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Cost Variation Analysis Of Various Antifungal Drugs Available In The Indian Market.

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ABSTRACT

Treating fungal infections are generally long-term and expensive. High medical care cost should be noted by policy makers and healthcare providers to reduce the economic burden from patients. This was a cross sectional study conducted to analyze the cost variation of antifungal drugs available in different formulations in our Indian market. The information on cost of each drug with its dosage and formulation was obtained from "Current index of medical specialties" (CIMS) April-July 2022 India, Indian Drug Review 28th year 2022 Issue 3 and Jan Aushadhi price list 2022 scheme. Cost ratio and percentage cost of drugs available in Indian market under different brand names manufactured by different pharmaceutical industries were calculated. **Results:** Highest cost ratio was observed with itraconazole 200mg Cap (30.6) and lowest with Caspofungin 70mg Inj (1.05). Percentage cost variation was maximum with itraconazole 200mg Cap for 1 tablet (2960%) and minimum with Caspofungin 70mg Inj (5.92%) for 1 tablet. Antifungal treatment is generally long term and it requires patient compliance and strict adherence to therapy. Since there is wide cost variation among antifungal agents available in Indian Market, cost policy regulation and sensitizing the physician for selecting the appropriate brand of drugs is required.

Keywords: Pharmacoeconomics; Antifungal Drugs; Cost ratio ; Percentage cost variation

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INTRODUCTION

Pharmacoeconomics is a branch of health economics. It is the study of economics that identifies, measures, and compares the costs and consequences of pharmaceutical products and services." [1] Analysing of the cost of drug therapy especially for chronic conditions is of vital importance in patients to check economic burden on patients and the healthcare system and to improve medication adherence. Cost analysis is a part of pharmacoeconomic study used in pharmacoeconomic evaluation of drugs. [2,3] Fungal infections are mainly of four types-cutaneous, subcutaneous, deep, and systemic. Cutaneous mostly involves keratin and found in skin and nails and is usually treated by local therapy. Superficial dermatophytic infections are treated with oral antifungals like itraconazole, fluconazole and griseofulvin along with topical application of drugs. [4] Subcutaneous infections are caused by organisms like Sporothrix. Deep fungal infections are generally caused by direct inoculation of organisms into deep soft tissues. Both infections respond well to systemic antibiotics. [5] Invasive fungal infections require prompt diagnosis and special consultation. Drugs like Voriconazole and Amphotericin B are used commonly for invasive fungal infections. The Echinocandins (like Caspofungin, Micafungin) are first line agent in invasive candidiasis. [6] With rise of immunosuppressant diseases in India like HIV and diabetes, fungal infections (both superficial and deep) are turning drug resistant and requiring long term therapy hence adding to the cost. Health care professionals and policy-makers need proper data on drug availability, price, and utilization to make necessary decisions. [7] Indian pharmaceutical market is over streamed with multiple brands and wide variation in cost between different brands of the same formulation is noted causing confusion in selecting the appropriate formulation by the prescriber. For chronic conditions like fungal infections patients may suffer financially when prescribed costlier brands. [5,8] Analysing the cost of antifungal therapy will be helpful for clinicians to select the appropriate P- drug and reduces the economic burden on the patient. As there are few studies reported in the Indian literature, on exploring the cost variation of antifungal drugs, the present study of the cost analysis antifungal drugs was taken up.

MATERIALS AND METHODS

A cross sectional study was done to analyse the cost variation of different antifungal drugs available in the Indian market under generic and different brands names. The study began with Institutional ethics committee clearance (IEC/A038/M/2022). "Current index of medical specialties" (CIMS) April-July 2022 India and from Indian Drug Review 28th year 2022 Issue 3 to know about price of various antifungal drugs and between different brands of antifungal drugs with same formulation. Cost of tablets/capsule for systemic and topical antifungal drugs was calculated. Drugs of different brand name with same formulation, dosage was included in the study.

Cost ratio and the percentage cost variation for different brand name drugs was calculated as follows.

$$\text{Cost ratio} = \frac{\text{Cost of the most expensive brand}}{\text{Cost of the least expensive brand}}$$

$$\text{Percentage cost variation} = \frac{\text{Maximum Cost} - \text{Minimum cost}}{\text{Minimum cost}} \times 100$$

RESULTS AND DISCUSSION

Increasing cost of medical care coupled with limited sources has led to more studies on pharmacoeconomic analysis in India. Aging, chronic diseases, new drugs, newer indication of current drugs, and development of pharmaceutical industry are the primary reasons behind it. The goal is to demonstrate the pharmacoeconomic value, i.e. maintaining a balance of economic, humanistic, and clinical outcomes [9].

Cost ratio and percentage cost variation of monotherapy antifungal drugs are presented in table 1. The different preparations of drugs are injections, tablets, disintegrating tablets and capsules. Amphotericin B and Caspofungin are available as Injectable preparation. Fluconazole, itraconazole, ketoconazole, terbinafine and voriconazole are available as oral preparations. Caspofungin is compared in 2 strengths, Fluconazole in 5 strengths and Itraconazole in 2 strengths. Amphotericin B, Ketoconazole, Terbinafine and Voriconazole are compared in single strength. Number of companies manufacturing

Amphotericin B are seven. Caspofungin manufactured by ten companies, Fluconazole by eighty-five, Itraconazole by ninety-seven, Ketoconazole by nine, terbinafine by three and Voriconazole is manufactured by two pharmaceutical companies. Highest cost ratio was observed with itraconazole 200mg Cap (30.6) and lowest with caspofungin 70mg Inj (1.05). Percentage cost variation was maximum with itraconazole 200mg Cap for 1 tablet (2960%) and minimum with caspofungin 70mg Inj (5.92%) for 1 tablet. More than 100% cost variation seen with Amphotericin B, Fluconazole, Itraconazole and Ketoconazole. In previous studies among oral antifungal drugs, Terbinafine 250 mg had highest cost ratio and cost variation. Griseofulvin 250 mg has lowest cost ratio and cost variation. Among parenteral antifungal drugs, Amphotericin B 50 mg has highest cost ratio and cost variation. Caspofungin (50 and 70 mg) has least cost ratio [10]. In a study by [11] by Spoorthy HV, Padma et al: In oral dosage form, Itraconazole showed the maximum cost variation. In a study by Tiwari A, Reddy P [12] 14 antifungal medications had percentage cost variation more than 100% and fluconazole 150 mg had maximum percentage cost variation while griseofulvin 500 mg had least percentage cost variation. From the above sources of data it shows that, a combination regime (Tinidazole 1g+ Fluconazole 150 mg) of systemic antifungal therapy was available. It is available as KIT and manufactured by two brands. Minimum price is 38 and maximum is 44. Cost ratio is 1.15 and % variation is 15.78.

Table 1: Cost ratio and percentage cost variation of monotherapy antifungal drugs

Drug	Strength (mg)	Formulation	No. of brands	Minimum price(INR)	Maximum price (INR)	Cost Ratio	% Variation
Amphotericin B	50 mg/1 vial	Inj	7	280	7858	28.06	2706.42
Caspofungin	50 mg/1 vial	Inj	5	6250	9990	1.59	59.84
	70 mg/1 vial	Inj	5	9990	10581.9	1.05	5.92
Fluconazole	50mg	DIS-TAB	5	5	11.9	2.37	138
		TAB	3	9.55	12.22	1.28	27.95
	150mg	DIS-TAB	3	10.30	22.31	2.16	116.60
		TAB	41	11.5	30	2.60	160.86
	200 mg	CAP	7	13.29	31.2	2.34	134.76
		TAB	13	13	21.07	1.62	62.07
		CAP	4	9.5	35	3.68	268.42
		TAB	2	19.5	21.45	1.1	10
300 mg	TAB	7	21	34.23	1.63	63	
Itraconazole	100 mg	CAP	42	9.0	189	21	2000
		TAB	7	7.2	28	3.88	288.88
	200mg	CAP	42	10	306	30.6	2960
		TAB	6	10	76.5	7.65	665
Ketoconazole	200 mg	TAB	9	19	44.58	2.34	134.63
Terbinafine	500 mg	Tab	3	17	25.28	1.48	48.70
Voriconazole	200mg	Tab	2	720	886.25	1.23	23.09

Table 2 shows cost ratio and percentage variation of topical antifungal drugs. These drugs are available in form of creams, lotions, ointment, gel, ternary solution, NLAQ. Clotrimazole and amorolfine are compared in 2 strengths each. Rest of the drugs are compared in single strength. Butenafine, ciclopirox, clotrimazole, sertaconazole, terbinafine, amorolfine, luliconazole and eberconazole are available as cream. Clotrimazole, ketoconazole, luliconazole are available as lotions. Ketoconazole is available as soap and shampoo. Ketoconazole and luliconazole available as ointment. Clotrimazole is available as TSOL, TGEL, T:PWD. Amorolfine available as NLACQ. Miconazole available as TGEL. Butenafine is manufactured in 2 brands. Ciclopirox manufactured in 1, Clotrimazole in 26, Ketoconazole in 29, Miconazole in 2, Sertaconazole in 2, Terbinafine in 21, Amorolfine in 3, Luliconazole in 31, Eberconazole in 2 brands. Maximum cost ratio is seen with Miconazole 2% TGEL 1g (78.57). Minimum cost ratio (1.04) seen with Clotrimazole 10 mg TGEL. Maximum percentage cost variation seen (7757.14) with Miconazole 2% TGEL and minimum percentage cost variation (4.97) seen in Clotrimazole 10 mg TGEL. More than 100% cost variation seen with Butenafine, miconazole, clotrimazole, and luliconazole. In previous studies [10] among single drug topical preparations, Clotrimazole 1% powder formulation has highest cost ratio and % price variation 22.48 and 2144.89%, respectively. Ketoconazole 2% solution formulation has least cost ratio and % price variation 1.233 and 23.33%, respectively. In a study by Spoorthy H. V [11] In topical single drug therapy luliconazole show maximum cost variation and Eberconazole cream 30 gm is manufactured by 16 companies showed minimum cost variation (33.4%).

Table 2: Cost ratio and percentage cost variation of different brands of topical antifungal drugs

Drug	Strength	Formulation	Number of brands	Minimum price(INR)	Maximum price(INR)	Cost Ratio	% Variation
Butenafine	1%w/v 1g	CRM	2	3.33	7.26	2.18	118.01
Ciclopirox	10 mg/g	CRM	1	1.03	1.87	1.81	81.55
Clotrimazole	1% w/w	CRM 1 g	6	1.8	3.05	1.69	69.44
		LOT 1ml	2	1.2	3.76	3.13	213.33
		T:PWD	14	0.79	1.6	2.02	102.53
		T:SOL	3	2	3.72	1.86	86
Ketoconazole	10 mg	T GEL	1	7.43	7.8	1.04	4.97
		CRM	8	3.64	10.93	3	200.27
		SOAP	14	0.93	2.38	2.55	155.91
		LOT	2	1.89	5	2.64	164.55
		SHAMP	3	1.32	5.98	4.53	353.03
Miconazole	2%	OINT	2	5.93	12.4	2.09	109.1
		TGEL 1g	2	1.26	99	78.57	7757.14
		CRM	2	9.5	12.06	1.26	26.94
		Terbinafine	1%	CRM	21	4.2	7.69
Amorolfine	0.25%	CRM	2	7.33	9.96	1.35	35.87
Luliconazole	5%	NLACQ	1	214	225	1.05	5.14
		CRM	23	7	15.75	2.25	125
		OINT	2	15	9.45	1.58	58.73
Eberconazole	1%	LOT	6	1	15.93	15.93	1493
		CRM	2	9,96	11.6	1.16	16.46

Table 3. Shows cost ratio and percentage variation of combination therapies of topical antifungal drugs.

Table 3: Shows cost ratio and percentage variation of combination therapies of topical antifungal drugs

Drug	Strength	Formulation	Number of brands	Minimum price(INR)	Maximum price(INR)	Cost Ratio	% Variation
Beclomethasone +clotrimazole+gentamicin	0.025% w/w+1% w/w+0.1% w/w	OINT	1	1.25	3.6	2.88	188
		CRM	3	6.9	9.7	1.4	40.57
Beclomethasone + clotrimazole	0.025% W/W+ 1%W/W	OINT	2	1.43	3	2.09	109.79
		LOT	2	4.52	6.4	1.41	41.59
		CRM	2	2.71	6.9	2.54	154.61
Beclomethasone + clotrimazole + Neomycin Sulphate	0.025% w/w+1% w/w+0.5% w/w	CRM	5	3.33	6.45	1.93	93.69
		LOT	9	1.73	3.93	2.27	127.16
Ketoconazole +Zn Pyrithone	2% w/v+1%w/v	SHAMP	13	1.45	299	206.20	20520.69
		SOAP	6	0.85	1.25	1.47	47.05
		SOAP	2	1.06	1.12	1.05	5.66
Cetrimide+ Ketoconazole	0.5%+2%	SOAP	2	1.06	1.12	1.05	5.66
Nadifloxacin + Mometasone + Miconazole	10mg+1mg+20 mg	CRM	3	7.2	9.922	1.37	37.80
Miconazole + Fluocinolone	2%+0.01%	OINT	1	13.7	6.33	2.16	116.42
Sertaconazole + Zn pyrithone	2%+1%	SHAMP	2	3	5.33	1.77	77.66
Oxiconazole+ Benzoic Acid	1%+0.2%/1g	CRM	1	3.07	5.15	1.67	67.75

They are available as ointment, cream, lotion, ointment, shampoo and soap.

Beclomethasone + Clotrimazole is available as cream, ointment, and lotion. Beclomethasone + clotrimazole + Neomycin Sulphate, Nadifloxacin + Mometasone + Miconazole and Oxiconazole+ Benzoic Acid are available as cream. Ketoconazole + Zn Pyrithone is available as lotion, soap and shampoo. Cetrimide+ Ketoconazole is available as soap. Sertaconazole + Zn pyrithone is available as shampoo. Beclomethasone + clotrimazole + gentamicin and Miconazole + Fluocinolone are available as ointment. Beclomethasone + clotrimazole + gentamicin is manufactured by 1 brand, Beclomethasone + clotrimazole by 7 brands, Beclomethasone + clotrimazole by 2 brands, Beclomethasone + clotrimazole + Neomycin Sulphate by 5 brands, Ketoconazole +Zn Pyrithone by 28 brands, Cetrimide+ Ketoconazole by 2 brands, Nadifloxacin + Mometasone + Miconazole by 3 brands, Sertaconazole + Zn pyrithone by 2 brands, Miconazole + Fluocinolone and Oxiconazole + Benzoic Acid by single brands each. Beclomethasone + clotrimazole combination is available in 2 strengths. Rest all drugs are available in single strength. Maximum cost ratio is seen with Ketoconazole 2%w/v +Zn Pyrithone 1%w/v (206.20). Minimum cost ratio (1.05) seen with Cetrimide 0.5%+ Ketoconazole 2%. Maximum percentage cost variation seen (20520.69) with Ketoconazole 2%w/v +Zn Pyrithone 1%w/v and minimum percentage cost variation (5.66) seen in Cetrimide 0.5%+ Ketoconazole 2%. More than 100% cost variation seen with Beclomethasone +clotrimazole+ gentamicin (0.025% w/w+1% w/w+0.1% w/w), Beclomethasone + clotrimazole (0.025% W/W+ 1%W/W and 0.05% W/W+ 1%W/W), Ketoconazole +Zn Pyrithone(2% w/v+1%w/v) and Miconazole + Fluocinolone(2%+0.01%).

Table 4 Shows Cost of generic drugs are less compared to branded drugs - Janaushadhi.gov.in. Highest difference was seen between the minimum cost brand of Fluconazole 150 mg tab with its generic drug cost (2.32) INR per tablet. Least difference between minimum brand cost and generics was observed for Ketoconazole 2% w/v Shampoo (0.6) INR. For systemic antifungal tablets on comparison between generic and brand drug we observed that minimum cost of branded antifungal drugs available in India are approximately five (05) times more than their generics.

Table 4: Shows Cost of generic drugs are less compared to branded drugs - Janaushadhi.gov.in

Drug	Strength	Formulation	Minimum cost(INR)	Maximum cost(INR)	Generic cost(INR)	Difference b/w generic cost of drug and minimum cost of brand
Fluconazole	150 mg	TAB	11.5	30	2.32	9.18
Itraconazole	100 mg	CAP	9	189	4.7	4.3
Ketoconazole	200 mg	TAB	19	44.8	2.59	1.69
	2% w/v	SHAMP	1.32	5.98	0.52	0.6
	2% w/w	LOT	1.89	5	0.4115	1.47
	2% w/w	CRM	3.64	10.93	1.16	2.48

Overall, with rise of diseases in India like HIV AIDS and diabetes which causes immunosuppression, fungal infections (both superficial and deep) are turning drug resistant and requiring long term therapy hence adding to the cost. Previous studies exploring the cost analysis of antifungal drugs have been done but knowledge has to be updated from time to time. In our study more than 100 % variation in the drug cost of majority of drugs (monotherapy, FDC) are seen. Thus, Indian patients have to spend more money to buy the branded drugs causing more economic burden which affects their medication adherence. In treatment of chronic conditions, a more effective drug can have poor medication adherence and compliance if the cost of the drug is high. Hence studies on pharmaco-economic analysis can create awareness in physicians about wider cost variations of the drugs prescribed and aids in patient getting appropriate affordable medication.

Limitations of the study are that the sources of drug information are fixed (CIMS, IDR and Jan Aushadhi price list 2022 scheme) and it can have its own set of flaws. The investigator has attempted to take a bird's eye view of the different prices of drugs in the Indian market. A pharmaco-economic analysis of a particular disease has not been done. Strength -The study has been done as an attempt to guide health professionals to select the appropriate P drug for the patient considering the affordability and effectiveness.

CONCLUSION

Our study showed that antifungal agents are available in different brands in the Indian market with wide price variation. To prescribe drugs rationally cost is an equally important factor that gets ignored commonly. Hence such studies comparing the costs of various brands of a drug can help in prescribing drugs affordable to the public. Since fungal infections are common in India and they require a long duration of therapy cost of drugs used in management of such infections play an important role in patient compliance. Sufficient information should be given to the physicians regarding price and data regarding bioequivalence of drugs. The regulatory authorities, pharmaceutical companies, physicians, pharmacists, and the common people need to address the problem of huge variation of cost in the drugs of the Indian market.

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