Research Article

Cost variation study of various brands of drugs used in COVID-19 patients in India: A Pharmacoeconomic study

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Abstract

Background: For drugs approved for COVID-19 disease, physicians cannot be expected to know exact cost of each drug available in market, and are sold under different brands which put physicians in difficult state to choose the best drug for given patient. The present study was planned to get idea about costs of various brands of COVID-19 drugs, intending effective resource utilization.

Objectives: To find out and compare cost of drugs used in COVID-19 disease in the same dose and dosage forms being manufactured by different companies, to evaluate percentage variation of cost and cost ratio.

Methods: An observational, analytical study. Price in INR* (Indian National Rupees) of drugs used in COVID-19 manufactured by different pharmaceutical companies in India will be obtained from CIMS, NPPA website for cost variation analysis and cost ratio. The data obtained were analysed using Microsoft Excel software.

Results: Wide variations in the prices of different brands of the same drugs existed. Highest% cost variation in CIMS was observed for Vitamin -C (3767.6%), the lowest for Hydroxychloroquine 400mg (34.9%). As per NPPA, the highest % cost variation was observed for Ivermectin 12mg (4585.53%) and lowest for HCQs 200mg (37.22%). Cost ratio of drugs -CIMS: highest for Vitamin C (38.67) and lowest for HCQs 400mg (1.34), -NPPA: highest for Ivermectin 12mg (46.85) and lowest for Zinc 50mg (1.44).

Conclusion: Government should look into pricing control policy of drugs manufactured by various companies in India, so that it remains quality assured and affordable. Doctors must choose cost effective medicines based on country's health situation. **Keywords:** COVID-19, Cost ratio, Pharmacoeconomic study.

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1. Introduction

Pharmacoeconomic studies weigh the cost of alternative drugs and drug regimens against the outcomes they achieve to guide decisions and policies about which drugs should be used in general, which drugs should be paid for by the government or other third party payers, etc. The importance of pharmacoeconomic information to healthcare decision makers will depend upon the viewpoint from which the analysis is conducted. Pharmacoeconomics is needful in pharmaceutical industry, government, and in the private sector for comparing various cost consequences. The two fundamental components of pharmacoeconomic studies are measures of costs and measures of outcomes that are combined into a quantitative measure or ratio. [1]

Coronavirus disease 2019 (COVID-19) is a potentially severe acute respiratory infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The virus was identified as the cause of an outbreak of pneumonia of unknown cause in Wuhan City, Hubei

Province, China; in December 2019 [2] the clinical presentation is that of a respiratory infection with a symptom severity ranging from a mild common cold-like illness, to a severe viral pneumonia leading to acute respiratory distress syndrome that is potentially fatal. [3]

The pandemic of coronavirus disease 2019 (COVID-19) caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) presents an unprecedented challenge to identify effective drugs for prevention and treatment [4]

No proven effective therapies for this virus currently exist. The rapidly expanding knowledge regarding SARS-CoV-2 virology provides a significant number of potential drug targets. The most commonly used drugs are Favipiravir, Remdesivir and Steroids. Other drugs used are, Zinc, Vit C, and multivitamin supplements. [5]

Physicians cannot be expected to know the exact cost of each drug available in the market, because Indian markets are flooded with a large number of drugs used for COVID-19 and the same drugs are sold under different brands which put the prescribing physicians in a difficult state to choose the best drug for a given patient [6]. Due to lack of information on comparative drug prices and quality, non-availability of drugs and conflicts of interest are also responsible for physicians not prescribing of most economical treatment.

Generally prescribing physicians are under the influence of information provided to them in the form of formularies, promotional literature and marketing tactics of the medical representatives of that particular brand. The opinion that newer drugs are always better than older is also prevalent among physicians which need not be true always. This kind of biased information restricts both prescribers and patient's choices [7].

The objective of Pharmacoeconomics study is to influence policy formulation and effective decision making, rational prescribing behaviour and effective utilization of resources, to make a person or a group of people to change their behaviour and persuade them a new course of action that is more efficient. [8] The present study was undertaken to evaluate the cost variation amongst the different brands of anticovid drugs available in India.

1.1 Aims and objectives

- To find out and compare the cost of drugs used in COVID-19 disease in the same dose and dosage forms being manufactured by different companies.
- To evaluate the variation of cost among different brands for the same dosage and same active drug by calculating percentage variation of cost.
- To evaluate the cost ratio among different brands for the same dosage and same active drug.

- To compare costs of drugs mentioned in NPPA and DPCO.

2. Methodology

2.1 Study Design-This is an observational, analytical study.

-Price in INR* (Indian National Rupees) of drugs used in COVID-19 manufactured by different pharmaceutical companies in India, in the same strength and dosage form was obtained from the latest volume of Current Index of Medical Specialities (CIMS) i.e., October 2020-January 2021, NPPA website, DPCO 2020 and Jan Aushadhi drugs list for cost variation analysis, cost ratio and ceiling price comparison.

- Approval from Institutional Ethics Committee taken. IEC Reference no: BJGMC/IEC/Pharmac/ND-Dept 0321141-141

2.2 Selection Criteria

2.2.1 Inclusion criteria

The cost of drugs used in Covid-19 disease in the same dose and dosage forms being manufactured by different companies will be compared.

2.2.2 Exclusion criteria

- a. Anti-bacterial for treatment of superadded bacterial infection or atypical pneumonia prophylaxis.
- b. Multivitamins i.e., B- complex excluded.
- c. Drug formulations with no price information.

2.3 Analysis of Data

- To identify the price (in Indian rupees) of various brands of drugs used in Covid-19 disease- i.e. Minimum price (INR), & Maximum price (INR) (of a drug manufactured by various pharmaceutical companies in the same strength)
- The cost ratio: The ratios of the cost of the costliest to cheapest brand were calculated. This tells us how many times costliest brand costs more than the cheapest one in each generic group.

Cost Ratio = *Cost of costliest brand / Cost of cheapest brand*

- The following formula was used to analyse the cost variation.

% Cost variation =

<u>(Price of most expensive brand–Price of least expensive brand)</u>×100 (Price of least expensive brand)

 Ceiling price in INR was noted from Jan Aushadhi and DPCO list(2020)

2.4 Statistical analysis:

The data obtained from the mentioned sources were analysed using Microsoft Excel®software. The price variations have been expressed in percentages and the results have been shown in tables, bar charts.

3. Results:

3.1 Cost variation:

The prices of various drugs used in COVID-19 disease available in the Indian market and produced by different pharmaceutical companies were analysed. Wide variations in the prices of different brands of the same drugs existed, both in the Current Index of Medical Specialities (CIMS) and National Pharmaceutical Pricing Authority (NPPA) categories. We have mainly analysed single drugs except for one combination Lopinavir + Ritonavir. Among all the drugs used for treating Covid-19 disease, the highest percentage of cost variation was observed in CIMS was for Vitamin -C (3767.6%) and the lowest was for Hydroxychloroquine 400mg (34.9%).[Table 1] As per NPPA,

the highest percentage of cost variation was observed for Ivermectin 12mg (4585.53%) and lowest for HCQs 200mg(37.22%). [Table 2]

3.2 Cost ratio:

Cost ratio is the ratio of the cost of the costliest to the cheapest branded formulations of the same drug, which tells us by how many times the cost of the most expensive drug is higher than the cheapest one for each of the drugs considered for evaluation. Cost ratio of drugs according to CIMS is found highest for Vitamin C (38.67) and lowest for HCQs 400mg (1.34) [Table 1]. As per NPPA, the cost ratio was found highest for Ivermectin 12mg (46.85) and lowest for Zinc 50mg (1.44). [Table 2]

Table 1: CIMS

Sr. No	Drug Name	Dosage form	Strength	Min Price	Max Price	Cost Ratio	% Cost Variation
1.	Remdesivir	IV	100 mg	2800	5400	1.93	92.85
2.	Favipiravir	PO	200 mg	40	102.9	2.572	157.25
3.	Ivermectin	PO	12 mg	9.6	160	16.66	1566.66
4.	HCQ	PO	400 mg	9.7	13.093	1.349	34.9
			200 mg	3.4	8.5	2.5	150
5	Oseltamivir	PO	75mg	42.9	62.9	1.466	46.62
6.	Vit C	PO	500	0.71	27.46	38.67	3767.6
7.	Zinc	PO	50mg	Nil	Nil	-	-
8.	Methyl Prednisolone	IV	40mg	10.33	155	15	1400
9.	Dextromethasone	IV	4mg/ml	0.81	8.1	10.125	900
10.	Enoxaparin	SC	0.6ml/60mg	430	630	1.465	46.51
11.	Prednisolone	PO	5mg	0.39	1.05	2.69	169.23
			10 mg	0.736	1.704	2.31	131.5
			20 mg	1.24	3.5	2.82	182.25
			40 mg	2.52	6.8	2.69	169.84
12.	Heparin	SC	1000 IU/ ml	5.94	85	14.3	1330.9
			5000 IU/ ml	3.75	117	31.2	3020
13	LOPI + RITO	PO	200 mg + 50 mg	37.5	62	1.65	65.33

As per CIMS, there was only a single brand for Tocilizumab (ACTEMRA) and Itolizumab (ALZUMAB) and the price is mentioned in Table 3.

 Table 2: National Pharmaceutical Pricing Authority (NPPA)

Sr. No	Drug name	Dosage form	Strength	Min Price	Max Price	Cost Ratio	% cost Variation	Ceiling price
1.	Remdesivir	IV	100 mg	2800	5400	1.93	92.85	Pares
2.	Favipiravir	PO	200 mg	31.25	99	3.171	216.8	
3.	Ivermectin	PO	12 mg	3.18	149	46.85	4585.53	
4.	HCQ	PO	400 mg	3.4	8.5	2.5	150	
			200 mg	4.5	6.625	1.472	47.22	
5	Oseltamivir	PO	75mg	47.5	129	2.7	171.57	
6.	Vit C	PO	500					1.37
7.	Zinc	PO	50mg	4.5	6.52	1.44	44.88	
8.	Methyl Prednisolone	IV	40mg	26.8	70.53	2.63	163.17	
9.	Dextromethasone	IV	4mg/ml					4.64
10.	Enoxaparin	SC	0.6ml/60mg	218.75	491.73	2.24	124.79	
11.	Prednisolone	PO	5mg					0.56
			10 mg					0.97
			20 mg					1.95
			40 mg					2.8
12.	Heparin	SC	1000 IU/ ml					16.26
			5000 IU/ ml	9.418	29.76	3.15	212.99	
13	LOPI + RITO	PO	200 mg + 50 mg					45.43

As per NPPA, there was only a single brand for Tocilizumab (ACTEMRA) and Itolizumab (ALZUMAB) and the price is mentioned below.

Sr. No.	Drug Name	Dosage form	Strength	Cost			
1.	Tocilizumab	IV	400mg	40545			
2.	Itolizumab	IV	25mg/5ml	7950			
Table 3:							
Sr. No.	Drug Name	Dosage form	Strength	Cost			
1.	Tocilizumab	IV	400mg	40600			
2.	Itolizumab	IV	25mg/5ml	8230			

The percentage cost variation and cost ratio of various drugs used in COVID-19 as per CIMS and NPPA are depicted in Fig 1, Fig 2, Fig 3 and Fig 4.



Fig 1: Percentage cost variation -CIMS

Fig 2: Cost ration - CIMS









3.3 Comparison of the ceiling prices between NPPA and DPCO

It was found that the ceiling price of Dexamethasone was approximately four times higher in NPPA (4.65INR) as

compared to DPCO(1.15INR) [Fig 5]. The ceiling price of other drugs like Vitamin-C, Prednisolone, Heparin, Lopinavir+ ritonavir were more or less similar.



Fig 5: Comparisons of Ceiling Price of NPPA and DPCO

3.4 Jan Aushadhi:

Jan Aushadhi Scheme (JAS) which comes under Pradhan Mantri Yojana is a noble scheme launched by the government of India and would go a long way if the stores are offered to genuine owners and the process of providing generic medicines to the patients is followed in a transparent manner. Among the drugs used for COVID – 19 diseases, following drugs were included in JAS: Ivermectin, HCQs, Oseltamivir, Dexamethasone, Enoxaparin, Prednisolone, and Heparin. [Table 4]

Sr. No	Drug Name	Dosage form	Strength	Cost
1.	Ivermectin	PO	12 mg	2.1
2.	HCQ	PO	200 mg	3
3.	Oseltamivir	PO	75 mg	45.8
4.	Dexamethasone	IV	4 mg/ml	1.5
5.	Enoxaparin	SC	0.6ml/60mg	198
6.	Prednisolone	PO	5mg	0.33
			10mg	0.6
7.	Heparin	SC	1000IU/ml	8.2
			5000IU/ml	10

 Table 4: Cost as per Jan Aushadhi Scheme

(All the Costs are Cost per tablet or Cost per ml)

3.5 Drug price control order:

DPCO is an organization of the Government of India which was established, inter alia, to fix/ revise the prices of controlled bulk drugs and formulations and to enforce prices and availability of the medicines in the country, under the Drugs (Prices Control) Order, 1995. It included HCQs, Vitamin -C, Methylprednisolone, Dexamethasone, Enoxaparin, Prednisolone, Heparin and Lopinavir + Ritonavir. (Table 5)

Sr. No	Drug Name	Dosage form	Strength	Cost (March)	Cost (Sep)
1.	HCQ	PO	200mg	5.80	5.91
2.	HCQ	PO	400mg	11.69	11.91
3.	Vit C	PO	500 mg	0.89	1.37
4.	Methyl Prednisolone	IV	40 mg	52.81	53.81
5.	Dexamethasone	IV	4mg/ml	1.15	1.17
6.	Enoxaparin	SC	0.6 ml/60mg	99.48	101.35
7.	Prednisolone	PO	5mg	0.55	0.56
			10mg	0.95	0.97
			20mg	1.91	1.95
			40mg	2.75	2.80
8.	Heparin	SC	1000IU/ml	15.96	24.39
			5000 IU/ml	39.61	60.54
9.	LOPI + RITO	PO	200mg+50mg	44.59	45.43

Table 5: Price as per DPCO

As we can see here in table 5, DPCO list was released in the month of March 2020 and September 2020 which coincided with the peak period of our pandemic. The prices of the drugs (mentioned as per tablet for oral drugs / per ml for injectables in the above fig) have increased considerably with almost doubling of cost for Heparin.

Table 6: Comparison of branded (as per CIMS and NPPA) and generic (as per JAS and DPCO):

Sr. No.	Drug Name	Strength (mg)	Cost -CIMS (min)	Cost- NPPA(min)	Cost- JAS	Cost – DPCO
1	Remdesivir	100	2800	2800		
2	Favipiravir	200	40	31.25		
3	Ivermectin	12	9.6	3.18	2.1	
4	HCQ	400	9.7	3.4		11.91
		200	3.4	4.5	3	5.91
5	Oseltamivir	75	42.9	47.5	45.8	
6	VIT C	500	0.71	1.37(CP)		1.37
7	ZINC	50	Nil	4.5		
8	Methyl Prednisolone	40	10.33	26.8		53.81
9	Dexamethasone	4	0.81	4.64(CP)	1.5	1.17
10	Enoxaparin	60	430	218.75	198	101.35
11	Prednisolone	5	0.39	0.56	0.33	0.56
		10	0.736	0.97	0.6	0.97
		20	1.24	1.95		1.95
		40	2.52	2.8		2.80
12	Heparin	1000IU	5.94	16.26(CP)	8.2	24.39
		5000IU	3.75	9.418	10	60.54
13	Lopi+ Rito	200+50	37.5	45.43(CP)		45.43

As per the above Table, we notice that the cost of least expensive brand in CIMS was cheaper than the generic drugs cost from JAS and DPCO.

4. Discussion

In this Pharmacoeconomic studies, result shows wide variation in the pricing of drugs used for COVID-19. The cost variation and cost ratio were found to be more for Vit C and Ivermectin tablets as per the results of the study. The reason could be due to preferential use of costly branded drugs overs the generics. What the prescriber should be made aware of is that the generics are equally efficacious. Cost of the drug is one of the important factors for the compliance of the patients or adherence to treatment because the patient feels that the cost of therapy is a financial burden, then the compliance with therapy will be compromised [11]. It is also estimated that around 20 million people in the nation fall below the poverty line due to health-related expenditures each year [12]. Therefore, the medicines are required to be made available at affordable prices for the masses in general. Drug discovery is an expensive process and most of the pharmaceutical companies try to recover the investments in a short period of time, ignoring the resultant financial burden on the patients.

India had delayed the imposition of drug price control by almost a decade in order to balance the promotion of the domestic pharmaceutical industry and access to essential drugs.[13] The NPPA controls the price of the drugs using a market-based mechanism. There were two major policy changes in DPCO 2013, both of which have some issues. Firstly, there is a selective imposition of price control to selective formulations of a particular drug, based mainly on their dose strengths, and excluding other doses and FDCs. This is creating incentives for companies to aggressively market non-regulated formulations of the drugs.

Secondly, the ceiling price is based on the simple average of the prices of the top brands of a particular drug in the market having a market share of at least 1%. This also takes into consideration the costlier time-release formulations of the drugs, and if they happen to hold more than 1% of the market share, they will push up the ceiling prices as a whole.

There are several ways to combat these problems. One way is to discard the policy of partial price control and impose price control on all formulations of a drug. Another way is to refine the method of determining the ceiling price to make it more effective. Recently, the Government of India has started collecting price data from individual manufactures. If this process can be speeded up, the regulation can become more effective as the firms will not be able to coordinate and push up their prices before the regulation order.

Another alternative is to promote generic medicines. Some studies based on the comparative effectiveness of generic versus brand-name medications have found the clinical outcomes associated with both quite comparable; this should instil more confidence in the patients and healthcare providers on the quality of generic medicines [14,15]. The pharmacists are also not inclined towards selling generic medicines due to low profit margins. Various regulators have suggested that de-branding generic drugs is likely to be more effective than price regulations to bring down the prices of drugs. To promote this, legislative measures to mandate doctors to prescribe generic drugs rather than brand names have been taken [16].

Doctor's ignorance of costs, combined with their tendency to underestimate the price of expensive drugs and overestimate the price of inexpensive ones, demonstrate a lack of appreciation of the large difference in cost between inexpensive and expensive drugs. This discrepancy in turn could have profound implications for overall drug expenditures. [17] Most of the treating physicians must keep in mind the financial condition of the patient and adopt a shared decision-making approach in prescribing medications. Results from a study have indicated that providing doctors with a manual of comparative drug prices including most of the available brands in the country is associated with a reduction in the patient's expenditure on medications. [18]

5. Conclusion

Our study concludes that a wide variation in pricing is found in the Indian market for various drugs used to treat COVID-19 disease. Reducing the cost variation and thereby improving the affordability of drugs would improve medication compliance, the health status of the community, and the national economic burden due to healthcare expenditures. Physicians should be made aware of the prices of various drugs while encouraging them to prescribe generic medicines. Government should look into the pricing control policy of these drugs manufactured by various companies in India, so that pricing of various brands remains uniform and cost effective. Doctors must prescribe rationally. Rational prescribing means choosing cost effective and safe medicines based on country's health situation. A collective effort would propel us towards the goal of "Health for All."

Strengths

This study is first of its kind for drugs used in COVID 19. The prices have been extracted from most of the sources of pricing information like CIMS, NPPA, JAS and DPCO.

Limitations

Antibacterial drugs were excluded from our study because their use differs based on the superadded bacterial infections and the data would have been extensive to assess brands of different antibiotics from all the sources which were considered for the study. The same was for multivitamins. The strengths or the doses for multivitamins were not constant.

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