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Pharmacoeconomic Evaluation of Drug Brands for Angina Pectoris and Decompensated Cardiomyopathy in Tertiary Care Teaching Hospitals

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Abstract

Background: Pharmacoeconomics is a specialized branch of health economics that evaluates the costs and benefits associated with drug therapy, guiding resource allocation and planning in healthcare. The World Health Organization emphasizes the importance of understanding drug utilization, including its marketing, distribution, prescription, and societal impacts. Effective therapeutic practice relies on evidence from pre-marketing clinical trials, although supplementary post-marketing data are crucial for informed drug therapy implementation.

Objective: This study aims to conduct a pharmacoeconomic evaluation of various brands of drugs used in the treatment of angina pectoris and decompensated cardiomyopathy in a tertiary care setting.

Methods: A prospective observational study was conducted in the cardiology ward of Narayana Hospitals, Nellore, over a two-year period. A total of 300 patients with angina pectoris and decompensated cardiomyopathy were assessed, with 250 patients meeting the inclusion criteria. Inclusion criteria encompassed patients aged 30 to 60 years, with various types of angina and decompensated cardiomyopathy, co-morbid conditions, a history of heart complaints, and willingness to participate. Exclusion criteria included pregnant women, those unwilling to provide information, pediatric patients, individuals with poor verbal communication, and unconscious patients. The study utilized an informed consent form and a specially designed quality of life (QOL) questionnaire.

Results: The findings from this study will provide valuable insights into the economic implications of drug therapy for angina pectoris and decompensated cardiomyopathy, highlighting potential benefits for patients and informing healthcare decision-makers.

Keywords: *Pharmacoeconomics, angina pectoris, decompensated cardiomyopathy, drug therapy, quality of life, tertiary care, health economics.*

INTRODUCTION

Pharmacoeconomic is a branch of health economic, which particularly focuses upon the cost and benefit of drug therapy [1]. Pharmacoeconomic serves to provide a guide for decision making on resource allocation and in planning process. The World Health Organization addressed drug utilization as the marketing, distribution, prescription, and use of drugs in a society considering its consequences, either social or economic. The therapeutic practice is expected to be primarily based on evidence provided by pre-marketing clinical trials [2] but complementary data from post marketing periods are needed to provide an adequate basis for implementing drug therapy**.** Angina pectoris is the medical term for chest pain or discomfort due to coronary heart disease. It occurs when the heart muscle does not get as much blood as it needs. Dilated cardiomyopathy (DCM) is a condition in which the heart's ability to pump blood is decreased because the heart's main pumping chamber, the left ventricle, is enlarged and weakened.

MATERIALS AND METHODS:

PLACE OF STUDY:

The study "**Pharmacoeconomic evaluation of various brands of drugs used in the treatment of angina pectoris and decompensated cardiomyopathy in tertiary care teaching hospitals"** which was carried out in the **"Department of cardiology"** IP at Narayana Hospitals, Nellore, **STUDY DESIGN:** The study was a prospective observational study conducted in cardiology ward of tertiary care teaching hospital.

STUDY POPULATION: This study was done in 300 patients who are suffering with Angina pectoris and Decompensated cardio myopathy and 250 are included.

STUDY DURATION: This study was conducted for 2 years.

INCLUSION CRITERIA:

All the patients suffering with different types of Angina and Decompensated cardiomyopathy.

Patient age in between 30 to 60yrs.

Patients with co-morbid conditions.

Who are willing to give information?

History of any heart complaints.

Patient with alcohol and smoking habits

EXCLUSION CRITERIA:

Pregnancy women.

Lack of interest to give information.

Pediatrics.

Whose verbal communication was poor.

Unconscious patients

STUDY MATERIAL:

Patient informed consent form.

A specially designed QOL questionnaire.

STUDY METHOD:

The study will be initiated after obtaining the permission from the institutional ethical committee. The patients will be enrolled in the study after taking informed consent from them. The enrollment of patients will be done on the basis of inclusion and exclusion criteria.

RESULTS:

Table 1: Shows the demographic details of the patients such as age, sex, employment, nutrition, hygienic conditions, employment and ethnicity.

DEMOGRAPHICS		**No. OF PATIENTS**	**PERCENTAGE**
AGE	**15 to 25**	56	22.4 %
	26 to 40	82	32.8 %
	41 to 50	112	44.8 %
SEX	**MALE**	171	68.4 %
	FEMALE	79	31.6 %
EMPLOYMENT	**EMPLOY**	231	92.4 %
	UNEMPLOY	19	7.6 %
NUTRITION	**BETTER**	69	27.6 %
	AVERAGE	94	37.6 %
	POOR	87	34.8 %
HYGENIC CONDITIONS	**BETTER**	73	29.4 %
	AVERAGE	43	17.2 %
	POOR	134	53.6 %
ETHINICITY	**INDIAN**	250	100%

Table 2: Shows the reasons for the admission of the patient conditions such as Hypertension, congestive heart failure, angina pectoris, left ventricular hypertrophy, cardiac myopathy, stunt, hyperlipidemia and arrythmias.

REASONS FOR ADMISSION:		
CONDITION	**NO. OF PATIENTS**	**PERCENTAGE**
HYPERTENSION	59	23.6%
CONGESTIVE HEART FAILURE	120	48%
ANGINA PECTORIS	210	84%
LEFT VENTRICULAR HYPERTROPHY	33	13.2%
CARDIAC MYOPATHY	123	49.2%
STUNT	9	3.6%
HYPERLIPIDEMIA	67	26.8%
ARRYTHMIAS	83	33.2%

Table 3: Shows the drugs used for the condition of the patient.

S.NO	NAME OF THE DRUG	USED FOR CONDITION
1.	CLOPIDOGREL	Unstable angina
2.	ATORVASTATIN	Hyperlipidemia
3.	ISOSORBIDE DINITRATE	Angina pectoris Unstable angina Acute coronary syndromes
4.	HEPARIN	Anti-coagulation
5.	POTASSIUM CHLORIDE	Hypokalemia
6.	ASPIRIN	Anti-inflammatory
7.	INSULIN	Type 2 Diabetes mellitus
8.	METOPROLOL TARTRATE	Hypertension
9.	FUROSEMIDE	Angina pectoris
10.	PANTOPRAZOLE	Hypertension
11.	CREMAFFIN	Antacid Constipation
12.	NITRO GLYCERINE	Angina pectoris

Class and Cost of The Drugs:

Table 4: Shows the different brands of the clopidogrel drug and their costs.

S.NO	Generic Name	Class of The Drug	Brands of The Drug	Cost of The Drug
1.	Clopidogrel	Anticoagulant, Antiplatelet, Fibrinolytics	Aclotil	Rs.4.25
			Antiban	Rs.3.80
			Antiplar	Rs.3.64
			Anziolet	Rs.7.30
			Aptogrel	Rs.4.95
			Asogrel	Rs.4.50
			Atorfit-C	Rs.5.13
			Caplor	Rs.1.20
			Clopid	Rs.3.02
			Clopitorva	Rs.19.73
			Cloplat	Rs.13.50

Table 5: Shows the different brands of the atorvastatin drug and their costs.

S.NO	Generic Name	Class of The Drug	Brands of The Drug	Cost of The Drug
2.	ATORVASTATIN	Dyslipidemic agents	Aztor	Rs.6.00
			Avistatin	Rs.10.00
			Biostat	Rs.1.90
			Biovas	Rs. 43.92
			Daztor	Rs.13.0
			Dyslip	Rs.7.07
			Etovas	Rs.7.90
			Lipofix	Rs.5.70
			Jovastatin	Rs.12.00
			Movastin-10	Rs.3.60

Table 6: Shows the different brands of isosorbide dinitrate drug and their costs.

S.NO	Generic Name	Class of The Drug	Brands of The Drug	Cost of The Drug
3.	ISOSORBIDE DINITRATE	Antianginal drug	Anzidin	Rs.5.07
			Cardicap	Rs.1.23

			Isolazine	Rs.8.50
			Isordil	Rs.0.72
			Isorus	Rs.8.50
			Olvisol	Rs.4.80
			Sorbitrate	0.79ps
			Sorbitrate-HF	Rs.5.00

Table 7: Shows the different brans of the Heparin and their costs.

S.NO	Generic Name	Class of The Drug	Brands of The Drug	Cost of The Drug
		Anti-coagulants	Bioclot	Rs.85.00
4.	HEPARIN	Anti-platelets	Beparine	Rs.37.00
		Fibrinolytics'	Blockasol	Rs.164.00
			Caprin	Rs.80.00
			Celparin	Rs.98.00
			No-clot	Rs.88.00
			Neporin	Rs.225.00
			Heparen	Rs.210.00
			Thromboparin	Rs.78.00
			V-parin	Rs.90.00

Table 8: Shows the different brands of potassium chloride and their costs

S.NO	Generic Name	Class of The Drug	Brands of The Drug	Cost of The Drug
	POTASSIUM	Electrolytes	K-cl	Rs.23.50
5.	CHLORIDE		Kesol	Rs.147.00
			Kion	Rs.67.00
			Potklor	Rs.59.98
			Potride	Rs.8.60

Table 9: Shows the different brands of aspirin and their costs.

S.NO	GENERIC NAME	CLASS OF THE DRUG	BRAND OF THE DRUG	COST OF THE DRUG
6.	ASPIRIN	Anti-coagulants	Anacin	Rs.22.50
		Anti-platelets	Aspin	Rs.22.67
		Fibrinolytics	Colsprin	Rs.4.07
		NSAIDS	Delisprin	Rs.5.40
			Disprin	Rs.11.2
			Ecosprin AV 150	Rs.45.60
			Prin	Rs.1.50
			Monosprin	Rs1.65
			Zosprin	Rs.7.90

Table 10: Shows the different brands of Insulin and their costs

S.NO	GENERIC NAME	CLASS OF THE DRUG	BRAND OF THE DRUG	COST OF THE DRUG
7.	INSULIN	Hormone	Actrapid	Rs.265
			Apidra	Rs.1152.98
			Basalog	Rs.712. 59
			Basugine	Rs.598.40
			Biosulin	Rs.152.98
			Eglucent cart	Rs.678.00
			Actrapid	Rs.471.80
			flexepen	Rs.823.10
			Basaslog one	Rs.362.00
			Consegna	Rs.678.00

Table 11: Shows the different brands of metoprolol tartrate and their costs.

S.NO	Generic Name	Class of The Drug	Brands of The Drug	Cost of The Drug
8.	METOPROLOL TARTRATE	Beta- blocker Anti-anginal Calcium antagonist	Actocard	Rs.2.72
			ADBLOCK-MT	Rs. 3.90
			ACE-Revelol	Rs.22.11
			Amlong-MT	Rs.11.70
			Amlopin-M	Rs.9.84
			Asoprol	Rs.2.44
			Best beta-AM	Rs.7.50
			Betafit-AM	Rs.4.20
			Amlovas-M	Rs.8.55
			Amtas-M	Rs.10.5

Table 11: Shows the different brands of furosemide and their costs.

S.NO	Generic Name	Class of The Drug	Brands of The Drug	Cost of The Drug
	FUROSEMIDE	Diuretics	Diucontin-k	Rs.7.64
			Frusemene	Rs.2.92
			Frusenex	Rs.0.65
			Lasix	Rs.0.54
			Lasix high dose	Rs.0.54
			Urix	Rs.2.95
			Furoped	Rs.91.05
			Tebemid	Rs. 3.0

S.NO	NAME OF THE DRUG	CLASS OF THE DRUG	BRAND OF THE DRUG	COST OF THE DRUGS
9.	PANTOPRAZOLE	Antacids, Antireflux agents	Panzid	Rs.3.50
			P-Zole	Rs.4.40
			Zovanta	Rs10.30
			Xylopan	Rs.7.00
			Concid	Rs.6.00
			Xepenta	Rs.7.00
			Proloc	Rs.8.50
			Wypan	Rs.4.50
			Orcip	Rs.9.40

Table 12: Shows the different brands of cremaffin and their costs.

S.No	GENERIC NAME	CLASS OF THE DRUG	BRAND OF THE DRUG	COST OF THE DRUG
10.	CREMAFFIN (Liquid paraffin, Magnesium hydroxide)	Laxative Purgative	Abilax	Rs.74.00
			Agarol	Rs.59.51
			Acmeffin	Rs.68.00
			Allsuth	Rs.167.00
			Besmooth	Rs.135.00
			Asilax	Rs.56.00
			Bajoffin	Rs.59.00

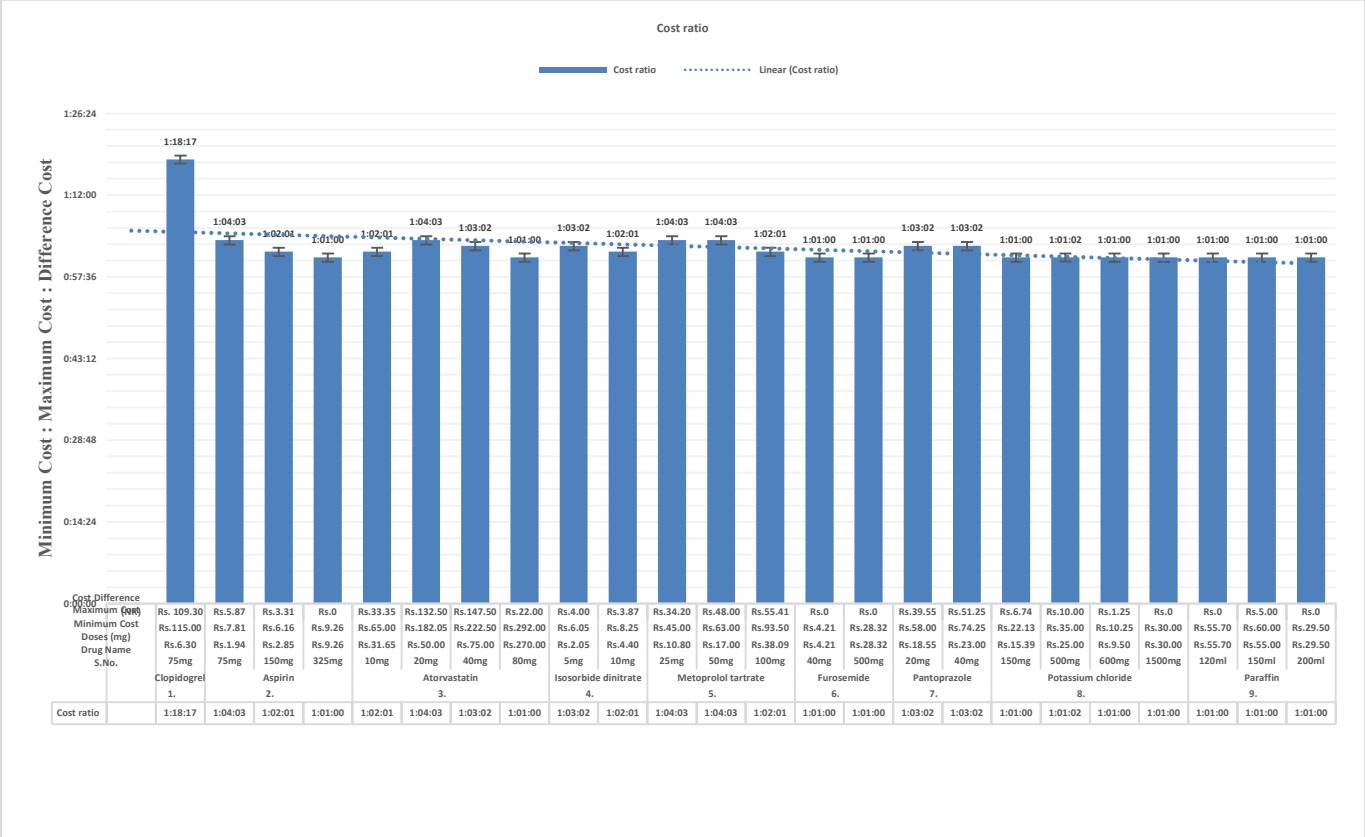
Table 13: Shows the percentage of drugs used for the patients.

TYPE OF THE DRUG	NAME OF THE DRUG	NO. OF CASES	PERCENTAGE
Anti-coagulant	Clopidogrel	250	100 %
	Heparin	217	87 %
	Aspirin	201	80.4 %
Anti-platelet	Clopidogrel	250	100 %
	Heparin	217	87 %
	Aspirin	201	80.4 %
Fibrinolytics	Clopidogrel	250	100 %
	Heparin	217	87 %
	Aspirin	201	80.4 %
Dyslipidemics	Atorvastatin	239	95.6 %
Anti-anginal	Isosorbide dinitrate	242	97 %
	Metoprolol tartrate	214	85.6 %
NSAIDS	Aspirin	243	97.2 %
Hormone	Insulin	224	89.6 %
Beta blockers	Metoprolol tartrate	214	85.6 %
Calcium antagonist	Metoprolol tartrate	214	85.6 %
Diuretics	Furosemide	195	78 %
Antacids	Pantoprazole	229	91.6 %
Laxative	Cremaffin	149	59.6 %
Electrolytes	Potassium chloride	176	71 %

Table 14: Shows the cost ratio of the drugs.

S.NO	Drug name	Strength and doses in form	Minimum tablet cost (INR)	Maximum cost (INR)	Difference (NR)	Cost ratio
1.	Clopidogrel	75mg	Rs.6.30	Rs.115.00	Rs. 109.30	1:18:17
2.	Aspirin	75mg	Rs.1.94	Rs.7.81	Rs.5.87	1:4:3
		150mg	Rs.2.85	Rs.6.16	Rs.3.31	1:2:1
		325mg	Rs.9.26	Rs.9.26	Rs.0	1:1:0
3.	Atorvastatin	10mg	Rs.31.65	Rs.65.00	Rs.33.35	1:2:1
		20mg	Rs.50.00	Rs.182.05	Rs.132.50	1:4:3
		40mg	Rs.75.00	Rs.222.50	Rs.147.50	1:3:2
		80mg	Rs.270.00	Rs.292.00	Rs.22.00	1:1:0
4.	Isosorbide dinitrate	5mg	Rs.2.05	Rs.6.05	Rs.4.00	1:3:2
		10mg	Rs.4.40	Rs.8.25	Rs.3.87	1:2:1
5.	Metoprolol tartrate	25mg	Rs.10.80	Rs.45.00	Rs.34.20	1:4:3
		50mg	Rs.17.00	Rs.63.00	Rs.48.00	1:4:3
		100mg	Rs.38.09	Rs.93.50	Rs.55.41	1:2:1
6.	Furosemide	40mg	Rs.4.21	Rs.4.21	Rs.0	1:1:0
		500mg	Rs.28.32	Rs.28.32	Rs.0	1:1:0
7.	Pantoprazole	20mg	Rs.18.55	Rs.58.00	Rs.39.55	1:3:2
		40mg	Rs.23.00	Rs.74.25	Rs.51.25	1:3:2
8.	Potassium chloride	150mg	Rs.15.39	Rs.22.13	Rs.6.74	1:1:0
		500mg	Rs.25.00	Rs.35.00	Rs.10.00	1:1:2
		600mg	Rs.9.50	Rs.10.25	Rs.1.25	1:1:0

		1500mg	Rs.30.00	Rs.30.00	Rs.0	1:1:0
9.	Paraffin	120ml	Rs.55.70	Rs.55.70	Rs.0	1:1:0
		150ml	Rs.55.00	Rs.60.00	Rs.5.00	1:1:0
		200ml	Rs.29.50	Rs.29.50	Rs.0	1:1:0
10.	Insulin	40IU/ml	Rs.129.24	Rs.158.58	Rs.29.34	1:1:0
		100IU/ml	Rs.284.4	Rs.763.31	Rs.478.91	1:3:2
11.	Heparin	10IU/ml	Rs.3.07	Rs.3.07	Rs.0	1:1:0
		200IU/gm	Rs.3.90	Rs.3.90	Rs.0	1:1:0
		1000IU/ml	Rs.27.00	Rs.79.95	Rs.52.95	1:3:2
		5000IU/ml	Rs.90.00	Rs.90.00	Rs.0	1:1:0
		25000Iu/ml	Rs.69.00	Rs.240.00	Rs.171	1:3:2



DISCUSSION: In our study, a total of 300 patients were assessed, with 250 agreeing to provide information. The age distribution of these patients ranged from 15 to 50 years: 56 patients (22.4%) were aged 15 to 25 years, 82 patients (32.8%) were aged 26 to 40 years, and 112 patients (44.8%) were aged 41 to 50 years. Our findings indicate a higher prevalence of cardiac problems among males, with 171 male patients (68.4%) compared to 79 female patients (31.6%). Regarding employment status, 231 patients (92.4%) were employed, while 19 patients (7.6%) were unemployed, highlighting that the majority of patients were in the workforce. Nutritional assessments revealed that 94 patients (37.6%) had an average nutritional status, 87 patients (34.8%) were classified as poor, and only 69 patients (27.6%) were identified as having a better nutritional status. Hygienic conditions among the patients were also evaluated, revealing that all patients were found to be in poor hygienic conditions. Specifically,

134 patients (52.6%) were categorized as poor, 43 patients (17.2%) as average, and 73 patients (29.4%) as having better hygiene. Notably, all patients in this study were of Indian origin. Data collection adhered to the guidelines set forth by the World Health Organization and other HRQOL (Health-Related Quality of Life) and QOL (Quality of Life) standards, with the primary reason for hospital admissions being cardiac issues.

Within the department, the majority of admissions were due to angina pectoris. Among the 250 patients, 210 patients (84%) presented with angina pectoris, 120 patients (48%) with congestive heart failure, 59 patients (23.6%) with hypertension, 33 patients (13.2%) with left ventricular hypertrophy, and 123 patients (49.2%) with cardiomyopathy. Other observed conditions included 9 patients (3.6%) with stents, 67 patients (26.8%) with hyperlipidemia, and 83 patients (33.2%) with arrhythmias. For treatment, various classes of drugs were employed, which are summarized in the results. Notably, anticoagulants, anti-platelets, and fibrinolytics were used in 100% of the patients. Additional medications included dyslipidemia agents (95.6% of patients), anti-anginal drugs (97%), NSAIDs (97.2%), insulin (89.6%), beta-blockers (85.6%), calcium antagonists (85.6%), diuretics (38%), antacids (91.6%), laxatives (59.6%), and electrolytes (71%). This diverse pharmacological approach was adopted to optimize patient outcomes in our cardiology department. Our study presents a pharmacoeconomic evaluation of various brands of drugs, with data collected through questionnaires from patients. The analysis employs standard deviation to examine the costs associated with drug therapy in the cardiology department, specifically focusing on the minimum and maximum drug costs, cost differences, and cost ratios. For instance, the cost of clopidogrel at a dosage of 75 mg ranges from a minimum of Rs. 6.30 to a maximum of Rs. 115, resulting in a cost difference of Rs. 109.30 and a cost ratio of 1:18.17. The price of aspirin at 75 mg is Rs. 1.94 at its minimum and Rs. 7.81 at its maximum, with a cost difference of Rs. 5.87 and a cost ratio of 1:4.3. Similarly, for aspirin at 150 mg, the minimum cost is Rs. 2.85, while the maximum is Rs. 6.16, yielding a cost difference of Rs. 3.31 and a cost ratio of 1:2.1.

For aspirin at a dosage of 325 mg, both the minimum and maximum costs are Rs. 9.26, resulting in no cost difference and a ratio of 1:1. Atorvastatin at 10 mg exhibits costs ranging from Rs. 31.65 to Rs. 65, which produces a cost difference of Rs. 33.35 and a cost ratio of 1:2.1. Atorvastatin at 20 mg has a minimum cost of Rs. 50 and a maximum cost of Rs. 182.50, leading to a cost difference of Rs. 132.50 and a ratio of 1:4.3. The cost of atorvastatin at 40 mg varies from Rs. 75 to Rs. 222.50, resulting in a cost difference of Rs. 147.50 and a ratio of 1:3.2. Atorvastatin at 80 mg has a minimum cost of Rs. 270 and a maximum of Rs. 292, yielding a cost difference of Rs. 22 and a ratio of 1:1.

For isosorbide dinitrate at 5 mg, the costs range from Rs. 2.05 to Rs. 6.05, resulting in a cost difference of Rs. 4 and a ratio of 1:3.2. Isosorbide dinitrate at 10 mg shows a minimum cost of Rs. 4.40 and a maximum of Rs. 8.25, which results in a cost difference of Rs. 3.87 and a cost ratio of 1:2.1.

The cost of metoprolol tartrate at 25 mg is Rs. 10.80 at minimum and Rs. 45 at maximum, leading to a cost difference of Rs. 39.20 and a cost ratio of 1:4.3. For metoprolol tartrate at 50 mg, the minimum cost is Rs. 17, while the maximum is Rs. 63, resulting in a cost difference of Rs. 48 and a cost ratio of 1:4.3. The costs for metoprolol tartrate at 100 mg range from Rs. 38.09 to Rs. 93.50, with a cost difference of Rs. 55.41 and a ratio of 1:2.1.

Furosemide at 40 mg presents a cost of Rs. 4.21 for both minimum and maximum, resulting in no cost difference and a ratio of 1:1. Similarly, furosemide at 500 mg has a consistent cost of Rs. 28.32 for both minimum and maximum, leading to no cost difference and a ratio of 1:1.

For pantoprazole at 20 mg, the costs range from Rs. 18.55 to Rs. 58.00, creating a cost difference of Rs. 39.45 with a ratio of 1:3.2. Pantoprazole at 40 mg has a minimum cost of Rs. 23.00 and a maximum of Rs. 74.25, yielding a cost difference of Rs. 51.25 and a ratio of 1:3.2.

Potassium chloride at 150 mg is priced between Rs. 15.39 and Rs. 22.13, resulting in a cost difference of Rs. 6.74

with a ratio of 1:1. For potassium chloride at 500 mg, the costs are Rs. 25.00 at minimum and Rs. 35.00 at maximum, leading to a cost difference of Rs. 10.00 and a ratio of 1:1.2. The costs for potassium chloride at 600 mg range from Rs. 9.50 to Rs. 10.25, resulting in a cost difference of Rs. 1.25 and a ratio of 1:1. For potassium chloride at 1500 mg, both minimum and maximum costs are Rs. 30.00, leading to no cost difference and a ratio of 1:1. The cost of paraffin at 120 ml is Rs. 55.70 for both minimum and maximum, resulting in no cost difference and a ratio of 1:1. For paraffin at 150 ml, the minimum cost is Rs. 55.00 and the maximum is Rs. 60.00, resulting in a cost difference of Rs. 5.00 and a ratio of 1:1. For paraffin at 200 ml, both the minimum and maximum costs are Rs. 29.50, leading to no cost difference and a ratio of 1:1.

Insulin at 40 IU/ml is priced between Rs. 129.24 and Rs. 158.58, leading to a cost difference of Rs. 29.34 and a ratio of 1:1. For insulin at 100 IU/ml, the minimum cost is Rs. 284.40, while the maximum cost is Rs. 763.31, yielding a cost difference of Rs. 478.91 and a ratio of 1:3.2. Heparin at 10 IU/ml has both minimum and maximum costs at Rs. 3.07, resulting in no cost difference and a ratio of 1:1. For heparin at 200 IU/gm, both minimum and maximum costs are Rs. 3.90, resulting in no cost difference and a ratio of 1:1. Heparin at 1000 IU/ml has a minimum cost of Rs. 27.00 and a maximum of Rs. 79.95, resulting in a cost difference of Rs. 52.95 and a ratio of 1:3.2. Finally, insulin at 5000 IU/ml has consistent pricing at Rs. 90.00 for both minimum and maximum, resulting in no cost difference and a ratio of 1:1. For insulin at 2500 IU/ml, the minimum cost is Rs. 69.00 and the maximum is Rs. 240.00, resulting in a cost difference of Rs. 171 and a ratio of 1:3.2.

Conclusions: Our study concludes that drugs used for the treatment of angina pectoris are effective, with variations observed in their cost-effectiveness. By analyzing the impact of these cost differences, we find that the highest-cost options may offer significant long-term benefits for patients, especially those from lower-middle-class and low-income backgrounds. Maximizing cost-effectiveness could help make treatment more accessible to these socioeconomically disadvantaged groups. We recommend that the government implement patient education initiatives on the costs and benefits of these drugs to alleviate the financial burden and improve health outcomes for those in need.

Consent: As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

Ethical Approval As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

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