WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 10, Issue 11, 1983-1951. Research Article ISSN 2277– 7105

EVALUATION ON PRESCRIBING PATTERN OF DRUGS IN CORONARY ARTERYDISEASE

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Article Received on
14 July 2021,

Revised on 03 August 2021,
Accepted on 24 August 2021

DOI: 10.20959/wjpr202111-21552

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ABSTRACT

Background: In spite of the convincing evidence stating the effect of medications in the secondary prevention of Coronary artery disease, an enormous number of drugs were prescribed. Studying prescribing patterns can help better understand the current trends in prescribing. **Aim:** To assess the prescribing pattern of drugs in patients with Coronary Artery Disease. **Materials and Methods:** A Prospective, Observational Study was conducted for 6 months among the inpatients presenting with coronary artery disease,150 inpatients from the department of cardiology were enrolled in the study. The data was collected analyzed and interpreted using descriptive statistics. **Results:** Out of 150 patients, 108 males and 42 females were enrolled in the study, accounting for about 72% of males and 28% of females. We observed that the maximum number of patients were from the age group 41-60 years with a proportion of 48%. Among the study population, the patients were diagnosed to have at least 1-2 co-morbidities. while assessing the prescribing pattern Antiplatelets (99.30%), Antihyperlipedimics (82.60%) and Antihypertensives (81.2%), Organic Nitrates (53%), Antianginal drugs (52%), Anticoagulant (24%), Antiarrhythmics (10.6%) were the prescribed cardiovascular drugs. Drug-drug interactions and adverse drug reactions were found. **Conclusion:** The study gave a clear image of prescriber preferences of drugs used in CoronaryArtery Disease. The results of the study can offer an outlook to physicians and may help them to improve rational prescribing. Systematic monitoring and productive strategies must be applied to enhance patient compliance to attain a better outcome.

KEYWORDS: Coronary Artery Disease, Cardiovascular drugs, secondary prevention

Comorbidity, medication.

INTRODUCTION

Cardiovascular diseases(CVDs) account for the number one cause of death globally, coronary artery disease is an important cause of morbidity and mortality in the world.[1,2] 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. IHD may present as an acute coronary syndrome (ACS, which includes unstable angina and non–ST-segment elevation or ST-segment elevation myocardial infarction [MI]), chronic stable exertional angina, ischemia without symptoms, or ischemia due to coronary artery vasospasm (variant or Prinzmetal angina)[1]. The main potentially modifiable risk factors for CHD have been considered to be hypertension, excessive alcohol consumption, cigarette smoking, raised serum cholesterol, diabetes, psychological stress, and abdominal obesity.[3]

Coronary artery disease is caused by the buildup of hard cholesterol substances(plaques) called atherosclerosis in the inner lining of the arteries that supply blood to the heart. The deposition of the plaques narrows the internal diameter of the arteries, this may cause to form a clot, obstructing the supply of oxygen and nutrients to the heart muscles, which is necessary for the healthy functioning of the heart. This may eventually result in the death of heart tissue, deprived of blood, which then leads to chest pain or heart attack.[4]

Secondary prevention of coronary heart disease involves the management of Both pharmacological and non-pharmacological therapies because they play a crucial role in symptom alleviation and can reduce the risk of future occurrences. The surgical revascularization procedures namely Percutaneous Transluminal Coronary Angioplasty(PTCA) and Coronary Artery Bypass Grafting(CABG) can reduce the symptoms. The medical therapy includes treatment with different categories of medication such as antiplatelets, anticoagulants, antianginals, beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARB), nitrates, statins, and calcium channel blockers.[5,6]

Shreds of evidence from randomized controlled trials had set up guidelines that recommend that aspirin, beta-adrenergic blockers, ACEI, and hydroxyl menthyl glutarate coenzyme A reductase inhibitors (statins)have been used in all patients with symptomatic chronic stable

angina or asymptomatic survivors of acute myocardial infarction and following the percutaneous coronary intervention or coronary bypass surgery for secondary prevention of myocardial infarction, stroke, and death.[7] it is proven that these medications, when used together are thought to minimize the long term risk of cardiovascular events and mortality.[4]

Rational use of medicines is considered a prime part of health care policy. based on which the most relevant medication is given to the patient for his clinical need in the right doses at the righttime in the acceptable cost.[8] According to WHO rational prescription must meet certain criteria such as appropriate indication, appropriate patient, appropriate medicine, appropriate information, and appropriate monitoring.[9] Prescribed medications are differentiated as essential medicines if it complies with the actual demand of subject population care services using standards like risk-benefit ratio, cost-effectiveness, and quality.[8] Irrational use of medicine is a major problem. Wastage of scant resources and widespread health hazards results from the misuse, overuse, and underuse of medicines.[9]

Knowledge of prescribing patterns can lead to improving rational drug use and aid in the implementation of initiatives to improve prescription habits. Identification of prescribing patternsbased on an assessment is one of the first stages toward enhancing medication quality and patientwellbeing.[10] Treatment necessitates the use of many essential drugs, these drugs when taken together can cause drug-drug interactions. Routine checks for drug interactions and adverse drug reactions can improve patient safety. This study aims to examine existing prescription trends in the treatment of coronary artery disease. The findings of this study are expected to offer the physicians with relevant and useful feedback.

MATERIALS AND METHODS

Study site: The study was conducted in a tertiary care hospital, at Tumkur.

Study period: The study was conducted for six months.

Study design: Prospective, Observational Study.

Study population: A total of 150 patients were enrolled in the study.

Study criteria: The study was carried out by considering the following inclusion and exclusioncriteria.

Inclusion criteria: The patient diagnosed with Coronary Artery Disease over the age group of40 years, with a length of the stay of more than a day were enrolled in the study.

Exclusion criteria: Pediatric patients, pregnant women, and the Subjects who are not willing toparticipate were excluded from the study.

Data Collection

During the study period about 150 case records of the CAD, patients were studied. The diagnosis with patient demographics and the drugs prescribed for individual patients, associated co- morbidities, were observed and recorded from the case records, other relevant data that cannot be obtained from the medical records were obtained by interviewing the patient through questionnaires. Information about the drugs such as drug dose, frequency, route of administration was noted. Laboratory parameters were monitored during the treatment and were recorded.

Study Procedure

It included 3 phases

Phase 1: we have prepared an informed consent form and data collection forms which are required to conduct the study. Obtaining signed informed consent from the subjects.

Phase 2: Investigators attended the ward rounds on daily basis with the physician for the identification of prescribing patterns.

Phase 3: All relevant information needed for the study was collected from the case records details about prescribed drugs, comorbidity, length of the stay, cardiology investigation results, drug interactions, adverse effects, drug dose, frequency were documented. The result was expressed as mean value and in percentages.

Statistical Analysis

Simple descriptive statistics were used to produce results in percentages and mean values.

Ethical Approval

The study was undertaken after obtaining Permission from the Institutional Ethics Committee of sree siddaganga college of pharmacy, Tumkur.

(Reference No: SSCPT/SHRC/PPD/2019-2020)

RESULTS

From the total of 150 patients' case sheets, 108 males and 42 females were enrolled in the study, accounting for about 72% of males and 28% of females. Thus the study showed that men are more liable to coronary artery disease than females. Most of the men included in the study were alcoholics and chronic smokers; this may be a major cause that the prevalence of men is higher than females. we observed that the maximum number of patients were from the age group 41-60 years with a proportion of 48% It is found that older adults become more

susceptible to disease, as people get older they will be more frequently associated with comorbid conditions that predispose to diseases. it was found that 72 from the total of 150 stayed in the hospital for 1-3 days and 67 stayed for 4-6 days and a very few about 11 from 150 stayed for 7-9 days, and they were severely affected.

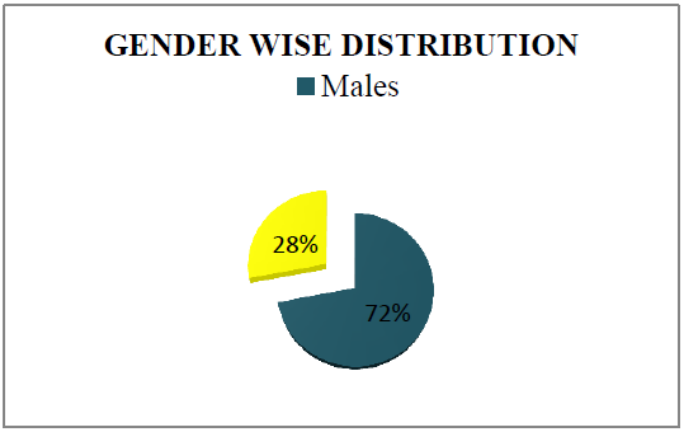

Figure 1: Sex wise Distribution.

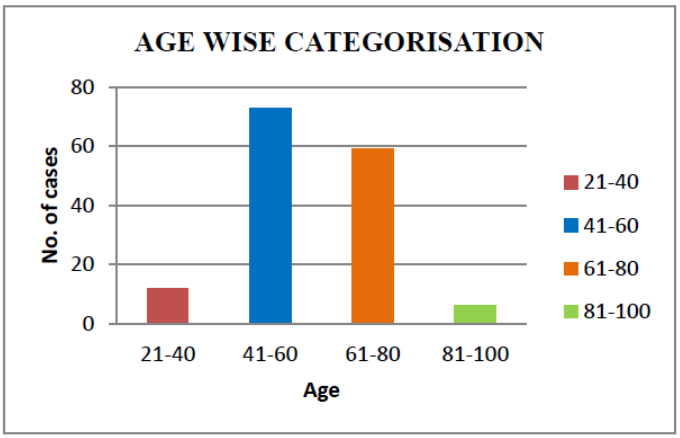

Figure 2: Age-wise Distribution.

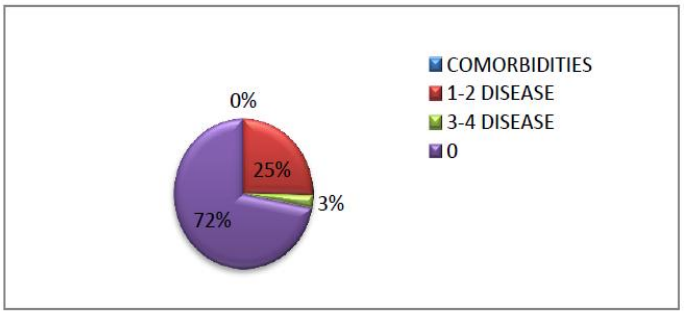

Figure 3: Details on comorbidity.

Patients with coronary artery disease are presented with 1 or more than 1 co-morbid condition. Patients with hypertension are found to be more in Coronary Artery Disease.

Table 1: Details of Patients Based on Co-Morbid Conditions.

Associated Disease	Total Number	Male	Female
Diabetes Mellitus	35	26	9
Hypertension	37	25	12
Diabetes Mellitus+Hypertension	31	9	22
Chronic Kidney Disease	5	5	0
Hypothyroidism	4	1	3

Drug Use Characterisation

In our study, it was observed that out of 150 prescriptions Antiplatelets (99.30%), Antihyperlipedimics (82.60%), and Antihypertensives (81.2%) were the most commonly prescribed Cardiovascular drugs. Heparin among the Anticoagulants, Ticagrelor among the Antiplatelets, Nitroglycerin among Nitrates, Amlodipine among the Calcium Channel Blocker, Ramipril among the ACE inhibitors, Metoprolol among the Beta-blockers, furosemide among the diuretics, telmisartan among the angiotensin II receptor blocker, Rosuvastatin among the Hypolipidemics, trimetazidine among the antianginal and digoxin among the antiarrhythmics were the most frequently prescribed.

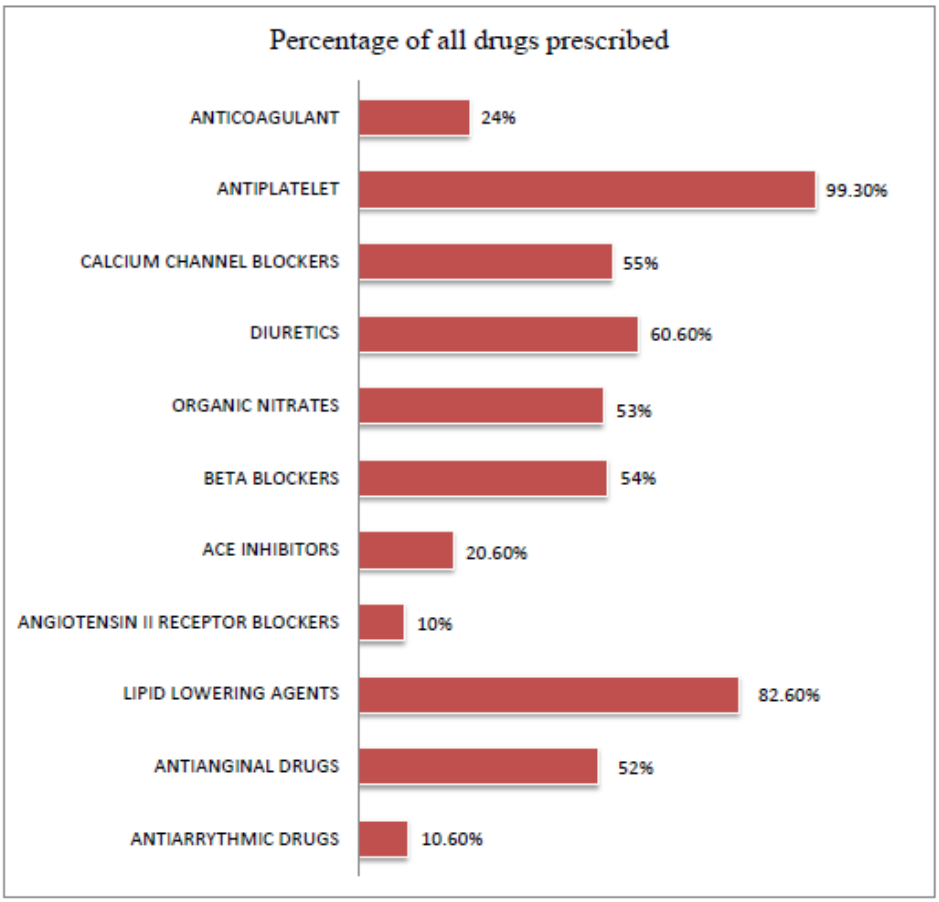

Figure 4: Percentage of Drugs Prescribed.

Table 2: Drugs Prescribed.

Therapeutic Class	Generic Name	No. of Rx	%	Total No. of Rx (n-150)	%
Anticoagulant	Heparin	19	51	37	24
	Enoxaparin Sodium	18	48		
Antiplatelet	Aspirin	60	40	149	99.3
	Clopidogrel	10	6.6		
	Ticagrelor	68	45		
	Tirofiban	11	7.3		
Organic Nitrates	Nitroglycerin	6	75	8	5.3
	Isosorbide Dinitrate	2	25		
Calcium ChannelBlocker	Amlodipine	46	55	83	55
	Diltiazem	23	27		
	Verapamil	14	1.6		
Diuretics	Hydrochlorothiazide	2	2.19	91	60.6
	Furosemide	51	56		
	Spironolactone	38	41.7		
Beta-Blockers	Metoprolol	45	55.5	81	54
	Carvedilol	22	27		
	Bisoprolol	1	1.23		
	Nebivolol	13	16		
ACE Inhibitors	Ramipril	29	93.5	31	20.6
	Enalapril	2	6.4		
Angiotensin II Receptor Blocker	Telmisartan	14	93	15	10
	Olmesartan	1	6.6		
Lipid-Lowering Agent	Atorvastatin	46	37	124	82.6
	Fenofibrate	1	0.8		
	Rosuvastatin	77	63		
Antianginal Drugs	Trimetazidine	9	11.3	79	52
	Ranolazine	6	7.5		
	Nicorandil	49	62		
Antiarrhythmic Drugs	Amiodarone	7	43.7	16	10.6
	Digoxin	9	56.2		

USE OF DRUG COMBINATIONS

Table 3: Details of the combination of drugs prescribed.

DRUG COMBINATION	NUMBER	PERCENTAGE
ASPIRIN +ATORVASTATIN	15	71%
CLOPIDOGREL+ROSUVASTATIN	2	9.5%
ASPIRIN+CLOPIDOGREL	4	19%

The three most commonly prescribed drugs in combination include aspirin + atorvastatin, clopidogrel+ rosuvastatin, aspirin+clopidogrel. Aspirin+clopidogrel account for 71% of the total drugs prescribed in combination, followed by, aspirin + clopidogrel 19%, and clopidogrel + rosuvastatin 9.5%.

Other Drugs

Other than Cardiovascular Drugs, Coronary Artery Disease Patients were also prescribed other medications like Antibiotics, proton pump inhibitors, vitamins as supportive therapy. Such drugs are mentioned in the below table.

Table 4: Details of various drugs prescribed along with Cardiovascular drugs.

Therapeutic class	Generic name
Antibiotics	Ceftriaxone, Clarithromycin Piperacillin+Tazobactum
Oral Hypoglycemic Agent	Metformin Glimipiride
Proton Pump Inhibitor	Pantoprazole Omeprazole Rabeprazole
NSAIDs	Acetaminophen
Antiasthmatic Drugs	Salmetrol Salbutamol IpratropiumFormoterol
Vitamin	Vitamin K

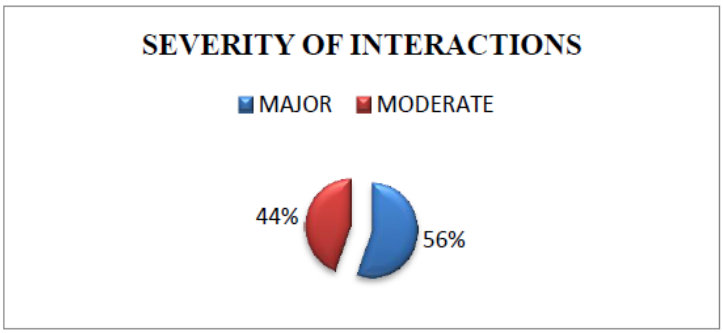

Figure 5: Details on the severity of Interactions.

A total of 108 interactions were found from 150 prescriptions. The interactions were checked using Medscape and Micromedex drug interaction checker The interaction were then grouped into 2 categories major and moderate based on the severity. Among which 55% account for major drug interactions and 44% account for moderate drug interactions. 21 adverse drug reactions were found.

DISCUSSION

A prescription by a prescriber is a representation of his /her attitude towards the medication and disease.[11] Evaluating a prescription is helpful to determine the behavioral pattern and use of medicines in a region.[12]

In the past few years, various research studies have been conducted to determine the safe and appropriate utilization of drugs denoting that inappropriate use of the drug is a universal phenomenon.[13] A total of 150 patient case sheets were analyzed during the study period and

the results depict that the frequency of Coronary Artery Disease was more in male patients(72%) than female patients(28%). The main reason for this high incidence in males is due to various risk factors and co-morbidities compare to females. This observation is supported with the demographics conducted by Nair S N et al in which 65.83% of males predominated over females(34.166%).[14] The studies conducted by Weidner G, Jousilahti P, and Chrysohoou C.[15-17] The reason for reduced predominance in females is due to the cardioprotective effect of estrogen.[14]

Among 150 patients the distribution of CAD based on the age group showed that more numberof patients suffering from CAD was present in the age group of 41-60(48%) followed by 61-80 years(39%). The study conducted by Vakade K P.[22] et al and Mukesh et al[18] suggest that 41-60yrs of age group are more susceptible to CAD.

Among the study population the patients were diagnosed to have 1-2 co-morbidities (25%) and 3-4 diseases (3%) 72% of the patients were presented with no co-morbidities. The most common co-morbidity seen is diabetes mellitus and hypertension in Coronary Artery Disease Patients.

This observation is supported by Celin et al[19] in which 39.8% are diagnosed with one co-morbidity and 17.6% with two co-morbidities and 40% of the patient with no co-morbidities.[19] The study conducted by Sowmya Shastri et al also supports the statement in which 25% were diagnosed with one comorbidity 37.25% with two co-morbidities.[20] Battu Rakesh et al conducted a similar study which concluded that diabetes mellitus and hypertension was the most common risk factor associated with the cardiovascular system. In the study conducted by Karthikeyan G, the average stay was found to be 7 days.[21] In our study, the average hospital stay was found to be6 days. It is also observed that Vakade K P et al[22], the average hospital stay was 5.75 days.

In our study, it was observed that out of 150 prescriptions Antiplatelets (99.30%), Antihyperlipedimics (82.60%), and Antihypertensives (81.2%) were the most commonly prescribed Cardiovascular drugs. It was supported by the study conducted by Shivraj Basavaraj Patil et al.[23] The most commonly used medication was Antiplatelets (90.24%) followed by Antihypertensives (87.80%) and Antihyperlipedimics (81.30%). In a study conducted by Jorg Muntwyler et al[24], the drug prescription rates for Antithrombotic agents (91%), Beta-blockers (58%), ACE inhibitors (50%), and lipid-lowering drugs (63%)

respectively. The prescription rate of Antihyperlipidemics in our study was comparatively higher than the previous study.

It was observed from a study conducted by Tasneem Sandozi and Fouzia Nausheen[25], the prescribing pattern in Antiplatelet drugs was Aspirin (25.71%) whereas in the present study the prescription rate for Aspirin was (40%) predominated by Ticagrelor (45%). The previous studieshave shown Aspirin is prescribed more frequently among the Antiplatelets. Our study found that Ticagrelor is prescribed over Aspirin.

In a study by Banerjee S et al[26], unfractionated Heparin was used in 36.8% of patients and low molecular weight heparin [LMWH] is 25.20%. In another study by Tasneem Sandozi and Fouzia Nausheen[25] the prescription rate for unfractionated Heparin (55.71%) and LMWH (20%).In the present study, Heparin was prescribed for 51% and Enoxaparin sodium 48%. The results of the study are consistent with the previous study whereas a study conducted by Dawalji Shruti et al[27], found that unfractionated Heparin was prescribed 40% and LMWH 62.73%. The result of the above study is not consistent with our study. In our study overall use of Antihypertensives in Coronary Artery Disease is as follows Diuretics (60.60%), Calcium Channel Blockers (55%), Beta-blockers (54%), ACE inhibitors (20.60%), ARBs (10%). In a study conducted by Supratim Datta[28], the overall use of Antihypertensives are Calcium Channel Blocker (73%), Beta-blockers (37.20%), ACE inhibitors (43.20%). A study conducted by Jorg Muntwyler[24] et al observed the drug prescription rates for Beta-blockers, ACE inhibitors as 58% and 50% respectively. The previous study indicated high use of Calcium Channel Blockers whereas in our study Diuretics were found to be the preferable choice of Antihypertensive. The result of our study shows a deviation from the previous studies as diuretics is prescribed over Calcium Channel blockers. Our present study is supported by Dawalji Shruti et al[27], in which diuretics are prescribed by 62.35%.

In a study conducted by Shredevi K.[29], et al the different statins prescribed were Atorvastatin (261 prescriptions), Rosuvastatin (26 prescriptions) in 1000 prescriptions. In another study Dawalji Shruti et.al, 27 Atorvastatin is prescribed in (143) prescriptions and Rosuvastatin (17). In the present study Rosuvastatin (63%) is prescribed more than Atorvastatin (37%), the study recorded the use of lipid-lowering agents as (82.60%). From the previous and present studies, the result of the study is not consistent with the previous studies, A greater variation in the use of Antihyperlipidemics was observed. The use of Rosuvastatin was much higher than Atorvastatin.

In a study conducted by Banerjee S et al[26], the commonly prescribed drug among the nitrates is Isosorbide mononitrate, clopidogrel among the Antiplatelet, Metoprolol among the Beta-blockers, Amlodipine among the Calcium Channel blockers, Ramipril among the ACE inhibitors, Atorvastatin among Hypolipidemics and unfractionated Heparin among the Anticoagulants. In the present study the commonly prescribed drugs were Nitroglycerin among Nitrates, Ticagrelor among the Antiplatelets, Metoprolol among the Beta-blockers, Amiodarone among The CCB, Ramipril among the ACE inhibitors, and Rosuvastatin among the Hypolipidemics and Heparin among the Anticoagulants.

A variation in the prescribing of organic Nitrates, Antiplatelets, and Antihyperlipidemics is observed when compared to earlier studies. Management of CAD is a complex process involved in multiple therapeutic regimens. Drug-drug interactions are a major issue in these patients. In this study out of 150 cases, 108 drug interactions were noted. The severity of drug interaction was categorized as major and moderate. Regular monitoring and timely assessment of patient conditions and laboratory parameters may help in managing ADR. Blessy et al conducted a studysharing a similar conclusion.

CONCLUSION

Today in this modern world there is a profound increase in cardiovascular-related disease which leads to increased morbidity and mortality. Smoking, stress, workloads, obesity, sedentary lifestyles provided a great pathway to these diseases. The pattern of a prescription can be improved by decreasing the total number of medications. Very few drugs were prescribed by generic name most of the drugs were prescribed by brand names. The study gave a clear image of prescriber preferences of drugs used in Coronary Artery Disease. The prescribers have strictly adhered to the treatment guidelines that resulted in an ideal prescription writing. The results of the study on prescribing pattern of drugs can offer an outlook to physicians and may help them to improve rational prescribing. Systematic monitoring and productive strategies must be applied toenhance patient compliance to attain a better outcome.

ACKNOWLEDGEMENTS

We are extremely thankful to our guide and all our beloved teachers of Sree Siddaganga College of pharmacy Tumkur for their encouragement, support, and guidance during the study. We express our sincere gratitude to all the study participants and hospital staff for their support timeand cooperation.

CONFLICT OF INTEREST

There is no conflict of interest in this work.

ABBREVIATIONS

WHO: World Health Organisation, **CAD**: Coronary Artery Disease, **CVD**: Cardiovascular Disease, **MI**: Myocardial Infarction, **ACS**: Acute Coronary Syndrome, **PTCA**: Percutaneous Transluminal Coronary Angioplasty, **CABG**: Coronary Artery Bypass Graft, **ACEI**; Angiotensin-Converting Enzyme Inhibitors, **ARB**: Angiotensin Receptor Blocker, **CCB**: Calcium Channel Blocker, **ADR**: Adverse Drug Reaction.

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