



## A prospective observational study on prescribing pattern of myocardial infarction in a tertiary care hospital

Sujith S Nair, Pooja P\*, Chaithanya Dileep Kumar, Nayana

Department of Pharmacy Practice, Crescent College of Pharmaceutical Sciences, Madayipara, Kannur.

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### \*Corresponding author:

Email : poojaputhalath102gmail.com

Phone : +91 - 917559816701

### ABSTRACT

A prospective observational study was conducted in the Department of Cardiology at a Tertiary Care Hospital Kannur, Kerala including 120 patients for study duration of 6 months. The main objective of drug utilization research is to assess the rationality of drug use, associated drug interaction and comorbidities in Myocardial Infarction. Kuppusswamy scale was utilized to determine the relationship between socio economic status with risk factors and statistical analysis was done using Spearman's Coefficient method. Information regarding demography, BMI, disease state co- morbidities, medical or medication history, risk factors, laboratory values and drugs prescribed were obtained by referring the case sheets and patient interview. The drug interactions were determined by Medscape drug interaction checker. The rationality of the treatment was assessed by reviewing the prescription pattern and comparing with the Standard Guidelines for MI. Atorvastatin (92.38%), heparin (92.23%) and aspirin (39.57%) were most commonly prescribed in this hospital. The result suggests that the risk of MI increases with increasing age and frequently observed in male patients. Hypertension (82.39) and diabetes (49.98%) were the co- morbid conditions. The commonly prescribed drug classes or main indication in MI were antiplatelet (20.94%) followed by antihypertensives (16.82%), antianginal (13.13%), hypolipidemics (9.35%), anticoagulants (9.18%) and fibrinolytics (0.26%) respectively. Significant relationship was observed between education and income with risk factor ( $p < 0.05$ ).

### INTRODUCTION

Myocardial Infarction (MI) is a medical term related to heart attack. The complete blockage of a coronary artery caused by rupture of an atherosclerotic plaque is usually the underlying mechanism of an MI.[1] Prescribing pattern studies deduce to monitor, evaluate and insinuate modifications in the practitioner's prescription habits, so as to make patient care rational and cost effective.[2] Rational drug prescribing is defined as "the use of the least number of drugs to obtain the best possible effect in the shortest period and at a reasonable cost.[3] The INTERHEART study has identified 9 easily measured risk factors: Smoking, Lipids, Hypertension, Diabetes, Obesity, Diet, Physical activity, Alcohol consumption and Psycho-social factors. The INTERHEART investigators found that these risk factors are the same in almost every geographic region and every racial/ethnic group worldwide and consistent in men and women.[4] Effective risk factors on MI

which cannot be modified are age, sex and education, whereas the modifiable risk factors include hypertension, hypercholesterolemia, smoking, diabetes, alcohol consumption, lack of physical activity.[5]

### MATERIALS AND METHODS

#### STUDY CRITERIA

Patients admitted with MI under Cardiac inpatient Department and CCU over the age group of 18 years and patients with or without co-morbidities were included in the study whereas patients who were undiagnosed, pregnant women, mentally challenged and comatose patients were excluded from the study.

#### STUDY PROCEDURE

The study was approved by the Institutional human ethical committee. The detailed information regarding the study was

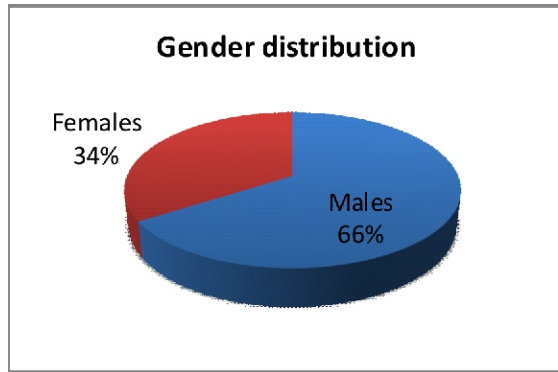


Figure 1 : Gender distribution

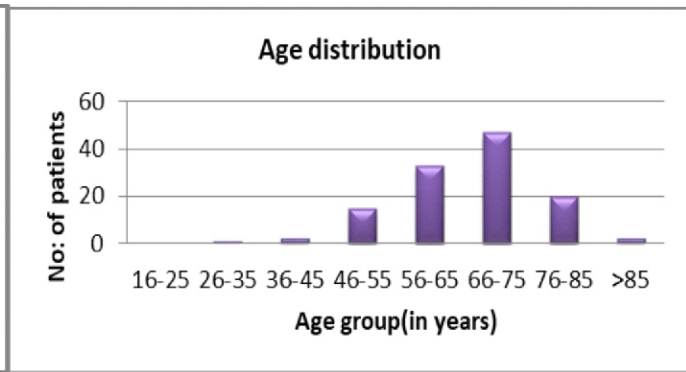


Figure 2 : Age distribution of patients

given to the participants under the Department of Cardiology. Informed consent was obtained from the participants who were willing to participate. A data collection form was developed and information regarding the age, gender, height, weight, BMI, disease state, co-morbidities medical or medication history, risk factors, laboratory values and drugs prescribed were obtained by referring their case sheet. Socio- economic factors and risk factors were obtained by interviewing the patient and the former was assessed by Kuppaswamy Scale.[6] The relationship between socio- economic factors and risk factors was statistically calculated from Spearman's co-efficient method.[7] The drug interactions were determined by Medscape drug interaction checker and classified according to their severity. The rationality of the treatment was assessed by reviewing the prescription pattern and comparing with the standard guideline for MI. All the relevant data were computed using MS Excel and SPSS Statistical package.

**RESULT**

**AGE AND GENDER DISTRIBUTION**

A total no. of 120 patients were enrolled in the study of which 79 (66%) were males and 41 (34%) were found to be female patients (figure 1). The male to female ratio among the patients

was 2:1. Age wise distribution shows that MI is most prevalent in age group of 66-75 (47) figure 2.

**TYPE OF MI AND CO-MORBIDITIES**

From the assessment of 120 patients, the most prevalent type of MI was found to be NSTEMI (41.66%) followed by AWTMI (31.66%), IWMI (21.66%) and STEMI (5%) as shown in figure 3. Data of 120 patients were analyzed and the total no. of drugs prescribed during hospitalization was 1122. The average no. of drugs per patient were 9.35. Various co-morbid conditions like

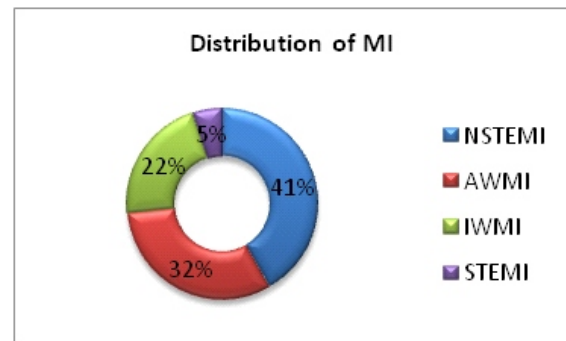
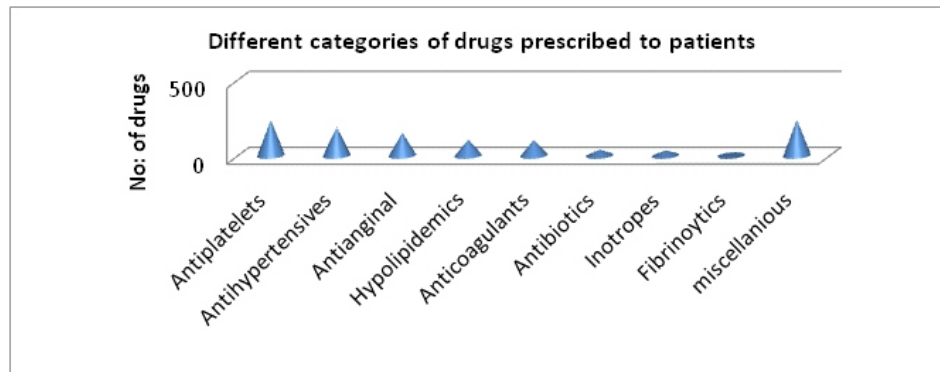


Figure 3 : Distribution of different types of MI

Table 1 : Distribution of co-morbid conditions in MI patients.

Co-morbid condition	No: of patients(n=120)	Percentage (%)
Hypertension	40	33.33
Hypertension + diabetes	38	31.66
Hypertension + others(HLP,CKD,hypothyroidism, COPD,asthma,stroke,seizure)	13	10.8
Hypertension + diabetes +others(HLP, Hypothyroidism, COPD, asthma)	8	6.66
Diabetes	8	6.66
Diabetes +others(HLP, hypothyroidism, COPD)	6	5
Others(Asthma, COPD, seizures)	4	3.33
None	3	2.5
HLP= Hyperlipidemia; CKD= chronic kidney disease; COPD= chronic obstructive pulmonary disease		



**Figure 4 :** Different categories of drugs prescribed

hypertension, diabetes mellitus, hypothyroidism, Hyperlipidemia were seen among patients and any of these were found to be risk factor of MI. Hypertension and diabetes were the two most common co-morbid conditions found in most of the patients which increase the risk of MI (table1).

#### PRESCRIBING PATTERN IN MI

Treatment of MI involves various categories of drugs namely anticoagulants, antiplatelets, fibrinolytics, antianginals, antihypertensives, hypolipidemics along with supportive therapy as show in figure 4.

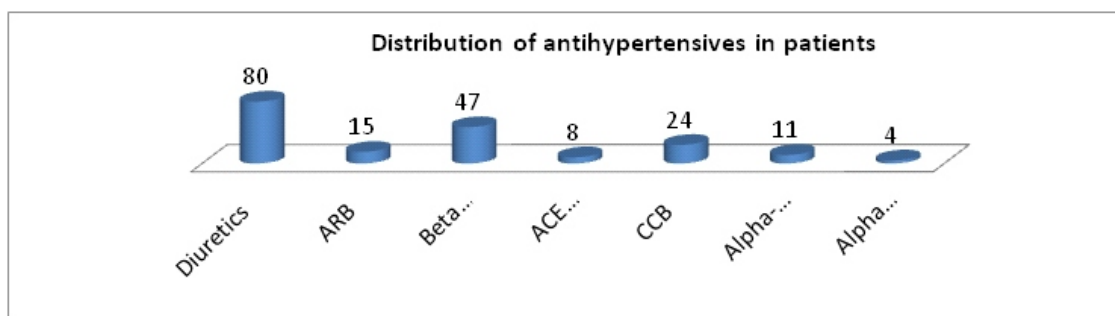
Among the total cases, majority were managed only with medical interventions (48%) and in others with surgical interventions like PTCA and CABG (52%) were performed. Antiplatelet drugs such as aspirin and clopidogrel are the inevitable drugs in MI to reduce the risk of further clot formation and helps in increasing the survival rate. Among the antiplatelet drugs prescribed 39.57% were on aspirin, 37.8% on clopidogrel, 8.08% on ticagrelor, 12.76% on tirofiban, 0.42% on prasugrel and 1.27% on cilostazol respectively.

**Anticoagulants** prescribed include heparin (92.23%) being the most prevalent drug used followed by enoxaparin (3.88%), warfarin and acenocoumarol 1.94% each respectively. The only fibrinolytics prescribed was streptokinase (2.5%).

**Antianginal drugs** prescribed include glyceryltrinitrate (46.66%), isosorbidedinitrate (8.66%), isosorbidedemonitrate (3.33%), sorbitrate (3.33%), nicorandil (25.33%), ranolazine (4%), ivabradine (4%), trimetazidine (2%), and isolazine (2.66%).

**Antihypertensives** prescribed include diuretics (42.32%), ARB (7.93%), beta blockers (24.86%), ACE inhibitor (4.23%), CCB (12.69%), alpha-beta blocker (5.82%) and alpha blocker (2.11%) as shown in the figure 5. Among the diuretics prescribed, the most frequently prescribed was loop diuretics (90%), followed by potassium sparing diuretic, spironolactone (8.75%) and osmotic diuretic mannitol (1.25). Among the loop diuretic, furosemide constitute 79.16% and torsemide 20.83%. Among the ARBs prescribed, the most prevalent constitute telmisartan (73.33%), followed by losartan (26.66%). Beta blockers prescribed include metoprolol (78.7%), bisoprolol (17.02%), nebivolol (4.25%). Ramipril and enalapril were the two ACE inhibitors prescribed which constitute 75% and 25% respectively. The frequency of calcium channel blockers prescribed includes amlodipine (41.66%), cilnidipine (29.16%), nifedipine (20.83%) and verapamil (8.33%). Carvedilol (5.82%) was the only alpha-beta blocker prescribed in the patients. The alpha blockers constitute tamsulosin (85) and prazosin (15%).

Among Hypolipidemics Atorvastatin was the most commonly prescribed hypolipidemic agent constituting 92.38% followed by rosuvastatin 7.61%. The inotropic agents prescribed were digoxin (8.82%), noradrenaline (11.76), atropine (26.47%), amiodarone (17.64%) and dopamine (35.29%). 75% of antibiotics prescribed in patients were cephalosporins. Others constitute flouroquinolones (5%), lincosamide (2.5%), oxazolidinone (12.5%) and macrolide (5%) (Table 8). Miscellaneous classes of drugs prescribed in MI and associated co-morbid conditions constitute PPI (23.84%), antidiabetic (9.20%), NSAIDs (12.55%), anesthetics (0.836%), bronchodilators (7.53%), H<sub>2</sub> receptor blocker (22.17%), benzodiazepines (9.20%), anti-



**Figure 5 :** Distribution of antihypertensive prescribed in patients

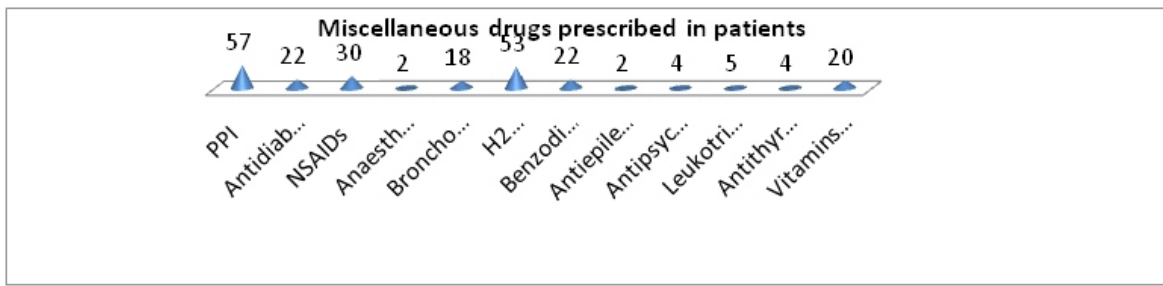


Figure 6 : Miscellaneous drugs prescribed in patients

epileptic (0.836%), antipsychotic (1.67%), leukotriene antagonist (2.09%), antithyroid (1.67%), vitamins and electrolytes (8.36%). The most commonly prescribed PPI was pantoprazole and H<sub>2</sub> receptor blocker was ranitidine.

**DRUG INTERACTION**

Out of the 120 cases studied 239 drug interactions were identified. Out of which 209 interactions were of moderate severity, while 30 interactions were of major severity (figure 7).

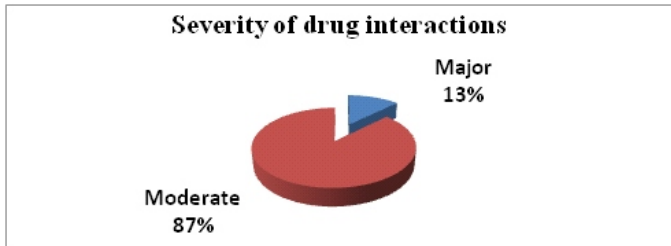


Figure 7 : Severity of drug interactions

From the 30 major interactions, the frequently occurring interactive pair was ceftriaxone- heparin(25) and commonly occurring interactive pair of moderate severity was aspirin-clopidogrel (59) and heparin- aspirin (58) (table 2).

**SIGNIFICANCE AND CORRELATION**

Significant relationship between education and income with risk factors was studied. No correlation was established between income and risk factors. But significant relationship was estimated between education and risk factors among the 120 patient profiles studied as the p value was found <0.05 (table 03).

**DISCUSSION**

Total 120 patient's case paper was analyzed during 6 months study period. Results point out that the frequency of MI was more in males (65.83%) than female patients (34.166%), which is in accordance with the study conducted by Weidner G, Jousilahti P and Chrysohoou C.[8-10]The reason for reduced incidence of MI in females is due to the cardio- protective effect of estrogen. As far as age factor is concerned, 39.16% patients belong to the age

Table 2 : List of potent drug-drug interactions:

Sl.No:	Interacting drug pairs	Mode of severity	Frequency
1	Ceftriaxone X heparin	Severe	25
2	Heparin X warfarin	Severe	1
3	Enoxaparin X heparin	Severe	2
4	Ceftriaxone X enoxaparin	Severe	2
5	Heparin X clopidogrel	Moderate	56
6	Heparin X aspirin	Moderate	58
7	Aspirin X clopidogrel	Moderate	59
8	Pantoprazole X clopidogrel	Moderate	19
9	Metformin X furosemide	Moderate	5
10	Metformin X telmisartan	Moderate	4
11	Aspirin X furosemide	Moderate	4
12	Aspirin X tirofiban	Moderate	4

**Table 3 :** Correlation between education and income with risk factors:

Spearman's rho	Risk factors	Income	Education	
		Correlation Coefficient	-.093	.208*
		Sig. (2-tailed)	.313	.022
		N	120	120

group of 66-75 years and 27.5% patients belong to 56-65 years. Hence 66.66% patients belong to the group 56-75 years. The study shows that only 2.5% of the patients were presented without any co-morbidity while rest 97.5% of patients were presented with co-morbidities with hypertension, diabetes, hyperlipidemia, etc. the commonest co-morbid condition was hypertension, followed by diabetes, hyperlipidemia and renal disorders which is in accordance with the study conducted by ShruthiDavalji, Venkateshwarlu K et al on Prescribing Pattern In Coronary Artery Disease, A Prospective Study.[11]

Average no: of drugs per patient during hospitalization was 9.35, which indicates polypharmacy and in most cases it was unavoidable which was similar to the ShruthiDavalji, Venkateshwarlu K et al on Prescribing Pattern In Coronary Artery Disease, A Prospective Study.[12]

The frequency of use of injectable preparations in our study was 26.71%. The rate is much higher when compared to the rate reported from a study Ravi P et al; where only 7.89% of the patients received injectable preparations. [13]

In our study 20.94% were antiplatelet, 16.84% antihypertensive, 13.13% antianginal, 9.35% hypolipidemics, 9.18% anticoagulants, 3.56% antibiotics, 3.03% inotropics and 0.265% fibrinolytics. In our study 36% of the patients have not received dual antiplatelet therapy (aspirin clopidogrel) which is in contrast with Kamath A et al study; where 90% of the patients receive dual antiplatelet therapy. [14]

The association of physicians of India recommends that all patients with MI, including those with STEMI should receive dual antiplatelet therapy.

In the present study, among the antihypertensives prescribed, diuretics constitute 42.32%, ARB 7.93%, beta blocker 24.86%, ACE inhibitor 4.23%, CCB 12.69%, alpha beta blocker 5.82% and alpha blocker 2.11%. This is in contrast to the study conducted by SupratimDatta; where the study indicated high use of CCB (73%).[13] Among the diuretics, loop diuretics 90% was the most frequently prescribed, followed by potassium sparing diuretic 8.75% and osmotic diuretic (mannitol) 1.25%. Furosemide was the most prescribed drug 79.16% among the loop diuretics due its low cost when compared with other drugs. Telmisartan 73.33% was used with higher frequency than losartan 26.66%. Further in our study, utilization rate of beta blockers (24.86%) and CCB (12.69%) was found to be much more than that of ARB and ACE inhibitors. Metoprolol (78.7%) was the frequently prescribed beta blocker, followed by bisoprolol (17.02%) and nebivolol (4.25%). 75% of ACE inhibitor constitutes ramipril followed by enalapril. Among the CCBs amlodipine constitute 41.66%, followed by cilnidipine 29.16%, nifedipine 20.83% and verapamil 8.33%. The alpha blocker prescribed was tamsulosin 85% and prazosin 15%. The only

alpha- beta blocker prescribed was carvedilol, which constitute 5.82%.

From our study, the most frequently prescribed anticoagulant was heparin (92.23%), followed by warfarin (1.94%), enoxaparin (3.88%) and acenocoumarol (1.94%) respectively. The most commonly prescribed anti- anginal agent was glyceryltrinitrate (46.66%) and the least prescribed was isolazine (2.66%) and trimetazidine (2%). Streptokinase was the only fibrinolytics prescribed.

In hypolipidemic drug therapy atorvastatin was the most commonly prescribed drug (92.38%), which is in contrast with Diane et al; study 40.1%. Many patients require HMG- CoA reductase inhibitors/ fibric acid derivatives because statin monotherapy may not be sufficient to manage the total lipid abnormalities of patient with the metabolic syndrome or insulin resistant. But in the present study statin monotherapy was only used and no combination therapy was included. Hence combination therapy may be frequently necessary to reduce CAD risk in these patients. But in the present study no combination therapy was observed.

34% of inotropics were prescribed in this study which includes 8.82% digoxin, 11.76% noradrenaline, 26.47% atropine, 17.64% amiodarone and 35.29% dopamine. The most commonly prescribed antibiotic was cephalosporin (75%). Amongst the non- cardiogenic drug PPI (pantoprazole) was found to be more prescribed (23.84%). In our study we noticed that the utilization rate of antiplatelet (aspirin and clopidogrel), anticoagulant (LMWH), statins (atorvastatin), nitrates (glyceryltrinitrate) were high. This finding correlates with standard guidelines mentioned for the use of drug in cardiovascular emergencies. These results were found to be similar to various studies conducted by Ian A Scott et al, VenuMenon et al, F Venturi et al. [14-16]

In this study, most of the interactions were moderate 87% and 13% are severe which is comparable to studies by Christiano Moura et al. [16] Patients with cardiovascular diseases are particularly vulnerable to interactions due to their advanced age, polypharmacy and other factors.

The present study estimated the relationship between the socio- economic status and risk factors of the patients enrolled in the study. No significant correlation was found between the socio- economic factor income with risk factors while significant relationship was established between the socio- economic factor education with risk factors as the p value was found, 0.022. Individuals with highest educational attainment presented higher physical activity, intake of fruits and vegetables and control of salt intake but also higher rates of current tobacco use and alcohol drinking, than those in lower education groups.

## CONCLUSION

In this study the data collected was evaluated for demography and treatment pattern. Atorvastatin, heparin and aspirin were most commonly prescribed in this hospital to treat various types of MI. It was observed that the risk of MI increases with increasing age and in male patients when compared to female patients. Hypertension and diabetes were the most common comorbid conditions associated with MI. The commonly prescribed drug classes for main indications in MI were antiplatelet (20.94%) followed by antihypertensives (16.82%), antianginal (13.13), hypolipidemics (9.35%), anticoagulants (9.18%) and fibrinolytics (0.26%) respectively. Extensive polypharmacy (9.35 drugs per prescription) was noticed in the prescriptions. The prescribing pattern can be improved by reducing the no. of drugs per prescription. The economic burden of the patients can be reduced by prescribing generic drugs. The potential drug interactions were more in the MI prescriptions with co-morbid condition. In addition to prescribing drugs patients should be educated about the risk factors of MI and how they can be prevented. The present study could serve as a reference for further studies to investigate the scope for educational interventions for improving prescribing practices.

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