International Journal of Basic & Clinical Pharmacology
Manimozhi K et al. Int J Basic Clin Pharmacol. 2024 Nov;13(6):799-804
http://www.ijbcp.com
pISSN 2319-2003 | eISSN 2279-0780

DOI: https://dx.doi.org/10.18203/2319-2003.ijbcp20243025

Original Research Article

Cost variation analysis of disease modifying anti rheumatic drugs in Indian market

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Received: 30 July 2024
Accepted: 03 September 2024

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ABSTRACT

Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease with systemic complications, necessitating treatment to manage inflammation and prevent joint damage. In India, significant cost discrepancies exist among branded formulations of generic drugs, posing a financial burden on patients and impacting treatment adherence. This study focuses on cost differences of disease modifying anti rheumatic drugs (DMARDs) among Indian brands and advocating strict adherence to drug price control order (DPCO) rules and suggests scheduling non-scheduled drugs under DPCO.
Methods: This observational study analysed the cost of 6 oral DMARDs across 16 tablet formulations using data from National Pharmaceutical Pricing Authority (NPPA) and DPCO ceiling prices 2024. Number of brands per formulation, cost ratios, percentage variations, and DPCO price violations was analysed. Statistical analysis was performed using Microsoft Excel Office 2021, and Zotero was utilized for managing references.
Results: This study highlights significant price variations among DMARDs in the Indian market, with methotrexate 2.5mg exhibiting the highest cost ratio (1:3.63) and percentage cost variation (263.6%). Azathioprine 50mg has the most brands available (23), while sulfasalazine 500mg, sulfasalazine 1000mg, and tofacitinib 11mg are among the formulations with the fewest brands (3 each). Notably, sulfasalazine 500mg and hydroxychloroquine 200mg showed the most frequent instances of pricing violations above DPCO recommendations.
Conclusions: Strict regulation for price control and monitoring should be implemented since the DPCO has not yet achieved its goal of enforcing price ceilings, and non-scheduled drugs should be included under DPCO regulations effectively to enhance adherence to RA therapy.

Keywords: Antirheumatic drugs, Cost analysis, DMARD, DPCO, NPPA, Rheumatoid arthritis

INTRODUCTION

Rheumatoid arthritis (RA) is one of the most common systemic inflammatory disease, typically affecting joints symmetrically. It can also manifest beyond the joints, causing rheumatoid nodules, vasculitis, eye inflammation, neurological issues, cardiopulmonary disease, lymph node enlargement, and spleen enlargement. While the disease generally follows a chronic course, some patients may experience spontaneous remission.[1] RA affects 40 per 100,000 people annually, with a 1% global prevalence varying by race and region, most common in North American and Northern European populations, and highest among Native American-Indians (5%-6%). Women are twice as likely as men to develop RA, typically starting in their 50s, and adults with RA face higher disability rates, workplace limitations, reduced earnings, and increased mortality, primarily due to cardiovascular disease, infections, cancers, depression, and lung disease, with

common comorbidities including diabetes and autoimmune thyroid disease.[2] It is triggered in genetically susceptible individuals by microbial factors, leading to immunologic disturbances and the production of autoantibodies such as rheumatoid factor (RF), with cell-mediated immunity involving CD4+ T-cells and macrophages activated by infections. Antigen exposure activates CD4+ T-cells, causing cytokine release (TNF-α, IF-γ, IL-1, IL-6) that results in inflammation, joint damage, pannus formation, bone and cartilage destruction, fibrosis, and ankylosis.[3]

Drugs for RA include disease-modifying antirheumatic drugs (DMARDs) like methotrexate, sulfasalazine, hydroxychloroquine, leflunomide, and biologics such as TNF inhibitors (e.g., etanercept, infliximab). These drugs suppress inflammation, prevent joint damage, and improve symptoms but do not provide immediate relief like NSAIDs. DMARDs require several months for onset of benefit and may be used in combination for better efficacy, especially in severe cases. Corticosteroids are used for short-term relief of severe symptoms but are not disease-modifying.[4]

However, patients with RA face a significant issue with cost-related non-adherence and often find themselves sacrificing basic needs more than older adults with multiple other chronic conditions. Despite efforts aimed at reducing high drug costs through policy changes, the situation did not improve for RA patients.[5] The increased costs associated with non-adherence do not seem to stem from more frequent visits to healthcare specialists or higher referral rates. Instead, the higher costs linked to non-adherence primarily arise from increased expenditure on medications. In other words, patients who do not adhere to their medications are primarily those who struggle to afford the higher costs of their treatments.[6]

In India, the market is saturated with numerous branded formulations for every drug molecule, each priced differently across various regions, which ultimately places the burden of healthcare costs primarily on patients.[7] The high expenses associated with medical care should be a significant concern for policymakers and healthcare providers.[8] Clinicians often lack awareness about drug costs and may inaccurately assess medication prices, assuming that inexpensive drugs are more costly and expensive ones are less so. This misunderstanding can lead to an increase in overall drug expenses.[9]

This study aimed to investigate and compare the cost differences among various brands of the same generic DMARDs. The study also recommends including non-scheduled drugs under the DPCO to enhance the management of RA. Understanding these cost variations can contribute to developing more economical treatment regimens, which could ultimately improve patient compliance and reduce therapy failure rates.

METHODS

The present record based observational study was conducted on July 2024. The prices of 6 oral antirheumatic drugs, available in 16 different formulations were analysed. The cost of a particular drug (per 10 tablets), in the same strength and dosage form manufactured by different companies, was obtained from "Pharma Sahi Daam", a website and application provided by the National Pharmaceutical Pricing Authority (NPPA) that is openly accessible to the public.[10] The ceiling prices for oral antirheumatic drugs were sourced from the NPPA's Integrated Pharmaceutical Database Management System 2.0 price list 2024, implemented under the Drug Price Control Order.[11] The unit prices for all oral antirheumatic formulations were used, as the DPCO sets ceiling prices for one unit in rupees (INR). The ATC code for all DMARDs was also obtained from WHO's website for ATC/DDD Index 2024.[12] Only oral DMARD drugs in tablet form were included in the study. Drugs that were manufactured by only one company were excluded from the analysis.

The following parameters were analysed in this study: 1) The total number of brands available for each drug formulation, 2) The minimum and maximum cost for each formulation, 3) The cost ratio, which compares the highest to the lowest cost of the same drug produced by different pharmaceutical companies, was determined as follows:[13]

$$Cost\ ratio = \frac{Maximum\ cost}{Minimum\ cost}$$

The percentage cost variation between the maximum and minimum prices was calculated as follows:[14-15]

$$\%\ Cost\ variation = \frac{(Maximum\ cost - Minimum\ cost)}{Minimum\ cost} \times 100$$

The percentage of brands with prices exceeding the DPCO ceiling price, calculated for each drug formulation as follows:[15]

$$\frac{Number\ of\ brands\ having\ ceiling\ prices\ more\ than\ DPCO\ ceiling\ price}{Total\ number\ of\ brands} \times 100$$

Microsoft Excel Office 2021 was used for the statistical analysis throughout the study, and Zotero, a data management software, was used for managing and organizing the collected reference articles.

RESULTS

This study indicates significant price variations among different brands of the same antirheumatic drugs in the Indian market. The highest cost ratio, at 1:3.63, and the highest percentage cost variation, at 263.6%, were observed for methotrexate 2.5 mg. This was followed by tofacitinib 5 mg [(1:2.73) and (173.6)], methotrexate 5 mg [(1:2.58) and (158.9)] and methotrexate 10 mg [(1:2.11) and (111.2)] (Table 1).

Table 1: Variation in cost of DMARDs.

Antirheumatic drugs (DMARDs)	Strength (mg)	Pack size	Min. unit cost (INR[a])	Max. unit cost (INR)	Cost ratio	% cost variation
Azathioprine	50	10	8.00	12.00	1.50	50
Hydroxychloroquine	200	10	5.59	10.67	1.90	90.8
	300	10	13.15	20.33	1.54	54.6
	400	10	10.80	15.46	1.43	43.1
Leflunomide	10	10	12.44	13.94	1.12	12.0
	20	10	14.19	27.23	1.91	91.89
Methotrexate	2.5	10	2.20	8.00	3.63	263.6
	5	10	3.82	9.89	2.58	158.9
	7.5	10	10.22	14.85	1.45	45.3
	10	10	6.60	13.94	2.11	111.2
	15	10	32.00	51.56	1.61	61.1
Sulfasalazine	500	10	5.28	5.29	1.00	0.1
	1000	10	11.55	17.55	1.51	51.9
Tofacitinib	5	10	19.00	52.00	2.73	173.6
	10	10	53.50	65.00	1.21	21.4
	11	10	55.00	75.00	1.36	36.3

a-Indian Rupees

Table 2: DPCO price variation in DMARDs.

Antirheumatic drugs (DMARDs)	WHO ATC[a] code	Formulations	Strength (mg[b])	No. of brands	DPCO price 2024	Brands (%) with price > DPCO
Azathioprine	L04AX01	1	50	23	11.26	52.17
Hydroxychloroquine	P01BA02	3	200	14	6.36	78.57
			300	7	NA[c]	NA
			400	12	13.80	50.00
Leflunomide	L04AK01	2	10	7	NA	NA
			20	11	NA	NA
Methotrexate	L04AX03	5	2.5	19	5.31	42.10
			5	12	9.43	58.33
			7.5	14	NA	NA
			10	10	13.29	60.00
			15	6	NA	NA
Sulfasalazine	A07EC01	2	500	3	4.72	100
			1000	3	NA	NA
Tofacitinib	L04AF01	3	5	8	NA	NA
			10	4	NA	NA
			11	3	NA	NA

a-Anatomical Therapeutic Chemical; b-Not Applicable; c-milligram

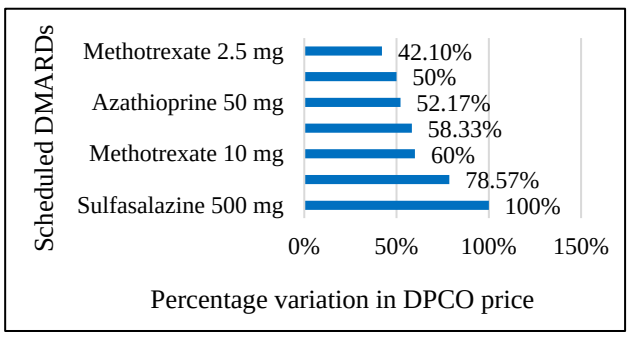

Figure 1: Percentage of price violation in scheduled DMARDs.

The antirheumatic drug with the most brands available in the Indian market is azathioprine 50 mg, with 23 brands, followed by methotrexate 2.5 mg, which has 19 brands. On the other hand, the least number of brands are available for sulfasalazine 500 mg, sulfasalazine 1000 mg, and tofacitinib 11 mg, with only 3 brands each for these formulations (Table 2).

Maximum price violation was noticed with sulfasalazine 500 mg with 3 out of 3 brands selling above the DPCO recommended price (100%) and hydroxychloroquine 200 mg with 11 out of 14 brands selling above DPCO ceiling price (78.57%) (Figure 1).

A total of 156 brands for all 16 formulations of antirheumatic drugs were identified. Among these, 63 brands (9 formulations) were not listed under the DPCO. The remaining 93 brand (7 formulations), were scheduled under the DPCO. Of these scheduled brands, 53 brands (56.98%) were priced above the DPCO recommended ceiling price, while 40 brands (43.01%) had prices below the recommended limit (Figure 2).

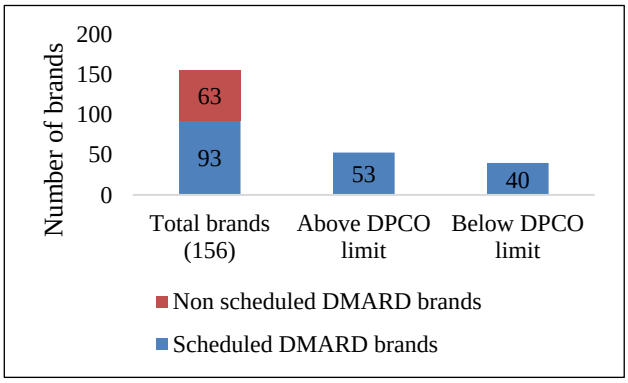

Figure 2: Number of brands violating DPCO price recommendations.

DISCUSSION

The Indian pharmaceutical market is dominated by branded generics, where multiple companies sell the same medication under various brand names alongside the original manufacturer. This diversity results in a vast array of pharmaceutical products, estimated between 60,000 and 70,000, leading to significant price discrepancies among available drugs.[16] Medication adherence plays a crucial role in achieving effective treatment outcomes, especially in chronic conditions like rheumatoid arthritis (RA). Regardless of a drug's efficacy, its benefits are only realized if patients adhere to their prescribed regimen. Poor adherence not only diminishes the potential benefits of medical care but also imposes substantial financial costs on both patients and the healthcare system.[17] Research indicates that non-adherence correlates with higher healthcare costs in rheumatology clinics, encompassing overall healthcare expenditures as well as those specifically related to rheumatology. Interestingly, this increased cost burden is primarily attributed to elevated medication expenses rather than an escalation in specialist visits or referrals.[6]

Our study reveals significant price disparities in the Indian market for DMARDs, highlighting both economic and regulatory challenges. Methotrexate 2.5 mg has the most notable price variation, with a highest cost ratio of 1:3.63 and a 263.6% difference between brands. Our study results are relevant to the study by Munshi et al, as they also found that the highest cost variation for DMARDs was for methotrexate 2.5 mg (378%) in the Indian market.[18] This inconsistency in pricing, also evident in other formulations like tofacitinib 5 mg and various dosages of methotrexate, indicates a systemic issue across the antirheumatic drug category. Such variations can lead to unequal access to treatment, where the financial ability of patients may dictate the quality and consistency of their care.

Market competition also plays a significant role in drug pricing. Azathioprine 50 mg, with 23 brands available, shows the highest level of competition, which could contribute to better pricing. In contrast, methotrexate 2.5 mg, despite having 19 brands, still experiences significant price disparities. Drugs like sulfasalazine 500 mg, 1000 mg, and tofacitinib 11 mg, each with only three brands available, highlight areas with limited competition, potentially leading to higher prices and reduced access for patients. Based on the drug molecules, the highest number of brands is for methotrexate (61), followed by hydroxychloroquine (33) and the drug with the least number of brands is sulfasalazine, with a total of 6 brands. Our study results are relevant to the study by Anzari et al, as they also found that the highest number of brands available in the Indian market is for methotrexate.[19]

The National Pharmaceutical Pricing Authority (NPPA) sets and revises prices of scheduled drugs under the Drug Prices Control Order (DPCO), 2013, ensuring essential medicines are available at reasonable prices. It monitors both scheduled and non-scheduled drug prices, taking action if prices exceed limits. The NPPA's regulation is based on principles from the National Pharmaceuticals Pricing Policy (NPPP), 2012, using the National List of Essential Medicines (NLEM) for price control. Monitoring involves inputs from Price Monitoring Resource Units (PMRUs), State Drugs Controllers (SDCs), market samples, databases, and public grievances through portals like Pharma Jan Samadhan and the Centralized Public Grievance Redress and Monitoring System (CPGRAMS).[20]

However, the DPCO is ineffective due to inadequate coverage and failing to meet its purpose. There's an urgent need to improve the price control criteria to impact the entire therapeutic category. To ensure drug security in India, strong regulatory institutions must be established or existing ones empowered.[21] Regulatory issues are highlighted by our findings, with sulfasalazine 500 mg showing 100% non-compliance with the Drug Price Control Order (DPCO) recommended price, and hydroxychloroquine 200 mg showing a high violation rate of 78.57%. This suggests a pressing need for stronger regulatory mechanisms and better market surveillance. The analysis of 156 brands across 16 drug formulations reveals that more than half of the DPCO regulated brands are priced above the ceiling, indicating inconsistent enforcement. These findings emphasize the need for improved regulatory oversight and innovative policy interventions to ensure fair pricing and access to antirheumatic drugs.

It is important to acknowledge the study's limitations. The study's focus was exclusively on oral Disease-Modifying Antirheumatic Drugs (DMARDs) in tablet form,

potentially overlooking other essential treatment options like injectable or topical formulations, which could have different pricing dynamics.

Additionally, our analysis was confined to data from a specific time point in July 2024. Drug prices are inherently volatile, influenced by factors such as manufacturing costs, regulatory changes, market competition, and economic fluctuations. Therefore, the prices observed in our study may not reflect long-term trends or seasonal variations accurately. Future research could enhance these findings by encompassing a broader range of medication forms and tracking price trends over an extended period.

CONCLUSION

In our country, even with a regulatory body overseeing pharmaceutical prices, there's still a significant price difference among DMARDs from different manufacturers. Despite severe penalties for companies that exceed ceiling prices, many brands continue to break these rules. As a result, the DPCO hasn't succeeded in lowering medicine costs as intended. To ensure compliance, strict regulations and better monitoring of drug prices are needed. We also recommend including non-scheduled drugs under price control to make essential medications more affordable. Additionally, more studies in other therapeutic areas are needed to highlight cost violations and encourage tighter government oversight.

ACKNOWLEDGEMENTS

Authors would like to thank all the staff in the medicine department for their support during study.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Manimozhi K, Abinish DG, Kalaivani S, Aswin J, Lokeshvaran D. Cost variation analysis of disease modifying anti rheumatic drugs in Indian market. Int J Basic Clin Pharmacol 2024;13:799-804.