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RESEARCH ARTICLE

PRESCRIBING PATTERN OF BETA BLOCKERS IN ACUTE CORONARY SYNDROME: A PROSPECTIVE STUDY

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INTRODUCTION

Coronary artery disease (CAD) is a leading cause of mortality and morbidity in India and worldwide Kenneth. CAD is the common form of Cardio vascular diseases (CVDs) and the commonest cause of death from CVD and one of the leading causes of disease burden. CAD is an emerging health problem in India Shruthi et al, Shwetha et al and also Indians seems to develop the disease at an earlier age Anand et al, Geever Z, Mckeigue et al. The global prevalence of CAD is rapidly increased in the last century. It affects millions of people all over the world. Studies estimates that India faces the greatest burden due to CAD. Asian Indians have considerably higher prevalence of CAD than many other ethnic groups Geever Vishwanathan et al. CAD is considered as an important health problem not only in the developed countries but also in developing countries like India Geever Z. Coronary artery disease (CAD) is also called Coronary heart disease (CHD) or

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Ischemic heart disease (IHD). CAD is a chronic disease that progresses over a period of years to decades Vishwanathan et al. It is mainly due to atherosclerosis of the inner lining of blood vessels that supply blood to the heart. CAD begins when plaques are deposited with in the coronary artery. These plaques narrow the internal diameter of the arteries which may cause a tiny clot to form, which can obstruct the blood flow to the heart muscle. This reduces the supply of oxygen and nutrients to the heart muscles, which is essential for the proper functioning of heart. This reduction will either manifest as angina or myocardial infarction (MI) Hatmi et al, Joseph TD et al, Shruthi et al. CAD is classified as stable angina pectoris and acute coronary syndrome (ACS). ACS includes unstable angina pectoris, ST-segment elevation myocardial infarction (STEMI) and Non ST-segment elevation myocardial infarction (NSTEMI) Da et al, Joseph et al.

Acute Coronary Syndrome

It refers to a group of conditions due to decreased blood flow in the coronary artery such that a part of the heart muscle is unable to function properly or dies. The cause of an ACS is erosion or rupture of an atherosclerotic plaque with subsequent platelet adherence, activation, aggregation, and activation of the clotting cascade. The most common symptom is pain, often radiating to the left arm or angles of the jaws, associated with nausea and sweating. ACS refers to acute myocardial ischemia caused by atherosclerotic coronary disease and includes STEMI, NSTEMI and unstable angina Joseph *et al*, Leon *et al*.

Unstable angina

Unstable angina lies between stable angina on the one hand and myocardial infarction on the other. It is caused by disruption of an atherosclerotic plaque with partial thrombosis and possibly embolization or vasospasm. Angina is considered unstable and require further evaluation if patient experience,

- Rest angina, which usually prolonged > 20 minutes occurring within a week of presentation.
- Severe new onset of angina
- Increasing angina refers to previously diagnosed angina that is distinctly more frequent, longer in duration, or lower in threshold.
- Decreased response to rest or nitroglycerine Leon *et al.*

Myocardial Infarction

The term myocardial infarction is thought to reflect death of cardiac myocytes due to prolonged ischaemia. Myocardial infarction is an acute coronary syndrome that can occur during the natural course of coronary atherosclerosis Fuster et al. Progression of atherosclerosis is triggered and enhanced by several factors, which can cause mediating diseases or directly affect the arterial wall. In advanced stages of the disease process, atherosclerotic plaques develop. Initially, normal lumen cross-sectional area will be preserved, since coronary arteries undergo compensatory outward remodelling in relation to plaque area Glagov et al. Development of the disease might therefore be clinically silent for years. In the long run, however, stenosis become functionally important, and coronary artery disease becomes symptomatic. Pain is the cardinal symptom of myocardial infarction, but breathlessness vomiting and collapse are common features. The pain occurs in the same sites as angina, but is usually more severe and lasts longer.

Beta blockers in acute coronary syndrome

Beta blockers are the cornerstone of the drug therapy and are widely used to treat the variety of cardiovascular diseases like hypertension, angina, myocardial infarction, cardiac arrhythmias. These drugs aids in the relief of ischeamic pain, reduce the need for analgesics in many patients and reduce infarct size and life threatening arrhythmias . Betablockers are the cardioactive agents to cause significant reduction in sudden cardiac deaths. Commonly used betablockers proven to be effective include Metoprolol, Bisoprolol, Carvedilol, Propranolol and Timolol. Beta blockers were first discovered by sir james black. In 1962 at imperial chemical industries in the united kingdom and he was awarded the nobel prize in 1988 for advances in medicine. It was one of the major contributions to the clinical medicine in 20th century. Beta blockers are one of the most important proven medication in cardiovascular medicine, reducing both the morbidity as well morbidity Mukherjee et al. About 33% of lifesaving potential

have been found to the betablockers than the other agents Khan. There are more than 100 beta blockers have been developed and only about 30 are available for the clinical purpose Frishman *et al.*

Classification of beta blockers

Cardio selective beta blockers

[1] With intrinsic sympathomimetic activity (beta-agonist)

- Acebutolol (W)
- Celiprolol

[2] Without intrinsic sympathomimetic activity

- Atenolol
- Bisoprolol
- Betaxolol
- Bevantolol
- Esmolol
- Metoprolo l(L)
- Nebivolol

Non- selective beta blockers

[1] With intrinsic sympathomimetic activity

- Alprenolol
- Carteolol
- Oxprenolol
- Penbutolol
- Pindolol(l)

[2] Without intrinsic sympathomimetic activity

- Propranolol
- Nadolol
- Sotalol
- Timolol
- Carvedilol(L)

W; weak betal selectively, weak intrinsic sympathomimetic activity L; Lipid soluble **Khan MG**.

Contraindications to beta blocker use

Absolute contraindications include;

- Severe bradycardia
- High grade AV blocks
- Cardiogenic shock
- Frank LVH
- Severe bronchospasm
- Severe depression
- Symptomatic PAD

Adverse effects of beta blockers

• General: Tiredness, Dizziness, Depression, Shortness Of Breath, Bradycardia, Hypotension, Diarrhea, Pruritis And Rash.

- Cardiovascular: HF, Hypotension, Bradycardia, Palpitation, Firstdegree Heart Block, Cardiogenic Shock.
- Gastrointestinal: Diarrhoea, Nausea, Drymouth, Gastric Pain, Constipation, Abdominal Pain.
- Other: Tiredness, Peripheral Oedema, Chest Pain.
- Nervous System: Dizziness, Vertigo, Stroke, Headache.
- Respiratory: Dyspnoea, Wheezing
- Psychiatric: Depression, Insomnia, Nightmare.
- Dermatologic: Pruritis, Rash

Review of Literature

Sukesh Krishna Chaitanya Loka, et al. (2015) conducted a study on "Evaluation of beta blockers use at a tertiary care hospital". The present study aimed to evaluate the prescribing pattern of beta blockers use. A prospective, observational study was carried out in inpatients of general medicine, and surgical departments of tertiary care hospital. Shruthi Dawalji Venkateshwarlu et al. (2014) conducted a prospective observational study on "Prescribing Pattern in Coronary Artery Disease" in CAD Patients. The incidence of CAD was more common in male compared to the female and the Various comorbid conditions like hypertension, diabetes mellitus, hypothyroidism, dyslipidemia were seen among patients and many of these were found to be risk factors of coronary artery disease. Hypertension and diabetes were the two most common co-morbid conditions found in most of the patients which increase the risk of coronary artery disease. The most commonly prescribed drug classes for main indications in coronary artery disease were anti-platelet drugs followed by antihyperlipidemics, anti-anginal drugs This was followed by anti-hypertensives (beta blockers) and anticoagulants respectively. Sripal Bangalore, et al. (2014) conducted a study on "Clinical Outcomes with b-Blockers for Myocardial Infarction: A Meta-analysis of Randomized Trials" evaluates the contemporary treatment of betablocker use and outcomes in myocardial infarction patients. Betablockers reduce recurrent myocardial infarction and angina and reduces The risk of events including mortality. Marwan Sheikh-Taha and Zeinab Hijazi (2014) conducted a study on "Evaluation of proper prescribing of cardiac medications at hospital discharge for patients with acute coronary syndromes (ACS) in two Lebanese hospitals". The purpose of this study was to evaluate whether ACS patients, admitted into two tertiary referral medical centers in Beirut, Lebanon, are discharged on optimal medical therapy based on the current AHA/ACC guidelines.

Geevar Zachariah, Harikrishnan, et al. (2013) conducted a study on "Prevalence of coronary artery disease and coronary risk factors in Kerala, South India: A population survey e Design and methods". The main aim of the study was to determine the prevalence of CAD and risk factors of CAD in men and women aged 20-79 years in urban and rural settings of three geographical areas of Kerala. The importance of this study lies in the fact it provides data on a wide spectrum of parameters from rural and urban parts from across the state. The study is hoped to serve as a baseline data for comparison with similar studies from other parts of the country and also assessing for future trends in the prevalence of the disease. Pranay Wal et al. (2013) conducted a study on "Management of coronary artery disease in a Tertiary Care Hospital". The objective of the study was to study the prescribing patterns of drugs used in the coronary artery disease (CAD) and to identify, which drug is mostly prescribed at that hospital.

Relevance

The burden of CAD is increasing in parallel with the increase in life expectancy. Beta blocker therapy given for the management of Acute Coronary Syndrome has been shown to have a favourable effect on mortality. The use of beta blockers in patients recovering from Acute Coronary Syndrome improves survival through a reduction of cardiac mortality, sudden cardiac death and re-infarction. This study helps to select the beta blocker with least adverse drug reactions.

MATERIALS AND METHODS

Study design

Prospective observational study

Study site

Cardiology department in a 500 bedded tertiary care teaching hospital.

Study duration

The total study period was 9 months.

Study population

Not less than 100 Acute Coronary Syndrome patients.

Ethical approval

Ethical clearance was obtained from Institutional Ethics Committee

Study criteria

The study group consists of the In-patients who are diagnosed to have Acute Coronary Syndrome in the cardiology department during the study period and who met the following criteria.

Inclusion Criteria

- Patients who are willing to participate in the study
- In-patients ≥ 18 yrs of age.
- Patients prescribed with beta blockers
- Patients diagnosed with ACS

Exclusion Criteria

- Pregnancy and lactation
- Patients with psychiatric disorder

Study procedure

This is a prospective observational study which is planned to conduct in the cardiology department of the 500 bed tertiary care teaching hospital. All In-patients with ACS, who are willing to participate, after signing the informed consent form are included in the study. Each patient medication profile is reviewed and recorded in the customised data entry form and patient demographic details ,prescribing drugs and adverse drug reactions are noted from patients case sheet and patients interview.Patients prescribed with beta blockers will be assessed at the baseline and at the time of follow up after two months. To study the prescribing patterns, relevant details of drugs given to every in-patient with ACS were collected. The obtained data was recorded and subjected for suitable statistical analysis.

Statistical analysis

The data were analyzed by using SPSS(Statistical Package for Social Science) version 16.

RESULTS AND DISCUSSION

A total patients admitted in cardiology department during the study period were analyzed, among which 108 patients diagnosed as unstable angina and myocardial infarction were included in the study as per inclusion criteria, of which 69 were males and 39 were females. Patients prescribed with beta blockers were assessed at the baseline and also at the time of follow up after 2 months.

Age categorization

Table 1. Age categorization of study population (N=108)

Age	Frequency	Percentage	Mean \pm SD
20 - 45	7	6.5	
46 - 70	85	78.7	60.31 ±12.13
71 – 95	16	14.8	

The table I shows the age wise categorization of the study population (N=108). They were divided into three groups, 20-45, 46-70, 71-95 years. The maximum number of patient was in an age group of 46-70 years 78.7% (85) and 71-95 years it was 14.8% (16). Between 20-45 years the percentage of patients included in the study was 6.5% (7). The least patients were in an age group between 20-45 years was 6.5% (7). The mean age of the population was 60.31 ± 12.13 . The above said datas were also shown in the Figure No: 1. The minimum age of patients included in the study was 27 years and maximumwas 90 years with a mean age of 60.31 ± 12.13 . The prevalence of CAD in people below 46 years are lesser 6.5% (7), compared to patients at an age group of 46-60 years (78.7%, n=85) and 71-95 years it was 14.8% (16). Similiar results are shown in study conducted by Benjamin *et al.* (2000).



Figure 1. Age categorization of study population(N=108)

Gender categorization

The Table 2 shows the gender wise distribution of the study population. Out of total population (N=108), males were found

to be more predominant than females patients with a prevalence of 63.9% (69) and 36.1% (39) respectively. It was found in the study conducted by Chuey Yan Lee et al. found in their study that before menopause the CAD event rate in women is low, this is because estrogen have a regulatory effect on several metabolic factors, such as lipids, inflammatory markers and coagulant systems. After menopause atherosclerotic plaque composition changes into more vulnerable lesions with inflammatory factors involved. These datas were also shown in the Figure 2. In a retrospective study conducted by Tasneem et al. of the 140 patients was studied, 96 of these patients were men and 44 of them were women. In the present study, out of 108 patients, 69 % were male and 39 %. The results of this study were found to be in consistence with previous studies and indicated that male were more prone to coronary artery disease compared to female.

Table 2. Gender categorization of study population (N=108)

	Frequency	Percentage	Mean±SD
Male	69	63.9	59.52±10.74
Female	39	36.1	61.72±14.31



Figure 2. Gender categorization of study population(N=108)

Reason for admission

Table 3. Reason for admission of study population (N=108)

Reason for admission	Frequency	Percentage
Chest pain	34	31.5
Breathlessness	3	2.8
Chest pain+ Generaltiredness	7	6.5
Chest pain+sweating	33	30.6
Chest pain+breathlessness+dyspnoea	1	0.9
Chest pain+breathlessness+sweating	1	0.9
Chest pain+vomiting	12	11.1
Chest pain+sweating+vomiting	7	6.5
Breathlessness+vomiting	1	0.9
General tiredness+vomiting	1	0.9
Palpitation+sweating	1	0.9
Chest pain+breathlessness	6	5.6
Chest pain+sweating+palpitation+dyspnoea	1	0.9
Total	108	100.0

The Table 3 shows the reason for admission of the study population. 31.5% (34) of the study population complaints with chest pain and it was the most common symptom. The other common symptoms are breathlessness 2.8% (3), chest pain associated with sweating 30.6% (33), chest pain associated with General tiredness 4.6% (5), chest pain associated with vomiting 11.1% (12), chest pain associated with vomiting and sweating 6.5% (7), chest pain associated with breathlessness

5.6% (6), and chest pain associated with breathlessness with dyspnoea, chest pain associated with breathlessness with sweating, Breathlessness + vomiting, General tiredness + vomiting, Palpitation + sweating, Chest pain+ sweating + palpitation + dyspnoea are all 0.9%. The prevalence of various reason for admission among study population was assessed and among which the commonest presenting symptom was found to be chest pain (31.5%), followed by chest pain with sweating(30.6%) and chest pain with vomiting (11.1%). It occur in CAD due to deposition of atherosclerotic plaques, coronary arteries gets narrowed and decreases the amount of oxygen that can be delivered to heart itself. This can cause the classic symptoms of chest pain or tightness with radiating to arm or neck associated with breathlessness and sweating and vomiting. The similar datas are also shown in the figure No. 3. Sukesh Krishna et al. found in their study that chief complaints of admission include breathlessness, swelling, followed by generalized weakness and chest pain. In the study conducted by Alex A. Agostini-Miranda et al. found that seven million visits per year to the emergency department or chest pain units due to a chief complaint of chest pain, of which 1.6 million are admitted with a diagnosis of acute coronary syndrome (ACS). In the present study also chest pain was the major complaint for ACS patients.



Figure 3. Reason for admission of study population (N=108)

Past medical history

Table 4. Past medical history of study population (N=108)

Past medical history	Frequency	Percentage
Type 2 DM	22	20.3
Hypertension	20	18.5
Dyslipidemia	10	9.3
Type 2 DM +HTN	30	27.8
Type 2 DM+DLP	10	9.3
DM+HTN+DLP	16	14.8

The Table 4 shows the past medical history of the study population (108). Among the study population 20.4%(22) had type 2 DM and 18.5%(20) had hypertension and 9.3%(10) had dyslipidemia. Type 2 DM with hypertension was 27.8% (30), type 2 DM with dyslipidemia was 9.3%(10) and type 2 DM with hypertension with dyslipidemia was 14.8%(16). About 27.8% of the study population shows Past medical history of type 2 DM with hypertension. The same data is shown in the Fig. 4. Fauci *et al.* has found that beta blockers are preferable in patients with insulin requiring diabetes mellitus. Increased occurrence of the hypertension is mainly due to their social habits, physical inactivity and dietary habits Bangalore *et al.*

has found that beta blockers reduce heart rate and reduce the risk of CV events in patients with hypertension.



Figure 4. Past medical history of study population (N=108)

Categorization of acute coronary syndrome

Table 5. Categorization of Acute Coronary Syndrome (N=108)

	Frequency	Percentage
UA	51	47.2
NSTEMI	45	41.7
STEMI	12	11.1

The Table 5, reveals that about 47.2% (51) of the patients included were diagnosed to have Unstable Angina and 41.7% (45) of the patients have NSTEMI and STEMI 11.1% (12). The same data were shown in the figure No.5.study conducted by Meriam *et al.* also found that majority of the patients had NSTEMI while assesseing the categorisation of ACS.



Figure 5. Categorization of Acute Coronary Syndrome (N=108)

Prescribing pattern of beta blockers

Table 6. Prescribing pattern of betablocker (N=108)

Betablocker	Frequency	Percentage
Metoprolol	94	87.04
Bisoprolol	9	8.33
Carvedilol	5	4.63

The given table shows the prescribing pattern of betablockers in the study population. Among betablockers, metoprolol was prescribed for majority of patients. 87%(94)were prescribed with metoprolol and 8.3%(9) were with bisoprolol and 4.3%(5)were prescribed with carvedilol. Same datas were shown in the Figure 6. In the study conducted by Sukesh *et al.* that Beta blockers were mostly prescribed among the age group 50-69 years (50.3%) and the widely prescribed was metoprolol (39.2%). In the present study also metoprolol was the mostly prescribed betablocker (87%) among the age group 46-70 years (78%).



Figure 6. Prescribing pattern of betablocker (N=108)

Commonly prescribed drugs other than beta blockers

 Table 7. Commonly prescribed drugs other than beta blockers for the study population (N=108)

Drug name	Given frequency	percentage
Antiplatelet	102	94.4
Anticoagulant	98	90.7
Diuretics	36	33.3
Antihyperlipidemics	29	26.9
Nitrates	58	53.7
Antidiabetics	78	72.22
Antiemetics	13	12.0
Antibiotics	31	28.7
Anxiolytics	14	13.0
Antacids	44	40.7
Analgesics	27	25.0
Laxatives	16	14.8

Table 7 Shows the other commonly prescribed drugs of the study population.about 94.4 % are prescribed with the antiplatelets, 90.7% are prescribed with anticoagulants, 33.3 % are prescribed with diuretics, 26.9 % are prescribed with antihyperlipidemics, 53.7% are prescribed with nitrates, 78% are prescribed with antidiabetics, 12 % are prescribed with antiemetics, 28.7% are prescribed with antibiotics, 13% are prescribed with anxiolytics, 40.7% are prescribed with antacids, 25% are prescribed with analgesics, 14.8% are prescribed with laxatives. same datas were shown in the figure No.15. In the study conducted by Shruthi et al. in 170 patients, The prescription pattern of various cardiovascular drugs were found to be as antiplatelet drugs (99.41%), antihyperlipidemic drugs 162 (95.29%), anti-anginal drugs (64.71%), anticoagulants (80.59%), antihypertensives (64.71%), diuretics (62.35%)and bronchodilators 31 (18.24%).



Figure 7. Commonly prescribed drugs other than beta blockers for the study population (N=108)

Doses of individual beta blockers

Metoprolol

Out of 108 patients, metoprolol 25 mg was prescribed for 60.185% and metoprolol 50 mg was prescribed for 13.88% and metoprolol 12.5mg was prescribed for 12.96% of the study population. Sukesh Krishna *et al.* found in their study that Out of 135 patients, metoprolol 25mg was prescribed for 22.9% of study population, 8.1% of patients were prescribed. with 12.5mg and 50mg.

Table 8. Prescribed doses of metoprolol in the study population (N=108)

Dose prescribed	Number of patients	Percentage
12.5 mg	14	12.96%
25 mg	65	60.185%
50 mg	15	13.88%



Figure 8. Prescribed doses of metoprolol in the study population (N=108)

Bisoprolol

Out of 108 patients, bisoprolol 2.5 mg was prescribed for 3.7% and bisoprolol 5 mg was prescribed for 4.6% of the study population.

Table 9. Prescribed doses of bisoprolol in the study population(N=108)

Dose prescribed	Number of patients	Percentage
2.5 mg	4	3.7%
5 mg	5	4.6%



Figure 9. Prescribed doses of bisoprolol in the study population (N=108)

Carvedilol: Out of 108 patients, carvedilol 3.125 mg was prescribed for 2.7% and carvedilol 6.25 mg was prescribed for 1.85% of the study population. Sukesh Krishna *et al.* found in their study that Out of 135 patients, Out of 135 patients, carvedilol 3.125mg was prescribed for 16.2% of study population, 10mg was prescribed for 7.4% and 0.7% of patients were prescribed with 6.25mg.

Table 10. Prescribed doses of carvedilol in the study population



Figure 10. Prescribed doses of carvedilol in the study population

Adverse drug reaction

Table 11. Adverse drug reaction of the study population (N=108)

ADR	Frequency	Percentage
Brady arrhythmia	5	4.6%
Pulmonary oedema	3	2.8%
Head ache	1	0.9%
Hyperkalemia	4	3.7%
Absent	95	88%

Table 11 Shows the Adverse drug reaction of the study population. 4.6 %(5) of the patients shows brady arrhythmia. 2.8%(3) of the patients show pulmonary oedema. About 0.9%(1) of the patients shows headache. 3.7 % (4) of the patients shows hyperkalemia. Brady arrhythmia found as the most predominant adverse drug reaction due to Metoprolol. No ADRs are found in 88% out of 108 patients. Same data's are shown in the Figure 11. Frishman *et al.* describes the adverse drug reactions of beta blockers in his study.



Figure 11. Adverse drug reactions of the study population (N=108)

Abbreviations

ACS Acute coronary syndrome ACEIs Angiotensin converting enzyme inhibitors ACCAmerican college of cardiology AHA American heart association AV node Atrioventricular node **BP** Blood pressure CA Coronary artery CADCoronary artery disease CHDCoronary heart disease CHF Congestive heart failure COPD Chronic obstructive pulmonary disorder CVD Cardio vascular disease DBP Diastolic blood pressure DM Diabetes mellitus **DLP** Dyslipidemia HDL High density lipoprotein HMGCoA Hydroxyl methyl glutaryl coenzyme A HTN Hypertension IHD Ischemic heart disease LDLLow density lipoprotein LVHLeft ventricular hypertrophy MI Myocardial infarction NSAIDs Non steroidal anti-inflammatory drugs NSTEMI Non ST-Segment elevation myocardial infarction PADPeripheral artery disease STEMI ST-Segment elevation myocardial infarction SBP Systolic blood pressure TC Total cholesterol TG Triglycerides T2DM Type 2 diabetes mellitus UAUnstable angina VF Ventricular failure

Conclusion

The present study was performed to assess the prescribing pattern Acute Coronary Syndrome patients. The study concluded by stating that beta blocker prescribed for majority of patients was Metoprolol than Bisoprolol and Carvedilol. Beta blockers was found to have very fewer adverse drug reactions.

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