Research Article

PATTERN OF PHARMACOTHERAPY AND ASSESSMENT OF DRUG RELATED PROBLEMS IN ISCHEMIC HEART DISEASE PATIENTS

Soumya Shastry¹, Ramakrishna Prudhivi^{2*}, Vidhya S¹, Alison Lugun¹, Thota Sai Mounika¹, Sunil Christopher³

¹Department of Pharmacy Practice, Dayananda Sagar College of Pharmacy, Kumaraswamy Layout, Bengaluru-560078, India

²Faculty of Pharmacy, Department of Pharmacy Practice, College of Pharmaceutical Sciences, Dayananda Sagar University, Kumaraswamy Layout, Bengaluru-560078, India

³Consultant Internal Medicine, Sagar hospitals, Banashankari, Bengaluru- 560078, India

*Corresponding Author Email: ramakrishna.prudhivi@gmail.com

Article Received on: 08/12/18 Approved for publication: 22/01/19

DOI: 10.7897/2230-8407.100392

ABSTRACT

Aim: To study the prescribing patterns of drugs used in Ischemic Heart Disease (IHD) patients and to identify Drug Related Problems (DRPs) associated with treatment. **Methodology:** 120 patients from the cardiology inpatient department who were suffering from IHD were included in this prospective, observational and analytical study conducted in Sagar hospitals, Kumaraswamy layout, Bengaluru, India. **Results:** Out of a total of 120 patients, 76 (61.67%) were males and 46 (38.33%) were females. Subjects of age group 61-70 (25.0%) were found to be more susceptible to IHD. Most of the prescriptions were prescribed with Lipid lowering agents (12.16%), followed by β -blockers (11.10%), Anti-Platelets (8.72%). A total of 221 DRPs were identified. Drug interactions (41.63%) were the most common drug related problems observed, followed by Untreated indications (25.79%), Medication use without indication (9.05%), Adverse Drug Reactions (ADRs) (9.05%), Overdose (6.79%), Sub-therapeutic dose (3.17%). The most common drug-drug interaction was Clopidogrel+Aspirin (6.52%), followed by Furosemide+Aspirin (6.52%) and Atorvastatin+Clopidogrel (5.43%). The most offending drug involved in the drug-drug interactions was observed to be Aspirin. **Conclusion:** Our study suggests that Statins, Anti-Platelet and Anti-Anginal/Ischemic drugs are major cardiovascular drugs used in the treatment of IHD. The various DRPs were observed to be due to polypharmacy practiced in the treatment of IHD which emphasizes the importance of early detection, evaluation and documentation of DRPs for better patient care and quality of life of patients with IHD.

Keywords: Ischemic Heart Disease (IHD), Drug Related Problems (DRPs), Adverse Drug Reactions (ADRs), Drug Interactions

INTRODUCTION

Cardiovascular diseases (CVDs) are a group of disorders of the heart and blood vessels and they include: coronary heart disease, cerebrovascular disease, peripheral arterial disease, congenital heart disease, deep vein thrombosis and pulmonary embolism.¹ Coronary heart disease (CHD), sometimes described as coronary artery disease (CAD) or ischemic heart disease (IHD), is a condition in which the vascular supply to the heart is impeded by atheroma, thrombosis or spasm of coronary arteries.² In 2015, there were an estimated 8.92 million deaths due to IHD making it the leading cause of death in the world.³ But an estimated 17.92 million CVD deaths occurred registering a declining feature.⁴

Cardiovascular diseases have now become the leading cause of mortality in India. A quarter of all mortality is attributable to CVD. Ischemic heart disease and stroke are the predominant causes and are responsible for >80% of CVD deaths. The global burden of disease study estimate of age-standardized CVD death rate of 272 per 100,000 population in India is higher than the global average of 235 per 100,000 population.⁵ Autopsy data from Delhi suggest infrequent occurrence at all ages of severe grades of sclerosis and of thrombotic lesions.⁶

Study on pharmaco-therapeutic pattern on cardiovascular patients is rarely done. Irrational use of medicines is widespread

throughout the world. The main problems include the unnecessary prescription of drugs which cause DRPs. Rational use of medicines requires that patients receive medications appropriate to their clinical needs, in doses that meet their own requirements, for an adequate period of time and at the lowest cost to them and their community. The irrational use of drugs is a major problem of present day medical practice.⁷ In spite of extensive programs on rational use of drugs and the Emergency Medicine List (EML) of World Health Organization (WHO), which are being promoted by various national and international agencies working on health sector, irrational prescription is still a common practice.⁸

Cardiovascular diseases (CVD) account for high morbidity and mortality all over the world.⁹ A study of prescription pattern ensures rational pharmacotherapy and assures quality medical care to the patients. The primary aim is observation of the prescribing pattern of cardiovascular drugs among the patients admitted to intensive cardiac care unit (ICCU).

A drug-related problem is any event or circumstance involving drug treatment that interferes with the patient achieving an optimum outcome of medical care. In hospitalized patients where multiple changes are being made in patient's medication regimens, drug-related problems take place more commonly and may be accompanied by lack of continuity of care. Drug related

problems causes marked morbidity, mortality as well as surge in health care expenditure which again affects the patient's quality of life.¹⁰ Often cardiovascular patients have multiple comorbid conditions, thus they are prescribed with multiple drugs. So the chances of occurring drug related problems are elevated in such category of patients. Thus the secondary objective of our study is to identify the various types of DRPs and assess methods to avoid them.

MATERIALS AND METHODS

Study design, settings and criteria

A prospective, observational and analytical study was carried out in IHD patients in in-patient department of cardiology department at Sagar hospitals, Kumaraswamy layout, Bengaluru, India.

This study was approved by institutional ethics committee of Dayananda Sagar College of Pharmacy and issued ethical clearance certificate for the same (DSCP/ETH.COM/780/2018). The study was conducted for a period of 6 months (September 2017 - February 2018). The patients were enrolled in the study as per inclusion criteria: all the patients of either sex who were diagnosed with IHD and were above 18 years of age. Exclusion criteria stated that, those who are non-cooperative and not willing to participate in the study, including pregnant women and cancer patients, were excluded from the study.

Sources of data and study procedure

The study materials included the patient information sheet, informed consent form, predesigned patient profile form, Naranjo ADR probability scale, Hartwig severity assessment scale and Schumock and Thornton preventability scale.

An informed consent form was designed for the patient in consultation with the guide and the doctor. Patients who gave consent were enrolled in the study. The study followed AHA/ASA guidelines to check treatment options for IHD patients. Micromedex, Medscape and CIMS were used to identify the DRPs. Helper and Strand introduced several categories of DRPs. In this approach, problems and causes were not separated. Following is the Helper and Strand DRPs classification:- 1) Untreated indications, 2) Improper drug selection, 3) Sub therapeutic dosage, 4) Failure to receive medication, 5) Over dosage, 6) Adverse drug reactions, 7) Drug interactions, 8) Medication use without indication¹¹

Drug interactions were also found and analyzed by their type and severity using www.drugs.com, www.medscape.com, Clinirex and Micromedex 2.0. ADRs were found by patient interview and spontaneous reporting system by health care professionals. The degree of association of an adverse effect with a drug was done with the help of Naranjo's scale where it involves certain; probable; possible; unlikely¹². The severity of the ADR is analyzed using adapted Hart-wig severity scale. The scale was classified as mild; moderate; severe.¹³ Preventable adverse drug reaction was defined according to Schumock and Thornton.¹⁴

Statistical analysis

Data was recorded on a pre-designed proforma and managed on an MS Office Excel spread sheet. The descriptive statistics was represented by mean $\pm$ standard deviation and percentages. Graph Pad prism version 5.0 statistical software was used for the data analysis.

For all analyses, $p < 0.05$ was regarded as statistically significant.

RESULTS

Socio-demographic data

Out of 120 patients, 61.67% were males and 38.33% were females. We found that highest percentage (25%) of patients suffered from ischemic heart disease was observed in the age group of 61-70 years. The majority of patients stayed in the hospital for 1-5 and the average ($\pm$ SD) was 2.8 ± 1.3 days. Among the study population, 25% of patients were diagnosed to have one co-morbidity, 37.5% were having two co-morbidities. A various number of co-morbidities have been encountered with IHD, out of which HTN with DM was found to be 27.5%, and only IHD was found to be 25.83%. Most of the patients (70.83%) received 5-10 drugs, whereas least number of patients received <5 drugs. We assessed smoking status in patients where 69.17% did not indulge in smoking. 12.50% were non-smokers. It was found that 65.83% were of non-alcoholics whereas 34.17% consumed alcohol. (Table 1).

Prescribing pattern

In our study, we found that the most of the prescriptions were prescribed with lipid lowering agents (12.16%), followed by β -blockers (11.10%), anti-platelets (8.72%), diuretics (8.35%), GI drugs (7.49%), anti-anginals (6.75%), anti-coagulants (5.65%), antibiotics (4.29%), vitamins (3.95%), CCBs (3.68%), ACE inhibitors (3.43%), ARBs (3.43%) and other drugs as mentioned below in the Table 2. Maximum number of drugs given in one patient was 17, whereas 4 patients received least number of drugs. Among diuretics, Furosemide was prescribed more common (75%), whereas Spironolactone was prescribed with 8.82%. Among ACE inhibitors, major number of prescriptions were prescribed with Ramipril (75%) and 7 prescriptions were prescribed with Enalapril. Among ARBs, 57.14% prescriptions were prescribed with Telmisartan whereas 21.42% were prescribed with Olmesartan and Losartan. Among β -blockers, Metoprolol was preferred (71.11%). Major number of prescriptions were with Prazosin (44.44%), Clonidine with 33.33% and Moxonidine with 22.22%. Out of 30 CCBs, major number of prescriptions were prescribed with amlodipine (50%), whereas other CCBs like clindipine is prescribed with 26.66%, Nifedipine with 13.33% and Diltiazem with 10%. Out of all Lipid lowering agents, major number of prescriptions were prescribed with Atorvastatin (68.68%) and Rosuvastatin is prescribed with 31.31%. Among anti-anginals, major number of prescriptions were prescribed with Isosorbide Mononitrate (54.54%), whereas NTG is prescribed with 16.36%, Isosorbide Dinitrate with 9.09%, Trimetazidine with 5.45%, Ranolazine with 5.45%, Nicorandil with 5.45%, Tirofiban with 1.81%, and Ivabradine with 1.81%. There is only one agent prescribed under positive inotropic agent-Digoxin. Anti-platelets like Clopidogrel, Aspirin, and Ticagrelor were prescribed with 47.88%, 43.66% and 8.45% respectively. In our study, anti-coagulants like heparin, enoxaparin sodium, nicoumalone and Fondaparinux were prescribed with 71.73%, 19.56%, 6.52%, and 2.17% respectively.

Type of Intervention

Out of 120 patients, most of the patients (57%) received Pharmacotherapy, followed by Coronary artery bypass graft surgery-CABG (28 %) and Percutaneous Coronary Intervention-PCI (15%) (Figure 1).

Drug Related Problems

Among 120 prescriptions followed during the study period, a total of 221 DRPs were identified. The average number of DRPs was 1.84 for each patient. Drug interactions (41.63%) were the most common drug related problems observed in our study followed by Untreated indications (25.79%), Medication use without indication (9.05%), Adverse Drug Reactions (ADRs) (9.05%), Overdose (6.79%), Sub-therapeutic dose (3.17%), which were represented in Figure 2.

The most common Untreated indication was found to be Breathlessness (24.60%). The most common drug used without indication was identified as Albendazole (45%). The most common drug which is given in overdose is Aspirin (26.67%), followed by Multivitamin (26.67%) and Heparin (20%).

The most common drug-drug interaction was Clopidogrel+Aspirin (6.52%), followed by Furosemide+Aspirin (6.52%) and Atorvastatin+Clopidogrel (5.43%). The drug involved in the most interactions was observed to be Aspirin.

Most of the drug interactions (70.65%) were moderate in nature followed by minor (23.91%) and major (5.43%).

A total of 20 adverse drug reactions were identified among 120 patients. The most common ADR found was GI bleeding (20%) and reduced hemoglobin level (20%) followed by acute renal failure (15%). The list of ADRs are mentioned in the Table 3. Gastrointestinal ADRs were the most common (35%) followed by hematological (20%) and cardiovascular (15%). The gastrointestinal ADR includes GI bleeding and ulcer, hematological includes low Hb level and cardiovascular includes low blood pressure. The types of ADRs by system are mentioned in the Figure 3.

Most ADRs were classified as "possible" (50%) followed by "probable" (35%). Most of the patients had moderate ADRs (60%) and mild (40%). Most of the ADRs were not preventable (60%) followed by preventable (40%). A total of 14 drugs were found to be causing ADRs. The common drugs causing ADR were Heparin (20%) and Aspirin (10%).

Table 1: Socio-demographic data of IHD patients

Variable	Number of patients (n) (120)	Percentage (%)
Gender		
Male	74	61.67
Female	46	38.33
Age		
≤ 50	23	19.17
51-60	27	22.5
61-70	30	25.00
71-80	25	20.83
≥81	15	12.50
Hospital stay		
1-5	102	85.00
6-10	13	10.83
11-15	5	04.16
Number of co- morbidities		
0	19	15.83
1	30	25.00
2	45	37.5
3	17	14.17
4	6	05.00
5	2	01.67
6	1	0.83
Smoking status		
Never Smokers	83	69.17
Non-Smokers	15	12.50
Occasional Smokers	12	01.66
Recurrent Smokers	8	10
Chain Smokers	2	6.66
Alcohol status		
Alcoholics	41	34.17
Non-Alcoholics	79	65.83
Non-Alcoholics	79	65.83

Table 2: Prescription pattern of different therapeutic class

Therapeutic Class	Number of Prescriptions (n)	Percentage (%)
Diuretics	68	8.35
ACE Inhibitors	28	3.43
ARBs	28	3.43
B-blockers	90	11.10
Alpha blockers	90	1.10
CCBs	30	3.68
Lipid lowering agents	99	12.16
Anti anginals	55	6.75
Anti-Platelets	71	8.72
Anti-Coagulants	46	5.65
Positive inotropic agent	18	2.20
Anti-diabetics	17	2.08
Anthelmintics	21	2.57

Table 3: List of drug interactions

Drugs	Number (n)	Percentage (%)
Clopidogrel+Aspirin	6	6.52
Furosemide+Aspirin	6	6.52
Atorvastatin+Clopidogrel	5	5.43
Aspirin+Pantoprazole	5	5.43
Atorvastatin+Pantoprazole	5	5.43
Metoprolol+Aspirin	5	5.43
Furosemide+Pantoprazole	4	4.35
Clopidogrel+Pantoprazole	4	4.35
Aspirin+Ramipril	4	4.35
Digoxin+Atorvastatin	4	4.35
Heparin+Clopidogrel	4	4.35
Aspirin+Heparin	4	4.35
Aspirin+Telmisartan	3	3.26
Digoxin+Furosemide	3	3.26
Metoprolol+Digoxin	3	3.26
Digoxin+Metformin	3	3.26
Digoxin+Heparin	3	3.26
Furosemide+Metoprolol	3	3.26
Others	18	19.57
TOTAL	92	100

Figure 1: Type of Intervention

Figure 2: Types of DRPs

Figure 3: List of ADRs

DISCUSSION

According to our study, 76 (61.67%) patients with IHD were males and 46 (38.33%) patients were females. The main reason for this high incidence in male population is due to male gender predominance due to various risk factors and co morbidities compared to the female population. This observation is supported with the demographic reports of the study conducted by Ganachari M S et al., cited a predominance in male gender over female gender.¹⁵ The studies conducted by Alagiriswami et al., and Sathish Kumar et al., also shows an increase in number of male population than females.

Among 120 patients, the distribution of IHD based on the age group of patients showed that majority (25.0%) of the patients who suffered from ischemic heart disease were present in the age group of 61-70 years. In a similar study conducted by Ramanath et al., majority of patients (77.9%) were in the age group of 60 - 70 years.¹⁸

Among the study population, 25% of patients were diagnosed to have one co-morbidity, 37.5% of the patients were with two co morbidities, 14.17% were having three co morbidities, 5% were having four co-morbidities, two patients (1.67%) were having five co-morbidities, one patient (0.83%) was having six co-morbidities and 15.83% of the patients were not having any co morbidity. This observation is supported with the study conducted by Celin et al., where among the study population, 39.8% of patients were diagnosed to have one co-morbidity and 17.6% of the patients were with two co-morbidities and two patients (1.8%) were having three co-morbidities and 40% of the patients were not having any co morbidity.¹⁹

Patients with hypertension and diabetes are at increased risk of a wide range of complications and co-morbidities, which adversely affect quality of life and mortality. Cardiovascular diseases, most commonly ischemic heart disease is the primary causes of morbidity and mortality among patients with hypertension and diabetes. Uncontrolled high blood pressure can cause ischemic heart disease. This means the heart muscle isn't getting enough blood and uncontrolled glucose level leads micro and macro vascular complications which strongly related to development of ischemic heart disease and in long run affects major physiological system significantly increase the rate of suffering from, hyperlipidemia, stroke, retinopathy, nephropathy which will ultimately leads to multiple organ failure if there is no proper control over blood glucose level. In this study, majority of our patients were suffering from ischemic heart disease only (25.83%), but in terms of co-morbidity, patients of suffering from hypertension and ischemic heart disease was highest, i.e., 27.5%

of total patients. In a similar study conducted by Khan M.A et al., it was found that patients had higher rate of hypertension (29.33%), Diabetes mellitus (5.33%) and IHD followed by HTN and DM was found to be (32%).²⁰ In another study conducted by Dawalji S et al., it was found that patients had higher rate of hypertension (25.88%), Diabetes mellitus (5.88%) and other condition like COPD & Asthma (2.94%).²¹

During the hospital stay, majority of patients (70.83%) received five to ten drugs. The polypharmacy (≥ 5 drugs) was observed in 106 patients. This was because most of the patients had more than two co-morbidities, symptomatic treatment, or for preventing complication, etc. This might be the reason for prescribing polypharmacy or more drugs. The studies of Hajjar et al., Rahmawati et al., and Cunningham et al. showed the similar results.^{22, 23, 24}

An independent risk factor for ischemic stroke is cigarette smoking. In ischemic stroke, evidence suggests that exposure to environmental smoke increases the risk of cardiovascular disease. Smoking cessation is recommended in persons who have experienced a stroke or TIA.²⁵ The risk of ischemic heart disease is raised by cigarette smoking. When all the factors are combined, the risk is augmented. Smoking increases blood pressure, decreases exercise tolerance and increases the tendency for blood to clot.²⁶ In our study, we assessed that 69.17% did not indulge in smoking whereas 12.50% were non-smokers, 10% were occasional smokers, 6.66% were recurrent smokers and 1.66% were chain smokers.

Patients with ischemic stroke, TIA, or hemorrhagic stroke who are heavy drinkers should terminate or decrease alcohol intake (Class I; Level of Evidence C). Light to moderate quantities of alcohol intake (up to 2 drinks a day for men and up to 1 drink a day for non-pregnant women) may be reasonable, although nondrinkers should not be provoked to begin drinking (Class IIb; Level of Evidence B). There is some evidence that a regular pattern of drinking relatively small amounts of alcohol (as low as one standard drink every second day) reduces the risk of ischemic heart disease in people from middle age onwards.²⁷ In our study population, it was found that 65.83% were of non-alcoholics whereas 34.17% consume alcohol. In 1987, a study by Shaper et al. in 24 British towns showed that the presence of ischemic heart disease was higher among nondrinkers even when compared with light drinkers.²⁸

In this study, we found that, 69 (57.5%) patients, received only Pharmacotherapy, 33 (27.5%) patients have undergone coronary artery bypass grafting (CABG) and 18 (15%) patients undergone for percutaneous coronary intervention (PCI). Pharmacotherapy

was given to patients according to severity of disease and associated complications. Aim of this study was to investigate the pattern of pharmacotherapy and find the frequency of specific class of drug prescribed in the treatment of ischemic heart disease. During this study, we found that, all the prescriptions contained multiple medications.

Among many lipid lowering agents, statins are commonly used to reduce of cardiovascular events and also in the treatment of dyslipidemia. Many reports have demonstrated the efficacy of statins in patients with ischemic heart disease. The West of Scotland Coronary Prevention Study (WOSCOPS) demonstrated statin induced reduction of cardiovascular events and cardiovascular mortality in patients with high cholesterol level but without ischemic heart disease. As per Lim S Y et al., in the Cholesterol and Recurrent Events (CARE) trial, the cardio protective effects of statins were also demonstrated in patients with myocardial infarction and average cholesterol levels.²⁹

In this study, we found that, the use of lipid lowering agent was highest in the treatment (Number of prescriptions: 99, Prescription rate:12.16%) followed by β -blockers (No of prescription: 90, Prescription rate: 11.10%), Anti-Platelets (No of prescription: 71, Prescription rate: 8.72%), Diuretics (No of prescription: 68, Prescription rate: 8.35%), anti ischemic/anti anginal drug (No of prescription: 55, prescription frequency: 6.75%) followed by Anti-Coagulants, CCBs, ACE Inhibitors and ARBs and positive inotropic agents which is similar to the findings in the study by A. H. M. Nazmul Hasan et al., with 88.98% of lipid lowering agents.³⁰

According to Andersson C et al., β - blockers, ACE inhibitors, Angiotensin receptor blockers (ARBs), CCBs are commonly employed as an antihypertensive agent, but in current practice they have multiple functions in the management of cardiovascular patients. Depending on intensity of ischemic heart disease, combination these drugs are used for proper management except there is any contraindication for patients.³¹

Most of the prescriptions contained combination drug products of a single therapeutic category and was observed in case of anti platelet, anti ischemic/anti anginal and anti hypertensive agents. In our study we found the combination use of furosemide and spironolactone compared to single use of either agent or any other single diuretic. As such combination of diuretics do not cause electrolyte imbalance compared to single use of diuretic, preferred by most physicians. According to Giles TD, diuretic treatment in combination with standard therapy of ischemic heart disease might bring positive outcome as diuretics reduce peripheral resistance ultimately reduce cardiac work load and prescribed to patients upon consideration of overall pathological condition.³²

Platelet plays an essential role in the pathogenesis of ischemia in coronary circulation, platelet aggregates together to form thrombus leads blockage in coronary circulation. In a study setting conducted by Clappers N et al., Anti-Platelet drug therapy is obvious in the management of ischemic heart disease as a primary and secondary preventive measure to reduce mortality.³³

In terms of use of Anti-Platelet agents, frequency and prescription rate of combination of clopidogrel and aspirin was highest. In terms of use of single lipid lowering agent in a prescription, frequency of use of Atorvastatin was most compared to Rosuvastatin. Patients suffering from ischemic heart disease required anti ischemic/anti anginal drug therapy. In 2008, Karalis DG and in 1998, Ebrahim et al., found that high blood cholesterol

level is also associated with the patients of diabetes and is one of the vital reasons that of high risk factor for the diabetes patients to develop ischemic heart disease. Other risk factor for high blood cholesterol includes life style and food habit.^{34, 35}

DRPs can affect the goals of the treatment and may even have a negative outcome on the patient's health and wellness.³⁶ Among 120 prescriptions followed during the study period, a total of 221 DRPs were identified. The frequency of DRP was 1.84 per patient. This observation was similar to the study conducted by Urbina O et al., where the frequency of DRP was high.³⁷

Drug interactions were the most common drug related problems observed in our study with 41.63% which agrees with the study conducted by Shareef J et al., which reported that drug interaction with 49.05% of the total DRPs, followed by Untreated indications (25.79%) and Medication use without indication (9.05%).³⁸

A total of 57 (25.79%) untreated indications were identified. This was found to be more when compared to the studies carried out by Shareef J et al., with 3.77%. The most common indication was found to be Breathlessness (24.60%), followed by Diabetes mellitus (12.28%) and others.³⁸

This study reported that 10 (4.52%) improper drug selections were identified. A total of 20 (9.05%) medication use without indication were identified which is similar to the findings in the study by Shareef J et al., with 5.66% and the drugs often used without indication in their study were Ranitidine, Pantoprazole.³⁸ The most common medication use without indication in this study was identified as Albendazole (45%), followed by Pheniramine (15%). In many cases there were no indication to start a drug treatment or most of the reasons were found to be due to prophylactic reasons. 9 (3.17%) drugs were found to have sub-therapeutic dose among 120 patients. A total of 15 (6.79%) drugs were identified to have overdose.

In our study a total of 92 drug interactions were found. Among these, major was 5.43%, moderate was the most common drug interaction 70.65% and minor was 23.91%. This was in contrast with the study conducted by Jimmy O.D et al., where 24.85% were major, 53.33% were moderate and 21.82% were minor interactions.³⁹ Among 120 patients involved in drug interactions the male patients had 55 (59.78%) drug interactions and the female patients had 37 (40.22%) drug interactions. The most common drug-drug interaction was Clopidogrel+Aspirin (6.52%). This is comparable to the study done by Ghulam Murtaza et al., were the common drug-drug interaction was Clopidogrel + Aspirin (22.79%).⁴⁰

In this study, 20 (9.05%) adverse drug reactions were identified. Other than the unwanted effect of ADR for the patient, it can cause a significant financial burden to both patient and the health care system. The common ADR found was GI bleeding (20%) followed by reduced Hb level (20%) and acute renal failure (15%). Gastrointestinal ADRs were the most common (35%) followed by hematological (20%) and cardiovascular (15%). A study conducted by Muthiah P et al., also showed that Gastrointestinal ADRs (20.7%) was the most common system to be affected.⁴¹

Most ADRs were assessed as "possible" (50%) according to the causality assessment scale.

This finding is similar to the study done by Wankhede et al., where they report the most ADRs were scored as possible (96%).⁴²

Most of the patients had moderate ADRs (60%) and mild (40%) according to severity scale which is comparable to the study conducted by Sriram S et al., where they observed the severity of 49% of reactions (using Hartwig scale) was reported as moderate.⁴³

Most of the ADRs were not preventable (60%) followed by preventable (40%) according to the Schumock and Thornton. This finding agrees with the study conducted by Celin et al., where most of ADRs were not preventable.¹⁹

The common drugs causing ADR were Heparin (20%) and Aspirin (10%). The findings in this study differs from the study conducted by S Kaur et al., where they found the most common drug causing ADRs were nitrates (37%) followed by Diuretics (24%).⁴⁴

CONCLUSION

Our study suggests that statins, anti-platelet and anti-anginal/ischemic drugs are major cardiovascular drugs used in the treatment of ischemic heart disease. Addition of β blockers, ACE inhibitors, ARBs, diuretics to standard therapy bring better therapeutic outcome and reduce ischemic mortality rate. Depending on the intensity of pathology, revascularization and PCI is done to the patients.

As the goal of ischemic therapy is to lower the blood cholesterol level, prevention of further platelet aggregation, control of hypertension in hypertensive ischemic patients, a combination of drugs from different pharmacological category is required. Along with pharmacotherapy and surgical intervention, cardiac rehabilitation and change in life style are also essential for better therapeutic outcome. High blood cholesterol, diabetes, hypertension associated with life style is major risk factors for the development of ischemic heart disease. The various DRPs were observed to be due to polypharmacy practiced in the treatment of IHD. It was observed that most prevalent DRP was drug interactions and it was mostly seen in male patients.

The therapeutic outcome of the patient can be improved by early detection and documentation of DRPs. Following the guidelines for the prescription and treatment would help in minimizing the DRPs. Our study emphasizes on the importance of evaluation of DRPs for better patient care and overall quality of life.

ACKNOWLEDGEMENTS:

Authors are thankful to the head of Sagar Hospital, Kumaraswamy Layout, Bengaluru, India and staff members of Cardiology clinic for providing support and facilitating the data collection.

ABBREVIATIONS

ADR: Adverse Drug Reaction, **AHA:** American Heart Association, **ASA:** American Stroke Association, **CABG:** Coronary Artery Bypass Grafting, **CVD:** Cardiovascular Disease, **DRPs:** Drug Related Problems, **EML:** Essential Medical List, **IHD:** Ischemic Heart Disease, **PCI:** Percutaneous Coronary Intervention, **WHO:** World Health Organization.

REFERENCES:

1. Who-int [homepage on the internet]. Geneva: Cardiovascular disease and it's risk factors, Inc.;c2017-01 [updated 2017 May 17; cited 2018 Jan 15]. Available from:

- http://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds).
2. D. McRobbie. Coronary heart disease. In: Walker R, Cate Whittlesea, editors. *Clinical Pharmacy and Therapeutics*. 5th ed. Edinburgh: Churchill Livingstone; 2012. p. 312-32.
3. Donahue J. Coronary artery disease in offender populations: incarceration as a risk factor and a point of intervention. *Journal of Correctional Health Care*. 2014; 20(4):302-12.
4. Gregory Roth. CVD Causes One-Third of Deaths Worldwide Study Examines Global Burden of CVD From 1990 to 2015. *Journal of the American College of Cardiology*. 2017; 68(2):595-603.
5. Prabhakaran D, Jeemon P, Roy A. Cardiovascular diseases in India: current epidemiology and future directions. *Circulation*. 2016;133(16):1605-20.
6. Bhopal R, Unwin N, White M, Yallop J, Walker L, Alberti KG et al. Heterogeneity of coronary heart disease risk factors in Indian, Pakistani, Bangladeshi, European origin populations: cross sectional study. *British Medical Journal*. 1999;319(7204):215-20.
7. Ofori-Asenso R, Agyeman AA. Irrational use of medicines—a summary of key concepts. *Pharmacy*. 2016;4(4):35-47.
8. Soman B, Rahaman MA, Vijayaraghavan G. Influence of hypertension and diabetes mellitus in pattern of coronary artery disease in women. *Journal of Clinical and Preventive Cardiology* 2017;6(1):7-11.
9. Collins AJ. Cardiovascular mortality in end-stage renal disease. *American Journal of Medical Sciences*. 2003;325(4):163-7.
10. Abraham RR, Manjula Devi AS. Drug Related Problems and Reactive Pharmacist Interventions for Inpatients Receiving Cardiovascular Drugs. *American Journal of PharmTech Research* 2012;2(3):2249-3387.
11. Adusumilli PK, Adepu R. Drug related problems: an over view of various classification systems. *Asian Journal of Pharmaceutical and Clinical Research*. 2014;7(4):7-10.
12. Naranjo CA, Busto U, Sellers EM, et al. A method for estimating the probability of adverse drug reactions. *Clinical Pharmacology and Therapeutics*. 1981;30:239-45.
13. Hartwig SC, Siegel J, Schneider PJ. Preventability and severity assessment in reporting adverse drug reactions. *American Journal of Health-System and Pharmacy*. 1992;49(9):2229-32.
14. Schumock GT, Thornton JP. Focusing on the preventability of adverse drug reactions. *Hospital Pharmacy*. 1992; 27(6):538.
15. Ganachari MS, Shashikala C, Fibin M. Assessment of Drug Therapy Interventions by Clinical Pharmacist in a Tertiary Care Hospital. *Indian Journal of Pharmacy Practice*. 2010;3(3):22-8.
16. Satishkumar BP, Dahal P, Venkataraman R, Fuloria PC. Assessment of clinical pharmacist intervention in tertiary care teaching hospital of southern India. *Asian Journal of Pharmaceutical and Clinical Research*. 2013;6(2):258-61.
17. Alagiriswami B, Ramesh M, Parthasarathi G, Basavanagowdappa H. Clinical Pharmacist Initiated Changes in Drug Therapy in a Teaching Hospital. *Indian Journal Pharmacy Practice*. 2009;1(2):36-45.
18. Ramanath KV, Nedumballi S. Assessment of medication-related problems in geriatric patients of a rural tertiary care hospital. *Journal of Young Pharmacists*. 2012;4(4):273-8.
19. Celin AT, Seuma J, Ramesh A. Assessment of drug related problems in stroke patients admitted to a South Indian tertiary care teaching hospital. *Indian Journal Pharmacy Practice*. 2012;5(4):28-33.
20. Khan MA, Mairaj M, Khan A, Ahsan M, Ali SI, Nisa ZU et al. Assessment of direct cost of treatment of ischemic heart

- disease patient in tertiary care hospital in Karachi. *Journal of Bioequivalence and Bioavailability*. 2017;9(2):353-8.
21. Dawalji S, Venkateshwarlu K, Thota S, Venisetty PK, Venisetty RK. Prescribing pattern in coronary artery disease: a prospective study. *International Journal of Pharmaceutical Sciences Review and Research*. 2014;3(3):24-33.
 22. Hajjar ER, Caferio AC, Hanlon JT. Polypharmacy in elderly patients. *The American Journal of Geriatric Pharmacotherapy*. 2007;5(4):345-51.
 23. Rahmawati F, Pramantara ID, Rohmah W, Syed Sulaiman SA. Polypharmacy and unnecessary drug therapy on geriatric hospitalized patients in yogyakarta hospitals, Indonesia. *International Journal of Pharmacy and Pharmaceutical Sciences*. 2009; 1(1):6-11.
 24. Cunningham G, DODD TR, GRANT DJ, MCMURDO ME, Michael R, Richards E. Drug-related problems in elderly patients admitted to Tayside hospitals, methods for prevention and subsequent reassessment. *Age and ageing*. 1997;26(5):375-82.
 25. Kernan WN, Ovbiagele B, Black HR, Bravata DM, Chimowitz MI, Ezekowitz MD et al. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2014;STR-0000000000000024.
 26. Heart.org [homepage on the internet]. United States; Smoking & Cardiovascular Disease, Inc.; c2010-02 [updated 2014 Feb 17; cited 2018 Jan 20]. Available from: http://www.heart.org/HEARTORG/HealthyLiving/QuitSmoking/QuittingResources/Smo king-Cardiovascular-Disease_UCM_305187_Article.jsp#mainContent.
 27. Therightmix.gov [homepage on the internet]. Australia: Alcohol and heart disease, Inc.;c2000-01 [updated 2018 Feb 07; cited 2018 Mar 20]. Available from: <https://www.therightmix.gov.au/factsheets/alcohol-and-heart-disease>.
 28. Shaper AG, Phillips AN, Pocock SJ, Walker M. Alcohol and ischemic heart disease in middle aged British men. *British Medical Journal*. 1987;294(6574):733-7.
 29. Lim SY. Role of statins in coronary artery disease. *Chonnam Medical Journal*. 2013; 49(1):1-6.
 30. Hasan AN, Hasan SJ, Islam MA, Trina AA, Deepa KN, Asaduzzaman M. Pattern of Pharmacotherapy of Patients Having Ischemic Heart Disease at a Specialized Hospital in Dhaka, Bangladesh: A Survey Based Study on Patients Discharged from Hospital. *British Journal Medicine and Medical Research*. 2017;22(2):1-9.
 31. Andersson C, Shilane D, Go AS, Chang TI, Kazi D, Solomon MD, et al. beta blocker therapy and cardiac events among patients with newly diagnosed coronary heart disease. *Journal of American College of Cardiology*. 2014;64(3):247-52.
 32. Giles TD. Do diuretics diminish the predicted benefits on ischemic heart disease events of lowering blood pressure in hypertension. *Journal of Clinical Hypertension*. 2010;12(7):469-71.
 33. Clappers N, Brouwer MA, Verheugt FWA. Antiplatelet treatment for coronary heart disease. *British Medical Journal*. 2007;93(2):258-265.
 34. Karalis DG. The role of lipid-lowering therapy in preventing coronary heart disease in patients with type 2 diabetes. *Clinical Cardiology*. 2008;31(6):241-48. Ebrahim S, Smith GD, McCabe C, Payne N, Pickin M, Sheldon TA et al. Cholesterol and coronary heart disease: screening and treatment. *Quality in health care*. 1998;7(4):232-9.
 35. Ebrahim S, Smith GD, McCabe C, Payne N, Pickin M, Sheldon TA et al. Cholesterol and coronary heart disease: screening and treatment. *Quality in health care*. 1998;7(4):232-9.
 36. Zhao SJ, Zhao HW, Du S, Qin YH. The impact of clinical pharmacist support on patients receiving multi-drug therapy for coronary heart disease in China. *Indian Journal of Pharmaceutical Sciences*. 2015;77(3):306-11.
 37. Urbina O, Ferrández O, Luque S, Grau S, Mojal S, Pellicer R, Riu M, Salas E, Comin-Colet J. Patient risk factors for developing a drug-related problem in a cardiology ward. *Therapeutic and Clinical Risk Management*. 2015;11(11):9-15.
 38. Shareef J, Sandeep B, Shastry CS. Assessment of Drug Related Problems in Patients with Cardiovascular Diseases in a Tertiary Care Teaching Hospital. *Journal of Pharmaceutical Care*. 2014;2(2):70-6.
 39. Jimmy O.D, Shobha Rani R.H, Indira R, Ramjan S. Study of Drug-drug Interactions in the Medication Charts in Medicine Wards at a Tertiary Care Hospital, Bangalore. *Indian Journal of Pharmacy Practice*. 2012;5(4):61-64.
 40. Ghulam Murtaza, Muhammad Yasir Ghani Khan, Saira Azhar, Shujaat Ali Khan, TahirM. Khan. Assessment of potential drug-drug interactions and its associated factors in the hospitalized cardiac patients. *Saudi Pharmaceutical Journal*. 2016;24(2): 220-5.
 41. Muthiah P, Sandhiya S, Melvin G, Ganesan S, Steven A, Ajith P, et al. Pattern of Adverse Drug Reactions Reported with Cardiovascular Drugs in a Tertiary Care Teaching Hospital. *Journal Clinical Diagnostic Research*. 2015;9(11):1-4.
 42. Wankhede SY, Pardeshi ML, Ghorpade VV, Ghongane BB. An assessment of pattern of adverse drug reactions of cardiovascular drugs in a tertiary care institute. *International Journal Basic Clinical Pharmacology*. 2018;7(2):273-7.
 43. Sriram S, Ghasemi A, Ramaswamy R, Devi M, Balasuramanian R, Ravi TK, et al. Prevalence of adverse drug reaction at a private tertiary care hospital in south India. *Journal of Research Medical Science*. 2011;16(1):16-25.
 44. Kaur S, Kapoor V, Mahajan R, Lal M, Gupta S. Patterns of ADRs and risk factors involved: study in cardiology unit of an Indian tertiary care center. *International Journal of Pharmacology*. 2010;8(1):1-4.

Cite this article as:

Soumya Shastry *et al.* Pattern of pharmacotherapy and assessment of drug related problems in ischemic heart disease patients. *Int. Res. J. Pharm.* 2019;10(3):136-143 <http://dx.doi.org/10.7897/2230-8407.100392>

Source of support: Nil, Conflict of interest: None Declared

Disclaimer: IRJP is solely owned by Moksha Publishing House - A non-profit publishing house, dedicated to publish quality research, while every effort has been taken to verify the accuracy of the content published in our Journal. IRJP cannot accept any responsibility or liability for the site content and articles published. The views expressed in articles by our contributing authors are not necessarily those of IRJP editor or editorial board members.