited to dermatophytes	Oral only	Lower (due to limited efficacy)
Ketoconazole	Imidazole	Inhibits lanosterol 14α-demethylase	Good topically; risky orally	Both (prefer topical)	Moderate
Clotrimazole	Imidazole	Inhibits lanosterol 14α-demethylase	Effective for superficial infections	Topical only	High
Voriconazole	Triazole	Inhibits lanosterol 14α-demethylase	Broad-spectrum (especially molds like *Aspergillus*)	Oral only (no topical)	Expensive (life-threatening infections)

Table. 5: Cost Variation of Oral Antifungal

S. No	Drug of Choice	Dose	Maximum Cost	Minimum Cost	Cost Difference	Cost Variation
1	Terbinafine	Tab:125mg 2.5mg 250 mg	408 Rs 100 Rs 654 Rs	200 Rs 100 Rs 400 Rs	208 0 254	104.0% 0.0% 63.5%
2	Fluconazole	Tabs:150 mg Caps:50 mg, 150 mg 200 mg	172 Rs 967 Rs 731 Rs 2798 Rs	172 Rs 98 Rs 79 Rs 480	0 869 652 2318	0.0% 886.7% 825.3% 482.9%
3	Griseofulvin	Tabs:125 mg, 500 mg	386 Rs 175 Rs	58 Rs 45 Rs	328 130	565.5% 288.9%
4	Itraconazole	Caps:100 mg	347 Rs	140 Rs	207	147.9%
5	Ketoconazole	Tabs:200 mg	277 Rs	77 Rs	200	259.7%
6	Clotrimazole	Tabs: 100mg 500mg	65 Rs 65 Rs	60 Rs 64 Rs	5 1	8.3% 1.6%
7	Voriconazole	Tabs:40 mg 200mg	400 Rs 1100 Rs	400 Rs 1100 Rs	0 0	0.0% 0.0%

Table.6 Cost Variation of Topical Antifungal

S. No	Drug of Choice	Strength	Maximum Cost	Minimum Cost	Cost Difference	Cost Variation
1	Terbinafine	Cream 1 %w/w,	200 Rs	104 Rs	96	92.3%
		4 %w/w	0 Rs	0 Rs	0	0.0%
		Lotion: 1 %w/v	80 Rs	80 Rs	0	0.0%
2	Fluconazole	-	0 Rs	0 Rs	0	0.0%
3	Griseofulvin	-	0 Rs	0 Rs	0	0.0%
4	Itraconazole	-	0 Rs	0 Rs	0	0.0%
5	Ketoconazole	Cream 2 %w/w	90 Rs	38 Rs	52	136.8%
		Solution 2 %w/v	308 Rs	217 Rs	91	41.9%
		Lotion 2 %w/v	255 Rs	155 Rs	100	64.5%
6	Clotrimazole	Cream 1% w/w	98 Rs	21 Rs	77	366.7%
		2% w/w	70 Rs	60 Rs	10	16.7%
		10% w/w,	110 Rs	110 Rs	0	0.0%
		Lotion 1 %w/v	108 Rs	30 Rs	78	260.0%
7	Voriconazole	-	0 Rs	0 Rs	0	0.0%

4. CONCLUSION

This study highlights the comparative cost-effectiveness of topical and oral antifungal medications used in the treatment of tinea infections. Among the antifungal agents evaluated, Clotrimazole and Terbinafine emerged as the most cost-effective choices for superficial and dermatophytic infections, respectively, offering a favorable balance of efficacy and affordability. Topical antifungals were prescribed more frequently than oral agents, primarily due to their localized action, lower systemic side effects, and significantly reduced cost burden on patients. The analysis also revealed substantial price variations among different brands and formulations, particularly for Fluconazole and Griseofulvin, suggesting a need for greater market regulation and promotion of generic prescribing to enhance affordability. Drugs like Voriconazole, although clinically effective for invasive and resistant infections, were associated with prohibitively high costs and limited use in routine outpatient care. Ultimately, the findings underscore the importance of cost considerations in antifungal therapy, especially in resource-constrained settings. Encouraging effective topical formulations and economically viable generics can improve treatment adherence, reduce the financial burden on patients, and support rational prescribing practices. This study provides valuable insights for clinicians, pharmacists, and policymakers aiming to optimize antifungal therapy through evidence-based, cost-conscious decision-making.

5. Future Perspective

Future research should focus on evaluating the clinical outcomes associated with various antifungal regimens to correlate cost-effectiveness with therapeutic efficacy and patient adherence. Longitudinal studies assessing treatment success, recurrence rates, and resistance patterns will be valuable in optimizing treatment guidelines. Additionally, real-world pharmacoeconomic analysis involving direct and indirect costs (e.g., productivity loss, travel expenses, treatment duration) will

provide a more holistic view of antifungal cost-effectiveness. Development and dissemination of standardized prescribing protocols that consider both efficacy and affordability could help mitigate irrational prescribing and minimize unnecessary use of high-cost medications. Policymakers should also focus on regulating drug pricing, encouraging the availability of quality generic formulations, and incorporating antifungal agents into essential drug lists with cost transparency. Educational initiatives for healthcare providers regarding cost-awareness in prescribing can contribute to better resource utilization. Lastly, formulation innovation, such as fixed-dose combinations and longer-acting topical agents, may enhance patient compliance and reduce the overall cost burden by minimizing treatment duration.

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