WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 11, Issue 11, 854-863. Research Article ISSN 2277– 7105

ANALYSIS OF PRESCRIBING PATTERN AND COST OF PHARMACOTHERAPY AMONG MYOCARDIAL INFARCTION PATIENTS

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Article Received on
10 June 2022,

Revised on 30 June 2022,
Accepted on 20 July 2022

DOI: 10.20959/wjpr202211-25059

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ABSTRACT

Background: Cardiovascular diseases causes an estimated 17.9 million deaths each year as per World Health Organization among which 85% of this is due to heart attack and stroke. In India, the incidence of myocardial infarction is 64.37/1000 people in men aged between 29-69 years. **Aim:** To analyse the prescribing pattern and cost of pharmacotherapy among myocardial infarction patients. **Methodology:** A prospective observational study was conducted for a period of six months at the cardiology department of a tertiary care hospital, Bengaluru. Recruited patient's demographic characteristics, drug therapy, cost of pharmacotherapy and drug interactions were studied and analyzed. **Results:** Out of 150 patients recruited, majority were males. Commonly prescribed categories of drugs were antiplatelets (99%), lipid lowering agents (97.3%), anticoagulants (74%) proton pump inhibitors (90.7%), beta blockers (70.7%), loop diuretics (47.3%) etc. In about 99% of the patients dual antiplatelet therapy with Aspirin + Ticagrelor/Clopidogrel was prescribed. About 458 drug-drug interactions were identified among which 95% were of moderate severity. The average cost of pharmacotherapy for 3 days of hospital stay for each patient was found to be INR 979.62 and the cost ranged from INR 228. 42 to INR 4336.82. **Conclusion:** This study provides insight towards drug prescribing pattern and average cost of pharmacotherapy in MI patients.

KEYWORDS: Acute Myocardial Infarction, STEMI, NSTEMI, Aspirin, Cost of Pharmacotherapy.

INTRODUCTION

Cardiovascular diseases (CVDs) are the number one cause of death globally taking an estimated 17.9 million lives each year as per World Health Organization (WHO). 85% of the death among this is due to heart attack and stroke. Over three quarters of CVD deaths take place in low- and middle-income countries.[1] In India, the incidence of myocardial infarction (MI) is 64.37/1000 people in men aged between 29-69 years.[2]

Myocardial Infarction is classified into acute and chronic types. Acute MI is a clinical syndrome that results from sudden occlusion of coronary artery which causes infarction of cardiac myocytes in the region supplied by that artery.[3] Acute MI is of two types – ST Elevation (STEMI) and Non-ST Elevation myocardial infarction (NSTEMI). The mortality rate from MI is relatively high, with 50% of the patients' death is due to acute coronary occlusion within the first hour after the onset of symptoms. Death is commonly due to dysrhythmia and ventricular fibrillation.

According to the guidelines put forward by the Ministry of Health & Family Welfare, Government of India, the initial treatment of STEMI includes Aspirin and Clopidogrel. Opioid analgesics like Morphine should be given to the patient in order to relieve the pain. If systolic BP is $\geq$ 120 mmHg, nitrates should be administered. Reperfusion therapy with fibrinolytics like streptokinase should be initiated within 12 hours of appearance of symptoms. Following the treatment with fibrinolytic agents, thrombolytics like low molecular weight heparins should be administered as an adjunctive therapy. Other adjunctive agents include Beta-blockers (Ex: Metoprolol), Angiotensin Converting Enzyme Inhibitors (ACEI) (Ex: Ramipril) and Angiotensin II Receptor Blockers (ARBs) (Ex: Telmisartan). Statins should be initiated as early as possible as a part of secondary prevention measures. The drug therapy is almost similar for NSTEMI except for the fact that, fibrinolytic therapy is not advised as these agents are not beneficial to such patients.[4]

A study conducted by Mehra A et al showed that the commonly prescribed drugs for myocardial infarction were antiplatelets (Aspirin and Clopidogrel, 84%) followed by hypolipidemics (Atorvastatin, 91%), antianginals (Isosorbide dinitrate, 73.5%), proton pump inhibitors (Pantoprazole, 67%) and anticoagulants (Enoxaparin, 67.5%).[5]

Another study conducted by Manohar N et al. showed that the commonly prescribed drugs were antiplatelets (Aspirin, 92%, Clopidogrel, 80%), and statins (Atorvastatin, 96%), followed by anticoagulants (Ticagrelor, 40%, Low molecular weight heparins (32%), nitrates (Nitroglycerin, 68%) and potassium channel blocker (Nicorandil, 56%).[6] But there is no differentiation in the prescribing pattern between STEMI and NSTEMI clinical conditions and the above studies have not used standard treatment guidelines to compare their results. In addition, very limited number of studies used standard treatments guidelines such as Ministry of Health and Family Welfare Guidelines, GOI, available in India.

According to the statistical briefing done by Agency for Healthcare Research & Quality in 2013, acute myocardial infarction is one among the 5 most expensive conditions treated in US hospitals with aggregate hospital cost of $12,092 million constituting 3.2% of the national cost.[7] Although, thrombolytic therapy reduces early mortality and improves long term prognosis of AMI, it increases the economic burden on the patients. However, very few pharmacoeconomic studies are available on the drug therapy in MI patients in India.

The results of above studies indicate that there is a variation in the prescribing pattern of medications that are used for the treatment of patients with STEMI and NSTEMI. Few clinical studies are available on the pharmacoeconomics of drug therapy in these patients. Therefore, a prospective study was planned to assess the prescribing pattern of medications including pharmacoeconomics of the drug therapy used for the treatment of patients with STEMI and NSTEMI.

MATERIALS AND METHODS

Study Site

The proposed study was conducted at the Cardiology Department of Aster CMI Hospital, Hebbal, Bangalore, Karnataka.

Study Design

Prospective observational open labelled study.

Study Duration

Duration of the study was 6 months.

Sample Size

150 patients.

Study Criteria

Inclusion Criteria

- In-patients who are diagnosed as suffering from acute myocardial infarction (STEMI/ NSTEMI)
- In-patients of either gender and aged between 30 and 80 years

Exclusion Criteria

- Pregnant and lactating women
- Patients whose age is less than 29 years.
- Patients with history of drug abuse/substance abuse during the past six months

Study Procedure

Step 1: In-patients who meet the study criteria were enrolled into the study.

Step 2: Demographic, medical and medication data was documented

Step 3: Medication data of the patient were transferred to data collection form

Step 4: Prescribing pattern was assessed by comparing against standard guidelines put forward by Ministry of Health and Family Welfare, Govt. of India

Step 5: Cost of medicines prescribed over a period of 3 days was assessed as per standard price control web known as Drug Price Control Order

Step 5: In addition, potential drug-drug interactions associated with the prescribed medicines was assessed using Lexicomp database

Statistical Analysis

The data obtained was subjected to descriptive statistics.

RESULTS AND DISCUSSION

A total number of 150 patients were recruited in the study. Recruited patient's demographic characteristics, drug therapy, cost of pharmacotherapy and drug interactions were studied and analyzed. Out of 150 patients studied, 118 were male and 32 were female. Age wise distribution is given in Fig 1.

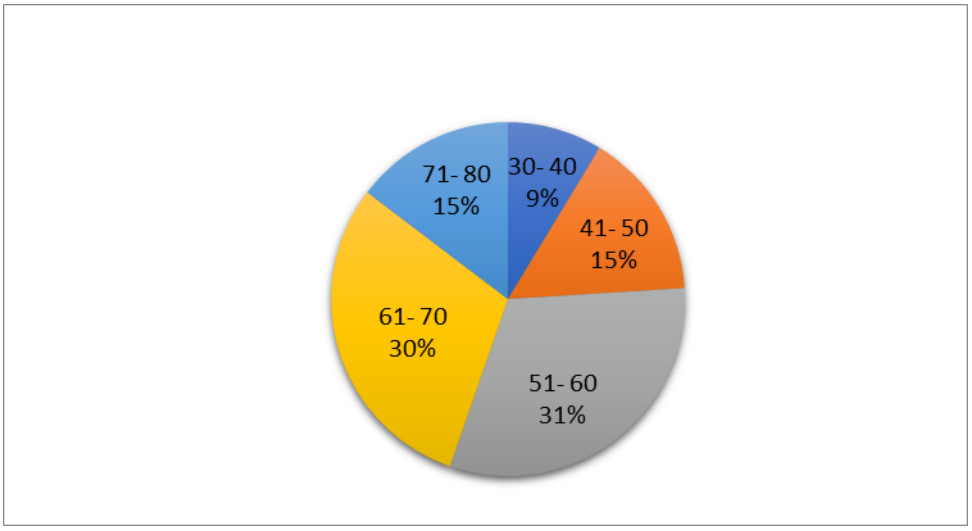

Fig 1: Age distribution.

Among the 150 AMI cases studied, STEMI was more prevalent type of MI compared to NSTEMI as shown in fig 2.

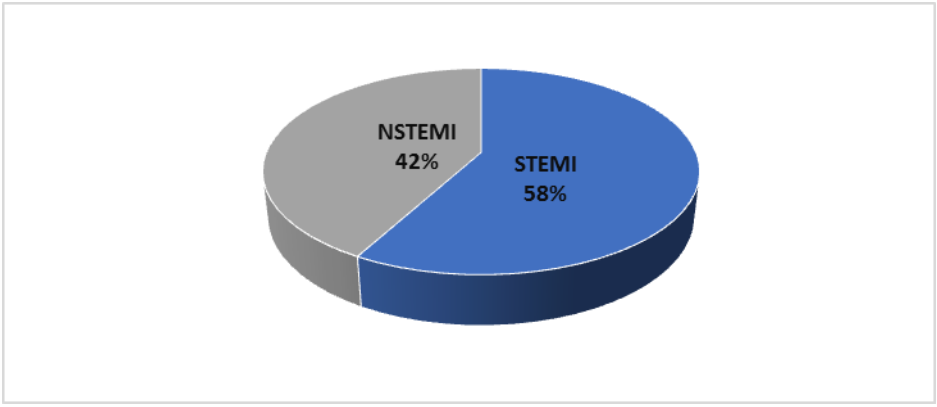

Fig 2: Distribution of MI.

Commonly prescribed categories of drugs were antiplatelets (99%), lipid lowering agents (97.3%), anticoagulants (74%), PPIs (90.7%), Beta blockers (70.7%), loop diuretics (47.3%) etc.

The distribution of different antiplatelet agents and anti-coagulants are as shown in Fig 3 and 4 respectively.

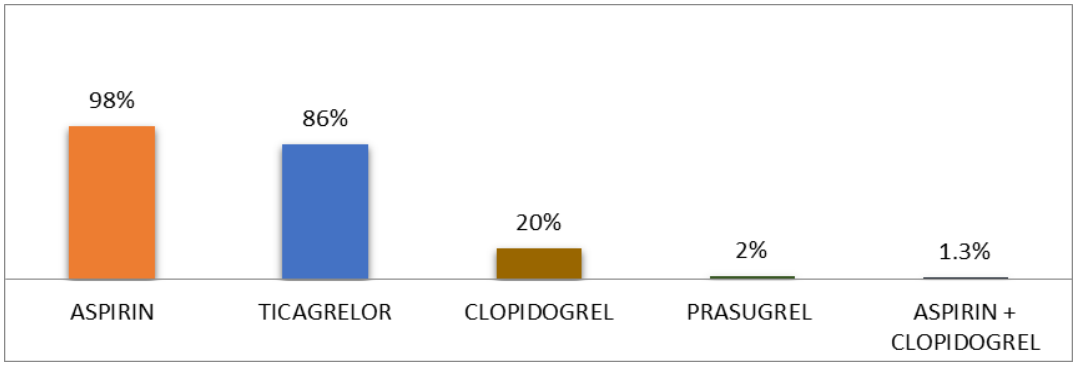

Fig 3: Distribution of Anti platelet agents.

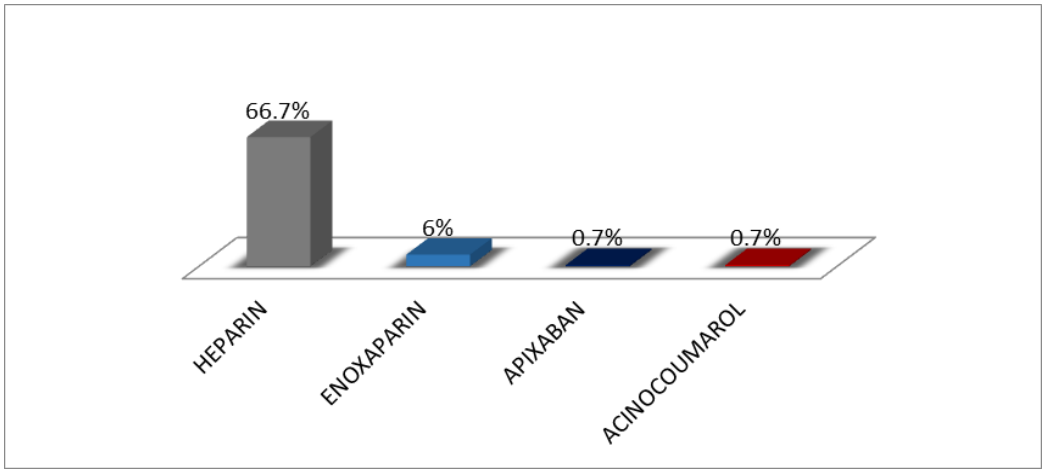

Fig 4: Distribution of Anti coagulants.

Anti- anginals prescribed includes Nitroglycerin (7.3%), Ivabradine (5.3%) and Nicorandil (4%). Anti- hypertensives prescribed include Beta- blockers (70.7%), Diuretics (54%), ACE-inhibitors (14%), Calcium channel blockers (9.3%), ARBs (2.6%) and Alpha blockers (0.7%). Beta – blockers prescribed include Metoprolol (54.7%), Carvedilol (8%), Bisoprolol (4.7%) and Nebivolol (3.3%).

Among Lipid lowering agents, Atorvastatin was the most commonly prescribed agent constituting 54.7%, followed by Rosuvastatin, 44.7%.

Proton pump inhibitor, Pantoprazole was prescribed in 90.7% of patients.

Out of 150 cases studied, 458 drug-drug interactions were found out. Among the total interactions, 437 were of moderate severity, 16 were of major severity and 5 of minor severity. The frequently occurring moderate drug interaction was between Aspirin and Heparin (95). Clopidogrel + Pantoprazole (16) was the only major DDI found in the study as shown in fig 5.

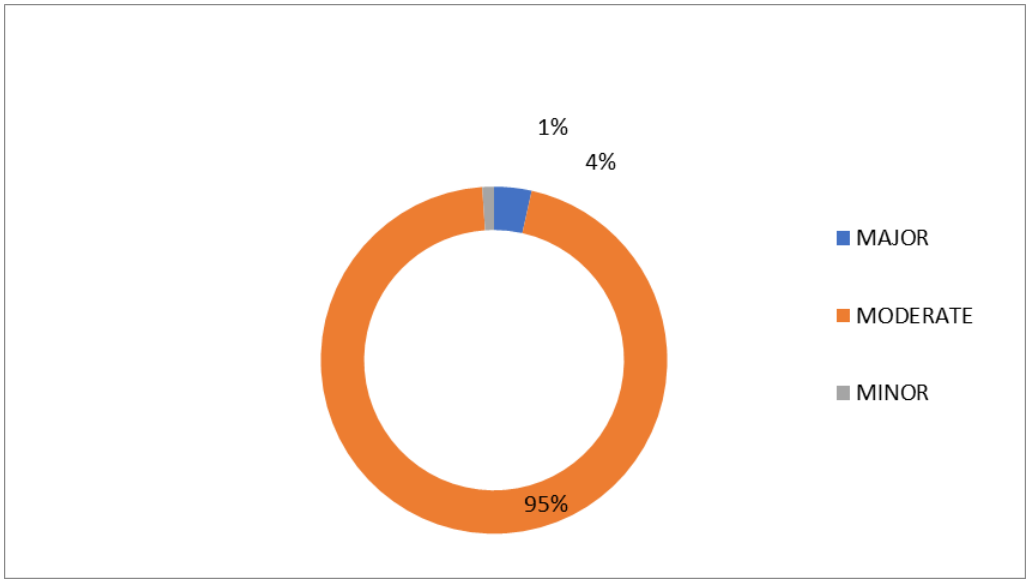

Fig 5: Distribution of drug-drug interactions.

The total cost of drugs per patient was calculated by multiplying all the drugs prescribed with the unit cost of each drug. The unit cost of each drug was obtained from Medguideindia.com. The average cost of pharmacotherapy for 3 days of hospital stay for each patient with AMI was found to be INR 979.62 and the cost ranged from INR 228. 42 to INR 4336.82.

In our study, the frequency of AMI was more in male (79%) when compared to female which is in accordance with the study conducted by Mehra A *et al.*[5]

The most common age group was 51- 70 years (61%) which is similar to the study conducted by Chaudhary *et al.*[8]

About 99% of the patients received dual anti platelet therapy (Aspirin + Clopidogrel/Ticagrelor) as the initial treatment choice in both STEMI and NSTEMI. Platelet activation places a key role in myocardial infarction and according to MOHFW, antiplatelet therapy should be administered once the diagnosis is confirmed which was followed in our study. This result was similar to the study conducted by Sainath S *et al* (100%).[9]

According to the guidelines of MOHFW, Ticagrelor has been found to be superior as compared to Clopidogrel in the treatment of ACS which is similar to the results of our study where Ticagrelor (86%) was prescribed more when compared to Clopidogrel (20%).[4]

Lipid lowering agents was prescribed in 97.3% of patients, among which Atorvastatin was prescribed more when compared to Rosuvastatin which was similar to the study conducted by

Vyas A *et al* (98%).[10] According to MOHFW, statin should be initiated as early as possible during hospital stay irrespective of cholesterol level as part of secondary prevention measures which was followed in our study as well.

In the present study, anti-coagulants were prescribed in 74% of patients which is similar to the study (76%) conducted by Shamna C *et al.* The drug prescription rates of Beta-blockers, Diuretics, CCBs, ARBs /ACE Inhibitors were 70%, 54%, 16.6% respectively which is similar to the study conducted by Jorg M *et al*, where the drug prescription rates for Beta blocker, Diuretics, ACE Inhibitors/ARBs, CCBs, were 67%, 50%, 20% and 15% respectively.[11]

Reperfusion therapy with Percutaneous Coronary Intervention (PCI) was instituted in most of the STEMI (95%) patients as advised by MOHFW, which is the most efficacious reperfusion therapy available. Also, fibrinolytic therapy was not given in any of the NSTEMI cases in accordance to the guidelines by Ministry of Health and Family Welfare.

The only major DDI found was between Clopidogrel and Pantoprazole. PPIs are recommended to use in combination with dual anti-platelet therapy in all coronary artery disease patients as a measure to minimize bleeding risk. The clinical significance of DDIs between pantoprazole and DAPT is less when compared to other PPIs like omeprazole or esomeprazole which shows high risk when used in combination with DAPT.

Anticoagulants contributed more than 40% of the total cost of pharmacotherapy. The variations in the cost of pharmacotherapy may be attributed to the physician's choice of drugs, comorbidities, dosage form of drugs, severity of illness etc.

CONCLUSION

This study provides insight towards drug prescribing pattern and average cost of pharmacotherapy in MI patients. It was observed that the risk of MI increases with increasing age and the incidence of disease was more in male as compared to female. The most commonly prescribed drug classes were antiplatelets, followed by lipid lowering agents, PPIs, anticoagulants, antihypertensives and vasodilators. The drug prescribing pattern for both STEMI and NSTEMI were found to be in accordance with the guidelines put forward by Ministry of Health and Family Welfare for the treatment of MI. Most of the drug- drug interactions found were of moderate intensity. The average cost of pharmacotherapy for 3

days of hospital stay for patients with AMI gives an understanding about the economic implications of the medications used in myocardial infarction.

ACKNOWLEDGEMENTS

We sincerely acknowledge the efforts of all those who have directly or indirectly have lent their helping hand in completing our project successfully.

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