Pharmacology and Clinical Pharmacy Research
Volume 6 No. 3 December 2021
ISSN:2527-7322 | e-ISSN: 2614-0020
doi: 10.15416/pcpr.v4i3.32488

A Pharmacoeconomic Comparison of Cost Variation among Hypolipidemic Drugs Available in Indian Market

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Abstract

Hyperlipidemia is a major cause of atherosclerotic coronary and cerebrovascular disorders affecting a large Indian population. The cost of various hypolipidemic drugs that are used for prevention and treatment of these afflictions largely vary in the Indian pharmaceutical market. Our study aimed to evaluate the cost variation of different brands of hypolipidemic drugs and to compare the branded prices with their corresponding generic and ceiling prices. The costs of various drugs were procured from the latest issue of the "Drug Today" from October to November 2020 edition which is a directory of all the drugs available in India published quarterly every year by Lorina Publications (India) Inc. Cost ratio, per cent cost variation, and daily defined dose (DDD) were calculated. We also compared the branded prices of drugs with their generic and ceiling prices available at the official website. A total of 9 single hypolipidemic drugs and 9 fixed dose combinations (FDC) showed a wide per cent cost variation. The highest percentage of cost variation was atorvastatin 80 mg (3284%) whereas fenofibrate showed the lowest percent cost variation (0.91%). The cost ratio was also found higher in 2 from 6 drugs. Among FDCs, atorvastatin 10mg + ezetimibe 10 mg (484%) showed a higher cost variation and rosuvastatin 20 mg + fenofibrate 160mg (0.6%) showed a minimum variation. The maximum cost variation from branded prices compared to generic prices was found in simvastatin 20 mg (544%) and atorvastatin 10 mg (155%). In summary, our study showed a wide variation in cost of hypolipidemic drugs available in Indian market which provides an insight to the prescriber, gives drug price control authorities to minimize the financial burden on the patient, and improve their compliance.

Keywords: Hypolipidemic, cost variation, Daily Defined Dose, generic, ceiling

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Received: 2 March 2021. **Revised**: 24 June 2021. **Published:** 6 December 2021

Introduction

Cardiovascular disease(CVD) is becoming more prevalent and is one of the leading cause of death globally.[1] The modifiable risk factors associated with CVD include dyslipidemia, hypertension, diabetes mellitus and smoking.[2] The prevalence of dyslipidemia in India is high affecting 25-30% of urban and 15-20% of population with raised total cholesterol, Apolipoprotein B (ApoB), Low Density Lipoprotein (LDL), Triglycerides (TG) and High Density Lipoprotein Levels (HDL).[3]

Drugs along with lifestyle modifications such as diet therapy, exercise and smoking cessation is important for the management of dyslipidemia.[4] There is a huge body of evidence suggesting the crucial role of lipid lowering drugs in correcting dyslipidemias.[5] The lipid lowering drug therapy include statins and non-statin therapy (fibrates, niacin, bile acid binding resins, ezetimibe, PCSK9 inhibitors, omega-3 fatty acid ethyl esters, mipomersen, and lomitapide).

The 2014 American College of Cardiology/ American Heart Association guideline recommend the use of statins to reduce atherosclerotic CVD risk and combining Non statin therapy in high risk group with care.[6] Statins are among the most effective and well tolerated drugs for treating dyslipidemias. Being HMG-CoA reductase inhibitors, they cause maximum reduction in lowering LDL cholesterol levels.

Statins are classified into High intensity statins which reduce LDL-C by approximately 50% and include atorvastatin 40-80 mg and rosuvastatin 20-40 mg; medium intensity statins which reduce LDL-C by approximately 30%-50% and include atorvastatin 10-20 mg, fluvastatin 40-80 mg, lovastatin 40 mg, pitavastatin 2-4 mg, pravastatin 40-80 mg, rosuvastatin 5-10 mg, and Simvastatin 20-40 and low intensity statins which reduce LDL-C by approximately <30% and include fluvastatin 20-40 mg, lovastatin 20 mg, pitavastatin 1 mg, pravastatin 10-20 mg, and simvastatin 10 mg.

In India, drugs are manufactured by a large number of pharmaceutical companies with different prices. Although government has fixed the prices of generic drugs under Jan Aushadhi Scheme[7] as well as ceiling prices are imposed by National Pharmacological Pricing Authority (NPPA) under Drugs Prices Control Order[8] to provide affordable medicines to the masses. In India, there is no provision of medical insurance for chronic diseases and the patients have to bear the cost of medicines by themselves.

Cost analysis studies are important to evaluate the price variations of commonly prescribed medicines so that physicians can use this information to reduce the cost of treatment significantly.[9] Our study aims to find out the variation in prices of different brands of the same drug bycalculating percent cost variation, cost ratio and the same in terms of Defined Daily Dose (DDD)[10] as well. Secondly, we also compared the brand prices with their corresponding generic and ceiling prices in terms of cost variation and cost ratio to analyse the pharmacoeconomic perspective of hypolipidemic drugs.

Methods

This research was an analytical and comparative type of economonic analysisof commonly available hypolipidemic drugs in India. We obtained the information about the available branded price of 9 single and 9 Fixed Dose Combinations (FDC) of hypolipidemic drugs from the latest issue of the "Drug Today" 2020 edition.[11] The generic costs of hypolipidemic drugs were obtained from the website of Bureau of Pharma PSU's of India (BPPI) and the ceiling price from the official

website-latest DPCO list 2020imposed by Government of India.

Case Definitions

1. DDD (Defined Daily Dose)

DDD denotes "the average daily maintenance dose or consumption used for a particular indication in an adult"[10]

2. Cost ratio

It is the ratio of the cost of the costliest to the cheapest branded formulation of a particular drug which gives an idea of how much is the expensive brand costlier than the cheapest brand of the same drug.[12]

3. Cost variation percent

It was calculated as follows

Cost variation%=

Maximum cost-Minimum cost: Minimum costx100[13]

The minimum and maximum price per unit (tablet/capsule) and per DDD of a particular drug, in the same and different doses was calculated and number of manufacturing companies were noted. Minimum and maximum price per DDD was also calculated by multiplying DDD with respective price of per unit. The difference in prices were compared and calculated in terms of cost ratio and cost variation percentage.

The drugs that out of our source were excluded from the study. Moreover, the minimum cost of branded drugs were compared with generic costs and the maximum cost were compared with the ceiling price. The data obtained was expressed in percentages and the results have been shown in tables and bar graphs.

Results and Discussion

Statins have shown proven benefit to decrease cardiovascular morbidity as well as mortality in primary and secondary prevention studies and showed 20%; 23%; and 17% decrease in CVD mortality, cardiovascular events and stroke respectively with every 39 mg/dl reduction in LDL-C.[14] These drugs are needed to be prescribed to a large population on a chronic basis for primary as well as secondary prevention. Therefore, it is necessary to evaluate the variations observed in the pricing of these commonly prescribed medicines as this can affect drug selection, cost regulation and formulary development decisions with the aim of reducing the economic burden on the patients. Earlier cost effectiveness analysis studies on Statins showed greater benefit of these drugs among high risk groups.[15] Our study compared the cost variation among various hypolipidemic drugs and also compared their cost with their generic and ceiling prices fixed by government of India.

A total of 9 single hypolipidemic drugs and 9 FDC showed a wide per cent cost variation. The highest percentage of cost variation was atorvastatin 80 mg (3284%) whereas fenofibrate showed the lowest percent cost variation (0.91%). Cost variation, cost ratio, and DDD of hypolipidemic drugs are presented in Table 1 and Figure 1. The maximum price per DDD was rosuvastatin 40 mg 77.28 Rs followed by gemfibrozil 600 mg 47.32 Rs and minimum price per DDD was of atorvastatin 10mg, 0.5.Rs.(Table 1,Fig.2)

Among 9 FDCs studied, cost variation was highest for atorvastatin 10mg + ezetimibe 10 mg (484%) and minimum was seen in rosuvastatin 20 mg + fenofibrate 160 mg (0.6%). Out of 9 FDCs, atorvastatin 10 mg + fenofibrate 160mg, atorvastatin 10 mg + ezetimibe 10 mg and rosuvastatin + cost ratio. The combination of atorvastatin 10mg + ezetimibe 10 mg was manufactured by maximum of 15 companies. Cost variation and cost ratio of FDCs of hypolipidemic drugs are presented in Table 2 and Figure 3.

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ISSN:2527-7322 | e-ISSN: 2614-0020

Table 1. Cost Variation, Cost Ratio and DDD of Hypolipidemic Drugs

Drug	DDD	Dose and No. of Brands	Minimum price/unit	Minimum price/DDD	Maximum Price/unit	Maximum Price/DDD	Cost Ratio	Cost Variation (%)
Gemfibrozil	1.2 g	300 mg (5)	3.80	15.20	11.83	3.11	211.31	211.31
		600 mg (2)	10.00	20.00	23.72	47.4	2.37	137.2
Bezafibrate	0.6 g	200 mg (1)	9.60	28,8	9.6	28.8	1	0
		400 mg (2)	9.01	13.51	19.95	29.92	2.21	121.46
Fenofibrate	0.2 g	145 mg (1)	14.60	20.13	14.60	20.13	1	0
		160 mg (1)	7.90	12.34	7.90	12.34	1	0
		200 mg (2)	7.85	7.85	15.00	15	1.91	0.91
Lovastatin	45 mg	10 mg (11)	2.50	11.25	7.50	33.75	3.00	200.00
		20 mg (12)	4.80	10.80	12.50	28.12	2.60	160.00
Simvastatin	30 mg	5 mg (6)	3.60	21.60	7.1	42.6	1.97	200.00
		10 mg (6)	5.80	17.55	11.1	33.3	1.91	169.00
		20 mg (4)	10.50	15.75	17.3	25.95	1.64	97.20
Atorvastatin	20 mg	5 mg (8)	1.50	6.00	9.30	37.20	62.00	520.00
		10 mg (51)	0.50	1.00	14.00	28.00	28.00	2700.00
		20 mg (26)	1.35	1.35	20.90	20.90	15.48	1448.00
		40 mg (11)	1.96	0.98	20.36	10.13	10.33	933.00
		80 mg (3)	1.43	0.35	48.4	12.10	33.80	3284.00
Rosuvastatin	10 mg	5 mg (14)	2.00	4.00	8.70	17.40	4.35	335.00
		10 mg (25)	2.90	2.90	15.30	15.30	5.27	427.50
		15 mg (1)	18.00	12.00	18.00	12.00	1	0
		20 mg (18)	2.43	1.21	30.80	15.40	12.67	1167.00
		30 mg (1)	30.00	10.00	30.00	10.00	1	0
		40 mg (3)	6.00	9.96	48.30	77.28	8.05	705.00
Pravastatin	30 mg	10 mg (1)	10.00	30.00	10.00	30.00	1	0
		20 mg (1)	16.50	24.70	16.50	24.70	1	0
Ezetimibe	10 mg	10 mg (4)	5.90	5.90	12.50	12.50	2.11	111.80

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ISSN:2527-7322 | e-ISSN: 2614-0020

Table 2. Cost Variation and Cost Ratio of FDCs of Hypolipidemic Drugs

Drug Combination	Drugs and No. of Brands	Minimum Price/unit	Maximum Price/unit	Cost Variation	Cost Variation (%)
Simvastatin+Ezetimibe	30+10 mg (1)	5.70	5.70	1.00	0
Atrovastatin+Aspirin	10+75 mg (5)	2.30	3.10	1.34	34.70
	20+75 mg (4)	2.50	2.50	1.00	0
Atorvastatin+Clopidogrel	10+75 mg (4)	12.50	18.30	1.46	46.40
Atorvastatin+Aspirin+ Clopdogrel	10+75+75 mg (2)	4.60	4.80	1.04	4.34
	20+75+75 mg (1)	6.40	6.40	1.00	0
Atrovastatin+Fenofibrate	10+145 mg (2)	9.90	15.00	1.51	51.50
	10+160 mg (8)	3.50	17.10	4.88	388.00
	20+160 mg (1)	20.34	20.34	1.00	0
Atrovastatin+Ezetimibe	10+10 mg (15)	3.90	22.80	5.84	484.00
	10+5 mg (15)	9.10	9.10	1.00	0
	5+10 mg (1)	8.00	8.00	1.00	0
	20+10 mg (1)	25.80	25.80	1.00	0
Rosuvastatin+Fenofibrate	5+145 mg (2)	14.00	16.00	1.14	14.28
	10+145 mg (8)	18.80	23.30	1.23	23.93
	10+67 mg (1)	20.85	20.85	1.00	0
	10+160 mg (4)	14.80	17.00	1.14	14.86
	20+160 mg (2)	32.30	32.50	1.00	0.60
Rosuvastatin+Aspirin	10+75 mg (2)	5.00	6.00	1.20	200.00
	10+150 mg (10)	6.00	6.00	1.00	0
	20+75 mg (1)	6.50	6.50	1.00	0
Rosuvastatin+Clopidogrel	10+75 mg (3)	9.60	15.00	1.56	56.25
	20+75 mg (1)	19.50	19.50	1.00	0
Rosuvastatin+Clopidogrel+Aspirin	10+75+75 mg (7)	7.16	19.60	2.73	173.70
	20+75+75 mg (4)	13.00	25.00	1.92	92.30

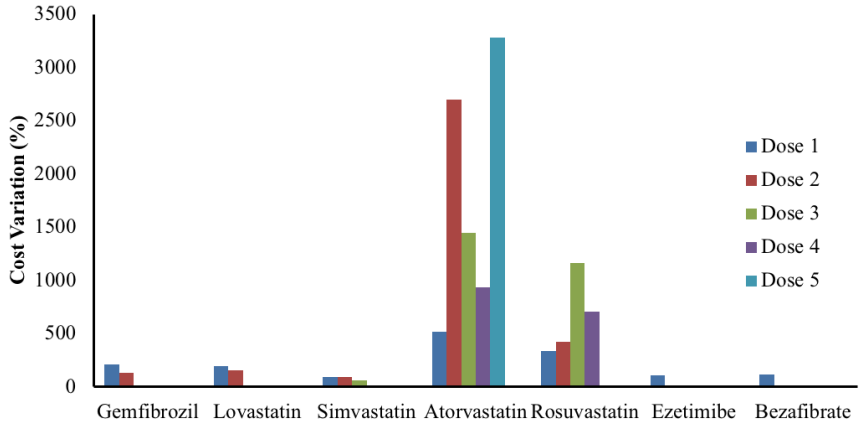

Figure 1. Cost variation (%) among Branded Hypolipidemic Drugs

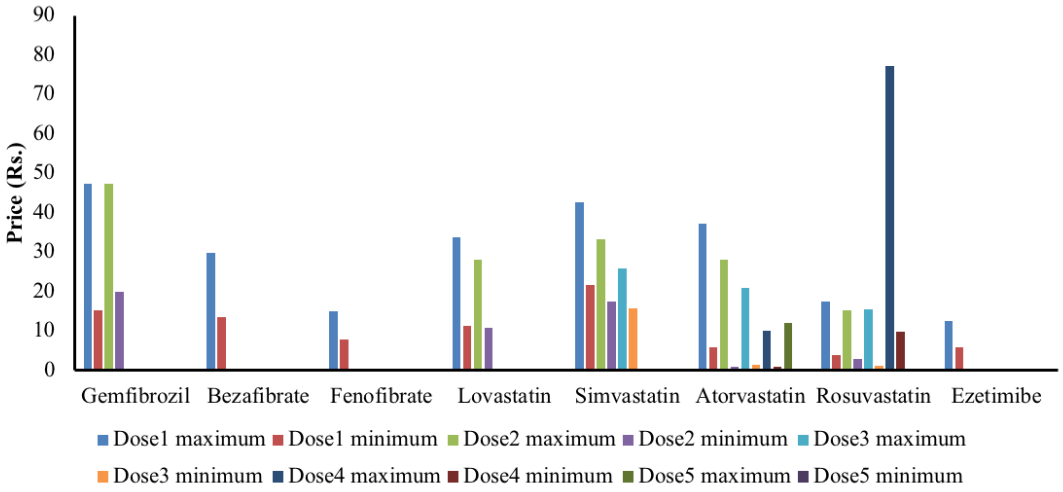

Figure 2. Comparison of Maximum and Minimum Price per DDD

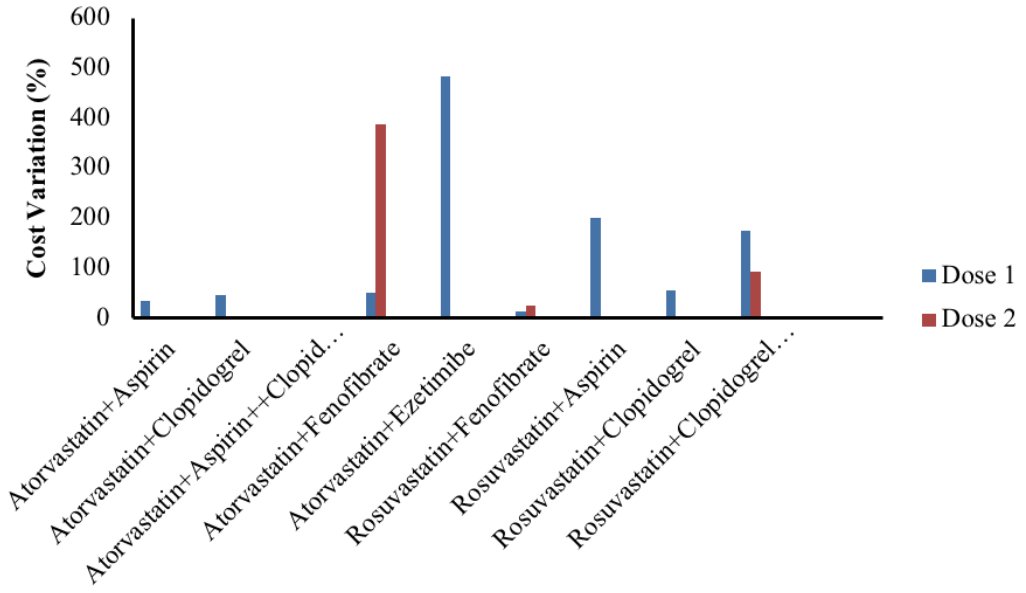

Figure 3. Cost Variation (%) among Branded FDC of Hypolipidemic Drugs

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ISSN:2527-7322 | e-ISSN: 2614-0020

Table 3. Comparison of Brand prices with Generic Prices of Hypolipidemic Drugs

Drug	Dose and No. of Brands	Minimum price Branded drug/unit	Generic Price/unit	Cost Ratio	Cost Variation (%)
Simvastatin	10 mg (6)	5.80	0.90	6.40	544.0
	20 mg (4)	10.50	1.20	8.75	775.0
Atorvastatin	5 mg (8)	1.50	3.82	0.26	-60.7
	10 mg (51)	0.50	0.56	0.89	10.7
	20 mg (26)	1.35	0.97	1.39	39.1
	40 mg (11)	1.96	1.80	1.08	8.8
Rosuvastatin	5 mg (14)	2.00	1.12	1.78	78.5
	10 mg (25)	2.90	1.40	2.07	107.0
	20 mg (18)	2.43	2.70	0.90	-10.0
Fenofibrate	160 mg (1)	7.90	2.40	3.29	229.0
Atorvastatin+Aspirin	10+75 mg (5)	2.30	1.20	1.91	91.6
	20+75 mg (1)	2.50	1.80	1.38	38.8
Atorvastatin+Fenofibrate	10+160 mg (8)	3.50	1.66	2.10	118.7
Atorvastatin+Clopidogrel	10+75 mg (4)	12.50	2.90	4.31	331.0
Atorvastatin+Clopidogrel+ Aspirin	10+75+75 mg (2)	4.60	3.60	1.27	27.7
Rosuvastatin+Fenofibrate	10+160 mg (4)	14.80	2.70	5.48	448.0
Rosuvastatin+Aspirin	10+75 mg (2)	5.00	4.40	1.13	13.12

Table 4. Comparison of Brand Drugs Prices with Ceiling Prices of Hypolipidemic drugs

Drug	Dose and No. of Brands	Minimum Price branded drug/unit	Ceiling Price/unit	Cost Ratio	Cost Variation (%)
Atorvastatin	10 mg (51)	14.00	5.47	2.55	155.00
	20 mg (26)	20.90	13.25	1.57	57.70
	40 mg (11)	20.26	19.24	1.05	5.30
Atorvastatin+Aspirin	10+75 mg (5)	3.10	3.80	0.81	-22.50
Rosuvastatin+Aspirin+ Clopidogrel	10+75+75 mg (4)	19.60	11.48	1.70	70.70
Rosuvastatin+Clopidogrel	20+75 mg (1)	19.50	16.77	1.16	16.27

When we compared the generic prices of various hypolipidemics with their minimum branded price, it was found that the maximum cost variation was seen in simvastatin 10 mg (544%). On the other hand, the minimum generic price of atorvastatin 5mg and rosuvastatin 20 mg was observed to be greater than the minimum branded price by 60.7% and 10% respectively. Additionally, simvastatin at two doses (10 and 20 mg) showed highest cost variation of 544 and 775% respectively as compared to generic counterparts. (Table 3)

Comparison of branded price with DPCO ceiling price was found that the highest cost variation was observed in atorvastatin 10mg (155%) and lowest cost was in atorvastatin 40mg (5.3%). The only exception was found in atorvastatin 10 mg + aspirin 10 mg FDC whose ceiling price was higher than the maximum branded price by 22.5%. (Table 4) Atorvastatin in different doses and its FDC with ezetimibe and Fenofibrate, showed maximum cost variation among hypolipidemics. Earlier studies have also reported maximum cost variation with Atorvastatin and its combination.[16]

Moreover, single atorvastatin and its combination with ezetimibe, is also being produced by highest number of pharmaceutical companies. This finding may be due to the fact that atorvastatin is one of the most widely prescribed hypolipidemic drug[17] and earlier studies have also demonstrated highest cost effectiveness of atorvastatin over other statins.[18]

On the other hand, lesser cost variation and cost ratio of <2 was found among different strengths of atorvastatin when compared with generic prices. Only the minimum price of 5 mg atorvastatin was found less than its generic price by 60.7%. When we compared the maximum brand price of atorvastatin with DPCO ceiling price, it was found that atorvastatin 10 mg was 2.5 times higher than its ceiling price. But the price of combination of Atorvastatin 10 mg with Aspirin 75 mg was surprisingly lower than its ceiling price by 22.5%.

Rosuvastatin is also a commonly prescribed Statin for controlling dyslipidemia. Rosuvastatin has shown superior efficacy in reducing LDL-C as compared to other statins.[19] It also showed a wide cost variation among its various doses with rosuvastatin 20 mg showing highest cost variation of 1167% (Table 1). FDCs of rosuvastatin with aspirin also showed a high percent cost variation of 200% followed by its combination with Aspirin and clopidogrel of 173.7% (Table 2). When we compared the generic counterpart

of rosuvastatin 5 mg and 10 mg, we found that cost variation was greater as compared to atorvastatin while rosuvastatin 40 mg generic was found to be costlier than the minimum brand price. (Table 3) We also found substantial cost variation of its combination with aspirin and clopidogrel as compared to DPCO by 70.7% (Table 4)

Simvastatin at two doses (10 and 20 mg) showed highest cost variation of 544 and 775% respectively as compared to generic counterparts (Table 3). The cost variation of non statins like ezetimibe, gemfibrozil, fenofibrate, and bezafibrate was found to be less than 200% probably because these drugs are commonly used as add on to statins.[20]

In summary, hypolipidemic drugs are widely prescribed in India for primary and secondary prevention of CHD and need to be used by a large population for a longer period of time. This imposes a great economic burden on the patients and adversely affects compliance. In India, different branded-generics are manufactured by a large number of pharmaceutical companies although generic drugs are also available at very low costs but Physicians as well as patients believe generics as inferior to branded drugs in terms of quality and therapeutic efficacy. Moreover to regulate the prices, ceiling prices of drugs has been fixed by DPCO. Inspite of these regulations our study revealed a large cost variation especially among most commonly prescribed statins, Atorvastatin and Rosuvastatin. The drugs which are to be used for prophylaxis as well as treatment of chronic diseases with high prevalence, must be available at affordable prices in order to increase patient care. Also manufacturing companies must strictly comply to the prices fixed by NPPA in accordance with DPCO and generic prices. Such cost analysis studies would help the physician for therapeutic decision making and to promote rational as well generic prescribing. The limitation of our study is that we included only those drugs whose prices were mentioned in our source.

Conclusion

Our study showed a wide variation in cost of hypolipidemic drugs available in Indian market which provides an insight to the prescriber, gives drug price control authorities to minimize the financial burden on the patient, and improve their compliance. Conclusion

Acknowledgements

None

Funding

Nil

Conflict of Interest

None

References

1. World Health Organization.Geneva: World Health Organization;c2019.Global Health Observatory(GHO) data[Internet] [cited2019 Jun20].Available from:http://www.who.int/gho/ncd/mortality-morbidity/ncd-total/en/index.html).
2. HC,Oh SM.Non communicable diseases: Current status of major modifiable risk factors in Korea. J*ournal of Preventive Medicine and Public Health*. 2013;46:165-172)
3. Gupta R, Sharma S.K. Recent trends in epidemiology of dyslipidemias in India. *Indian Heart Journal*.2017;69(3):382-392
4. Eun-Jung Rhee, Hyeon Chang Kim, In-Kyung Jeong.2018 guidelines for the management of dyslipidemia. *Korean Journal of Internal Medicine*. 2019;34(5):1171)]
5. Gurgle HE. Drug Therapy for

Dyslipidemias. In: Brunton LL, Dandan RH, Kollmann BC, Eds. Goodman & Gilman The Pharmacological Basis of Therapeutics.13th ed. New York, NY: McGraw-Hill;2018: 605-618.
6. ACCORD Study Group.Effects of combination lipid therapy in type 2 diabetes mellitus. *New England Journal Medicine.* 2010,362:1563-1574).
7. Bureau of Pharma PSUs of India (BPPI).2020.Accessed January15,2021. http://janaushadhi.gov.in/productList.aspx.
8. National Pharmaceutical Pricing Authority. Government of India. Available at http://www.nppaindia.nic.in/DPCO2013.pdf. Accessed January 12, 2021
9. Frazier LM,Brown JT,Divine GW,Fleming GR,Philips NM,Siegal WC. Can physician education lower the cost of prescription drugs? A prospective controlled trial. *Annals of Internal Medicine*.1991;115(2):116-21
10. Guidelines for ATC Cassification and DDD Assignment.3rd ed Oslo:WHO Collaborating Center for Drug Statistics Methodology 2020.
11. Hypolipidemic agent. Drug today 109 Vol.No.2. July-October 2020. Lorina Publications (India) Inc. 867-873.
12. Tiwari A, Reddy P. Cost analysis of Antifungal drugs available in India: A pharmacoeconomic perspective. Indian *Journal of Pharmacy and Pharmacology.* October-December 2016; 3(4); 192-196
13. Rao KS, Nundy M, Dua A S. National commission on macroeconomics and health. Financing and delivery of health care services in India. New Delhi: Ministry of health and family welfare. Government of India. Delivery of health in the private sector. 2005, 89-104.
14. Cholesterol Treatment Trialists (CTT) collaboration.Baigent C,Blackwell L,.Efficacy and safety of more intensive lowering of LDL cholesterol:A meta analysis of data from 170000 participants in 26 randomized trials. *Lancet.* 2010;376:1670-1681).
15. Oscar H F, Peters A. Cost effectiveness of statins in chronic heart disease. Journal of epidemiology and community health, 2005; 59(11).http..// jech.bmj.com/content/59/11/927
16. Padmavathi V, Kranti T.Analysis of cost variation among various statin preparations available in India. *Indian Journal of Pharmacy and Pharmacology*. Jan-Mar,2019;6(1):14-17
17. Sreedevi K. Venkateswara Rao. J. A study on prescription pattern of statins in cardiovascular disease; January 2011 *Der Pharmacia letter* 3(3):393-396
18. Dean G S, Christopher R MB. An economic analysis of the Atorvastatin comparative efficacy and safety study (ACCESS). *Pharmacoeconomics.* 2003; 21suppl1:13-23.
19. Carlo S. Clinical trials with Rosuvastatin: efficacy and safety of its use. *Italian Heart Journal*. 2003 Dec; 4 suppl 7:33s-46s.
20. Vavlukis M, Vavlukis A. Adding Ezetimibe to Statin Therapy: latest evidence and clinical implications. *Drugs in Context.* 2018; 7:212534.