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Assessment of Drug Related Problems in Cardiovascular Diseases and Prescribing Patterns of Cardiovascular Drugs in a Secondary Care Teaching Hospital

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ABSTRACT

Cardiovascular diseases (CVDs) are a serious public health concern that has risen to become the leading cause of death and premature death around the world, as well as a major contributor to rising health-care expenses. This study aimed to assess and determine the prevalence of drug related problems in cardiovascular disease patients along with identify prescription pattern of cardiovascular drugs during course of treatment in our study population. Prior authorization was received from the Institutional Ethics Committee. This prospective observational study involves 160 hospitalized patients in the in-patient department of a secondary care hospital. The prescribing pattern was analyzed and assessed during the period of 6 month and drug related problems in the following patients were reported. Of 160 patients, 102 (64%) were male and 58 (36%) were female. Subject of age group of 61-70 (n=51) were found to be more suspected. A total of 160 cases identified 366 DRPs. The most common identified DRP were the DDI 281 (77.41%), polypharmacy 42 (11.57%), no lab data or lack of monitoring 14 (3.82%), indication without drug 7 (1.91%), drug duplication 5 (1.36%), drug without indication, contraindication and ADR 3 (0.81%). The most common DDIs was aspirin + furosemide (n=23). The most offending drug involved in DDI was observed to be aspirin. Most of the prescription were prescribed with ant-platelet agent (41.22%), statins (15.71%) followed by CCBs (7.47%). Prescribing pattern of drugs in cardiovascular diseases concluded that optimized drug therapy lead to minimal ensuing DRPs. Clinical pharmacist recommendation in prevention of many DRPs can reduce the disease complication.

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INTRODUCTION

Cardiovascular diseases (CVDs) are a serious public health problem that has risen to become the world's

leading cause of mortality and premature death, as well as a major contributor to rising health-care expenses [1]. Coronary artery disease, cerebrovascular disease, peripheral artery disease, and congestive heart failure are only a few of the heart and blood vessel diseases.

CVDs are caused by high blood pressure, smoking, diabetes, lack of exercise, obesity, poor diet, high blood cholesterol, and excessive alcohol consumption [2]. Coronary heart disease (CHD), also known as Coronary artery disease (CAD) or Ischemic heart disease (IHD), is a condition in which atheroma (degeneration of arterial walls) blocks blood flow to the heart [3].

Cardiovascular illnesses have now become the top

cause of death worldwide. CVD is the leading cause of death in the United States, accounting for one-quarter of all deaths. IHD and stroke are the leading causes of death from CVD, accounting for more than 80% of all deaths. According to global burden of disease studies, India's age-standardized CVD death rate of 272 per 100,000 people is higher than the global average of 235 per 100,000 people [4].

According to the World Health Organization, nearly 17.7 million individuals died worldwide in 2015 as a result of Coronary Heart Disease [5, 6].

Coronary artery disease (CAD) is the major cause of CVD, accounting for almost 35 percent of the disease burden, according to a global burden of disease study done in India [6]. Consequently, the current study aims to examine current prescription patterns in patients with cardiovascular diseases in order to assure appropriate medicine use and thereby reduce disease morbidity and mortality [7].

Patients with CVDs require drugs, and the number of medications prescribed has consistently increased (Polypharmacy). This increase in the number of medications prescribed has been linked to bad health outcomes includes frequent Hospitalization, waste of resources and different DRPs [8]. Primary (trying to prevent yourself from acquiring an illness) and secondary (trying to detect a disease early and prevent it from growing worse) cardiovascular disease prevention may be relevant to pharmacists. A pharmacist can provide more direct interventions (such as medication education and illness management) in addition to distributing prescriptions, measure support for the physician's actions, and improve medication adherence, therapeutic outcomes, humanistic control, and economic outcomes [9, 10].

Drug-related difficulties (DRPs) are defined as any occurrence (or) situation involving drug therapy that interferes with the patient's capacity to attain the best possible medical outcome, either directly or indirectly. The focus of assessment and the final decision made in that step of the patient care process is the DRPs [11]. It exemplifies the pharmacist's truly distinctive contribution to patient care. DRP is linked to a longer length of stay, a higher financial burden, and a nearly 2-fold greater chance of death. It's also a prevalent occurrence in chronic noncommunicable disorders like cardiovascular disease [12].

The categories of medication-related problems include:

Untreated Indications: The patient has a medical problem that requires drug therapy (a reason to take

medicine), but he or she is not being treated for it. The patient, on the other hand, needs a medication that was not prescribed.

Improper drug selection: Although the patient has a therapeutic indication, he or she is taking the wrong prescription.

Sub therapeutic dosage: The patient is suffering from a medical problem that is being treated with insufficient medication.

Failure to receive medication: The medicine that was prescribed for a medical concern is not obtained or used by the patient. (For example: pharmacological, psychological, sociological, or economic reasons).

Over Dosage: The patient has a medical problem that is being treated with large quantities of a medicine that is considered safe (toxicity).

Adverse drug reactions: A unfavorable pharmacological reaction or side effect has caused the patient to develop a medical condition.

Drug interactions: A patient's medical condition has been exacerbated by a drug-drug, drug-food, or drug-laboratory test interaction.

Medication use without indication: The patient is taking a medicine for which there is no medical justification [1].

Prescription pattern is an useful exploratory method for evaluating current medication use habits and prescription appropriateness.¹³ Medical auditing entails the examination of prescribing patterns, as well as the monitoring and evaluation of prescribers, as well as the recommendation of necessary modifications to promote rational and cost-effective medical treatment [8].

Prescription pattern monitoring studies are DUE studies that focus completely on proper prescription prescribing, dispensing, and administration, as well as minimizing drug abuse and misuse. The appropriate use of medications is directed and promoted for prescribers, dispensers, and the general public. Because of an increase in the sale of new pharmaceuticals and delayed ADRs, as well as the cost of drugs, prescription capacity, and variation in prescribing and drug consumption, prescription pattern monitoring studies are becoming increasingly important. The goal of this study is to improve the population's rational/safe drug use [3, 13].

By actively participating in ward rounds and taking the patient's past medical, past medication histories, laboratory evidences, and patient clinical data, clinical pharmacists play an important role in improving patient pharmaceutical care and appropriate drug

administration, even lowering the cost of improper drug therapies. Clinical pharmacists are also competent advisors for answering drug-related inquiries from doctors, nurses, and patients. Clinical pharmacists' function has recently risen in prominence as more clinical pharmacists have joined the health-care team.

It's worth noting that each DRP could be subjected to multiple interventions. The pharmacist continued to monitor the patient after the interventions until discharge, intervening as needed for any future DRPs [6].

The study emphasises the importance of examining DRPs for better patient care and overall quality of life [3]. Prescription patterns should be investigated in order to verify that patients receive reasonable pharmacotherapy and high-quality medical care, and the prescribing pattern can be improved by reducing the number of pills per prescription [14]. It will assist prescribers in enhancing patient care by rationalizing prescribing techniques [15].

METHODOLOGY

Study Site

The research is being carried out at the Vivekananda Hospital in Deshpande Nagar, Hubballi, Karnataka, India.

Study Design

The patients are separated into interventional and control groups in this prospective observational trial.

Study Period

The research will take place over the course of six months.

Ethical Approval

The institutional Human Ethical Committee of KLE College of Pharmacy in Hubballi gave its approval for this investigation. The thesis comes with an ethical clearance certificate.

Study Sample

There were 160 cardiac patients that were followed up on during the study period and met the inclusion criteria.

Study Criteria

Inclusion Criteria

1. In patient of Vivekananda hospital
2. Subjects of all age groups
3. Male and Female Subjects

4. Hospital stay- more than 48 hours
5. Subjects of cardiovascular diseases
6. Past medical history of CVDs
7. Obstetrics and gynecology department

Exclusion Criteria

1. Outpatients
2. Hospital stay – less than 48 hours
3. Psychiatry patients
4. Pediatric patients

Source of Data

Medical case sheets, treatment chart, laboratory investigation, past medical history, clinical progress chart, nurse charts, interactions with patients, interactions with patient's caregiver, interaction with health care professionals.

Sources for Data Collection

Intervening students' clinical pharmacists were assigned to visit medicine units on a regular basis for a six-month period. Every day, all in-patients admitted to wards were assessed. All of these patients' medication information was gathered and recorded in specially prepared data collecting forms. The drug information resources consult by each student pharmacist for intervention are classified as following. Primary sources: scientific journals, literatures, abstracts; Secondary sources: data base (Micromedex, Medscape); Tertiary sources: Text-books such as Martindale, Stockley's drug interaction, Goodman Gillman of pharmacology and therapeutics, pathophysiology approach by Dipiro.

Statistical Analysis

Diagrammatic representation was used to perform descriptive statistics and a level of significance test. Data analysis was done by categorical data which were presented as percentage and the obtained data are represented in graphs.

RESULTS

During a six-month period, 160 patients who met exclusion and inclusion criteria as per the study protocol were reviewed in this prospective observational study on the assessment of Drug Related Problems in Cardiovascular Disease and prescribing patterns of cardiovascular drugs in a secondary care hospital.

Out of total 160 patients, Ischemic Heart Disease (in 64 patients) and Coronary Artery Disease (in 61 patients) were the most commonly found cardiovascular diseases with percentage of 40% and 38.125% respectively, followed by Myocardial Infarction in 4 patients (2.5%), Dilated cardiomyopathy in 6 patients (3.75%), Atrial fibrillation in 3 patients (1.875%), Double vessel disease in 4 patients (2.5%), Dyslipidemia in 2 patients (1.25%). Single vessel disease, Rheumatic heart disease and hyper dynamic heart failure were seen in 3 patients each (1.875%). Sclerotic aortic valve disease in 6 patients (3.75%) and other CVDs includes 7 patients (4.375%) respectively in our study.

Age-Gender distribution data was represented in Table 1. Co-morbidities of IHD and complications were depicted graphically in Figure 1, Figure 2 respectively.

Out of 160 prescriptions, 127 prescriptions were found to have potential drug related problems while remaining 33 prescriptions had no DRPs. 363 different drug related problem were found in our study population during the hospital admissions represented in Table 2.

By intervening all 160 prescription, 127 prescription were found with 281 potential drug-drug interaction with major 229 interaction, moderate 52 interaction and minor 3 interactions. By the following result, drug-drug interaction was found in 76.77% of the total DRP cases. Hence by assessing all the drug interaction in our study in CVD, Aspirin was majorly interacting with furosemide in maximum case that is 23 cases followed by aspirin with tirofiban and metformin in 20 cases respectively shown in Figure 3.

Carvedilol was found to be drug having maximum side effects of Bradyarrhythmia 3-10%, peripheral oedema 1-7%, abnormal weight gain 10-12% and hypotension 1.8-20.2%. Followed by Nifedipine causing pedal edema 7-29%, hypotension upto 5 %, palpitation upto 7%, cough and dyspnea. Tramadol used in CVD patients causing Constipation 10-46%, flushing 7-15%, pruritis 3-12%.

Drug without indication were found in 3 prescriptions. Fluconazole, clonazepam, chloroquine are drugs given for CVD patients without any indication. Drug duplication data was represented in Table 3.

The contraindication were found in the 3 different prescriptions by continuous use of contra indicating drugs, there was increased risk of getting other co-morbidities. Examples are Ivabradine + clarithromycin, Ivabradine + fluconazole leads to Increased exposure of ivabradine leads to QT inter-

val prolongation and Amiodarone + ketoconazole leads to Increased amiodarone plasma concentration leads to risk of cardiotoxicity.

Anemia was the most untreated indication as physician focus mainly on treating the CVD symptoms rather than hematological disorders. Whereas for untreated hypotension, which was seen in male patient with diagnosis of CAD along with hemiparesis and type 2 DM, physician managed the patient with Normal Saline. Furthermore, ALD with alcohol withdrawal syndrome / Anxiety were the commonest untreated indication for these kind of prescription, physician focusing on treating underlying cause that was hypertension, type 2 DM, CKD and other cardiac related condition.

Polypharmacy refers to a patient's use of multiple medications and here it ranks second among the DRPs.

Prescription Patterns

Monotherapy refers to use of a single drug to treat a disease or condition and monotherapy in CVD patients were depicted in Figure 4. Whereas, dual therapy and multiple therapy in CVD patients were depicted in Figure 5 and Figure 6 respectively.

DISCUSSION

The study included 160 patients with age group ranging from 21 to 100 years. Males made up 63.75 percent of the population, while females made up 36.25 percent. In a study conducted by Rakesh et al., 60.6 percent of the 99 patients were men, 39.4% were females, and 31.3 percent were over 60 years old [16]. The results of this study were found to be in consistence with previous studies and indicated that male with age of 61-70 more prone to CVD than the female and followed by 71-80. It shows that risk increase with increasing age. Our research looked into the prescribing patterns of drugs used to treat cardiovascular disease in tertiary care hospitals. The research was carried out over a six-month period.

An analysis of nature and frequencies of DRPs revealed that Drug interactions, Poly-pharmacy, Drug duplication and drug without indication were the most frequently occurring DRPs. These findings are in agreement with that of Amit Sharma et al. [17] who reported drug interaction (55.88%) and polypharmacy(48%)as the most frequent DRPs.

The most frequently documented the major interaction were Aspirin which causes increased risk of bleeding when administered along with Clopidogrel/enoxaparin/tirofiban.

Table 1: Age-Gender Wise Distribution of CVD

Age	Female	Male
21-30	0	4
31-40	3	5
41-50	6	4
51-60	14	25
61-70	16	35
71-80	11	26
81-90	8	2
91-100	0	1

Table 2: Identification of DRPs in the Study Population

S. No	Drug related problems	Number	Percentage
1	Drug Drug Interaction	281	76.77%
2	Adverse Drug Reaction	3	0.81%
3	Drug without Indication	3	0.81%
4	Drug Duplication	5	1.36%
5	Contraindication	3	0.81%
6	Indication Without Drug	7	1.91%
7	Inappropriate drug selection	2	0.54%
8	Polypharmacy	42	11.4%
9	Over dose	1	0.27%
10	Sub-therapeutic dose	1	0.27%
11	Drug Food interaction	2	0.54%
12	Drug-laboratory interaction	2	0.54%
13	N0 lab data or lack of monitoring parameter	14	3.82%

Table 3: The Drug Duplication in Study Subjects with their Respective Brand Name

S. No.	Duplicating Drugs	Brand Names
1	Pantoprazole	Inj. Pantodac and inj. Pantoheal
2	Metoprolol	Tab. Met XL and Tab. Prolomet
3	Atorvastatin	Tab. Atorva and Tab. Ecospirin AV
4	Clopidogrel	Tab. Clopid and Tab. Ecospirin Gold
5	Ticagrelor	Tab. Brilinta and Tab. Axcer

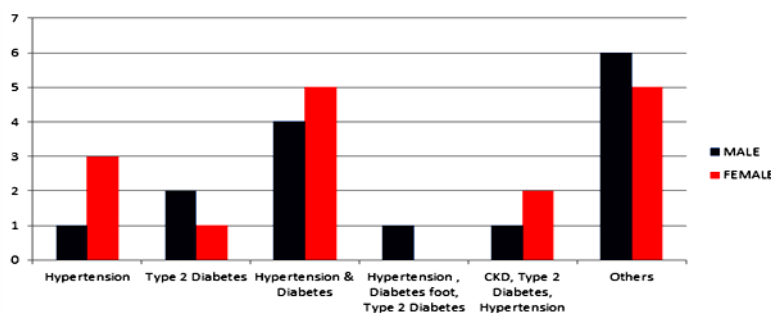


Figure 1: Graphical Representation of Co-morbidities of IHD

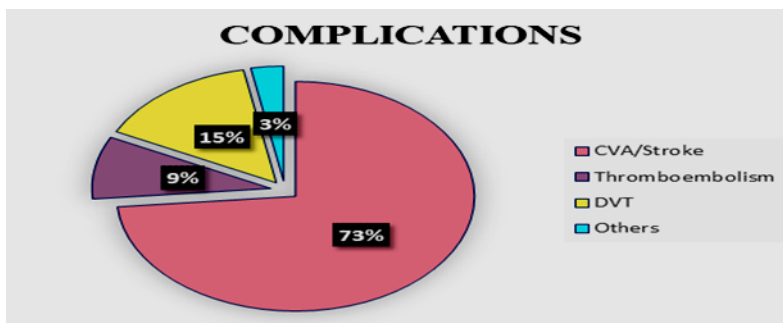


Figure 2: Complications

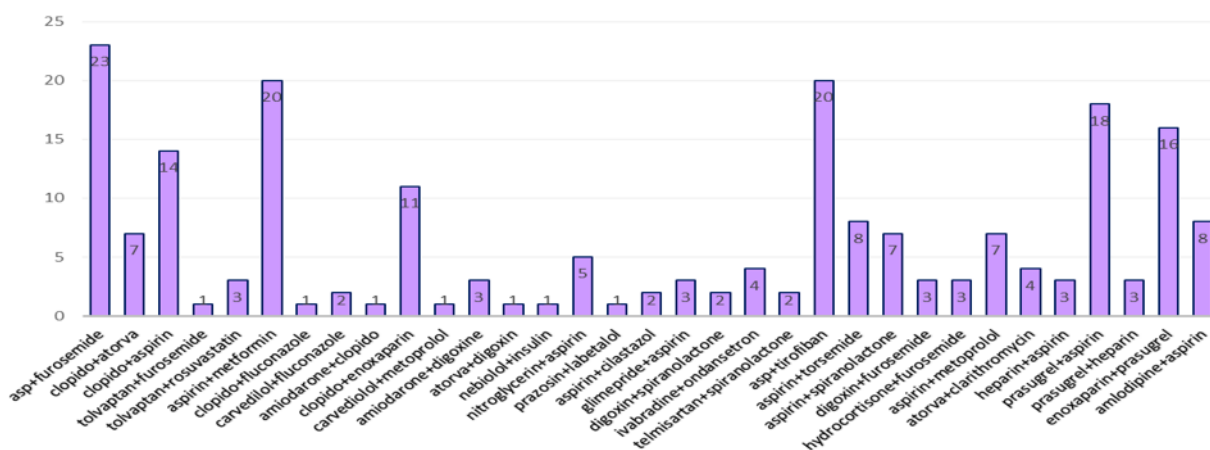


Figure 3: Graphical Representation of Drug-Drug Interaction Cardiovascular Diseases

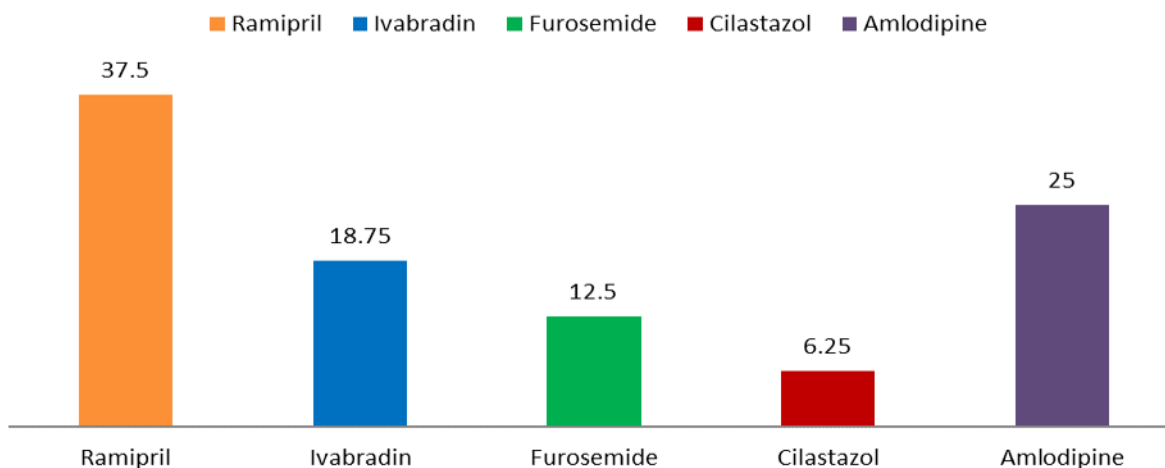


Figure 4: Monotherapy in CVD Patients

The most prevalent co-morbidities seen in both IHD (40%) and CAD patients are hypertension and Type 2 diabetes mellitus (38%). Stroke (73%) and Deep vein thrombosis (15%) were found the major complications of CVD. Complication findings are in agreement with that of Kaleab Gizaw et al. Pharmacist recommended either drugs de-challenge or dose reduction for all moderate to severe ADR observed [1]. Bradycardia as ADR was suspected in

a patient who taken Carvedilol. Nifedipine induced pedal edema was observed in a patient. Another ADR observed in tramadol induced constipation. Drug without indication was another type of DRPs identified. Another type of medication-related issue uncovered was drug duplication. This issue was particularly noticeable in the anti-hypertensive, anti-platelet, and anti-ulcer medication classes.

Administration of different branded pantoprazole

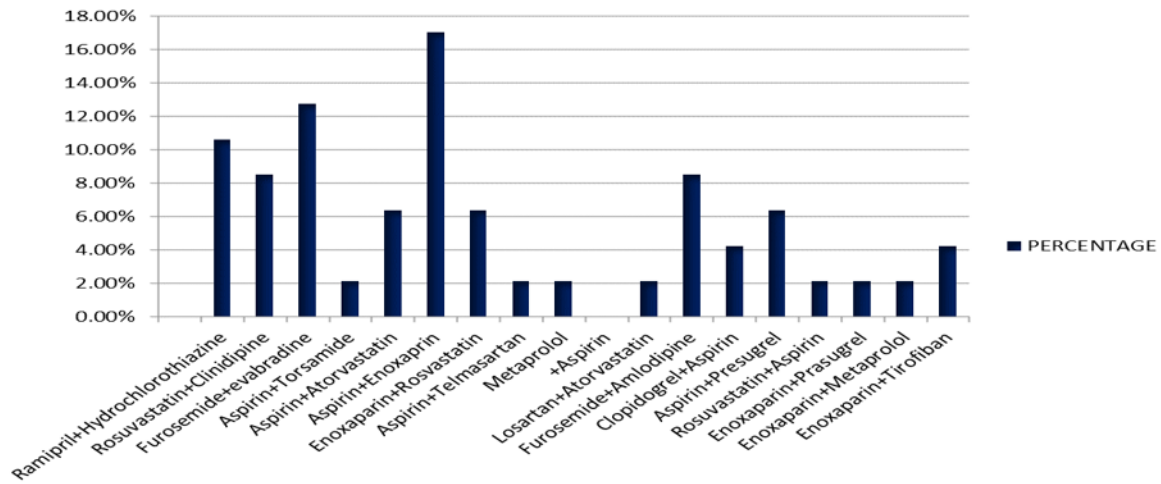


Figure 5: Dual Therapy in CVD Patients

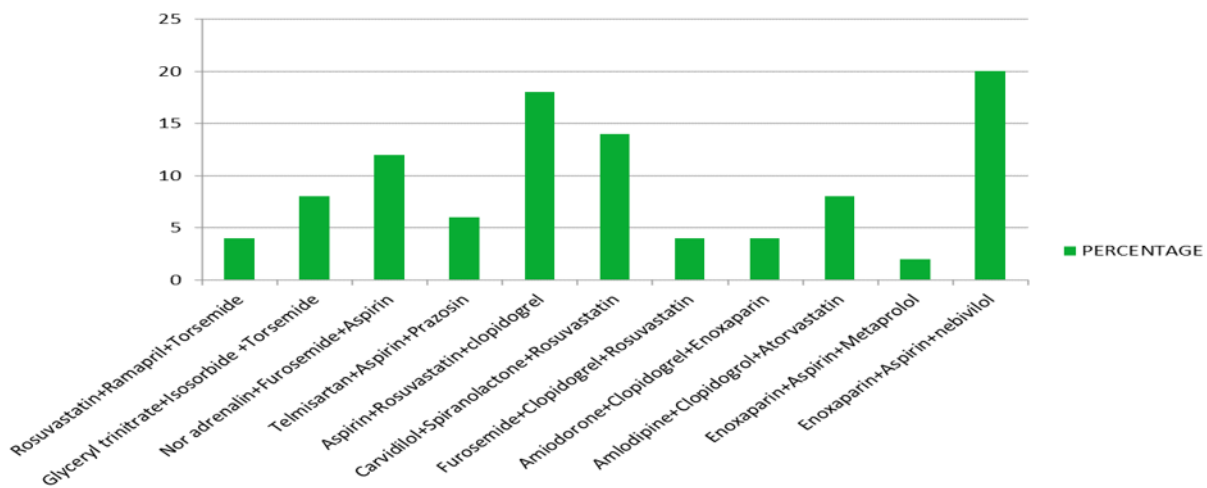


Figure 6: Triple Therapy in CVD Patients

concurrently was seen in few cases lead into duplication over dosage may lead to an increased risk of GI disturbances such as nausea, vomiting, diarrhea and stomach pain and few prescription were found to contain tab. Met XL and tab. Prolomet both of which contain metoprolol [11]. Overdosage due to metoprolol may cause acute symptoms like hypotension, dizziness and bradyarrhythmia. Another example is Clopid and Ecospirin gold both of which contain Clopidogrel, Overdosage leads to bleeding.

Contraindications were found in three different prescriptions with continuous use of contraindicating drugs. Concurrent use of Ivabradin and clarithromycin were contraindicated and increased exposure of Ivabradin leads to QT prolongation. Concurrent use is avoided and ECG monitoring was frequently to prevent further complication and worsening of patient condition. In our study, we found that untreated indication was to be 7 prescriptions (1.91%) out of 366 total drug related problems. This includes situations where a medicine

with a valid indication has not been prescribed. Hypotension, anaemia, ALD with alcohol withdrawal syndrome, and anxiety are among the treatable symptoms. This was shown to be similar to the work of Javedh Shareef and colleagues [1].

Inappropriate drug selection was found to be 0.54%. In our study, propranolol and metoprolol are contraindicated in asthmatic and diabetic patient who results in bronchospasm and severe hypoglycemia respectively. Polypharmacy is frequently cited as a risk factor that contributes to the incidence of DRPs in many research subjects. Polypharmacy was found to be strongly related with DRP in IHD and CAD patients, with at least one DRP found in 42 prescriptions, with five or more medicines. Polypharmacy has been linked to issues like poor medication adherence, possible drug-drug interactions, and drug adverse effects [17].

Overdose was found to be 0.27% among the study population. Amlodipine was overdosed 10mg BD

found as a DRP, and the corrected dose is 5mg OD. Subtherapeutic dosing was responsible for 0.27 percent of all drug-related issues. When compared to Elnaem et al. research's this was determined to be lower. The severity of drug-food interaction was assessed using IBM Micromedex drug interaction. Among these interactions it was found that grape fruit has major and moderate interactions with atorvastatin and ticagrelor which leads to myopathy and decreased anti-platelet activity. This study was less compared with wan-Tseng Hsu et al. [18]. Data shows drug laboratory interaction with aspirin which leads to false hypoglycemic effect. In our study also include the data that represents monitoring parameters for diagnosis of diseases.

Most commonly prescribed categories of drug were Antiplatelets (aspirin 17.65%, Clopidogrel 15.46%, prasugrel 8.11%), statins (rosuvastatin 7.98%, atorvastatin 7.73%) and calcium channel blockers (amlodipine 7.47%). Where as in Boggula N et al. study it was observed that heparin (64.957%), furosemide (27.35%), aspirin (17.088%) and atorvastatin (12.34%) [7]. In our study, most of the CVD drugs are prescribed as multiple therapies which include Aspirin, enoxaparin and nebivolol. Duplication of the drug product and cost effectiveness of drug can be minimized by prescribing drugs in generic name rather than brand names. In our study most of the drugs prescribed in generic names it was similar to the results of Ranjanandh et al. [16].

Most frequently prescribed drug class was antiplatelets in the form of Tablet (41.22%) followed by Statins (15.71%), this correlated with the observations made in the study of Patil S B et al. it contains most frequently prescribed drug class were anti Anginal [14, 19].

Studies show that monotherapy is less frequently used for treating CVD and the effectiveness of the treatment is less compared to the multiple therapies. A study conducted by Raj Kumar et al. indicates that CCBs 21.18%, Beta blockers 59.41%, ACEIs (27.06%) compared with our study shows Heparin (55.17%), furosemide (27.58%), Aspirin (17.67%) and Clopidogrel (15.46%) provide in different dosage form to achieve therapeutic outcome. In the previous studies indicated higher use of Beta blockers, were in the present studies heparin and aspirin in the Injection and oral dosage form are used more frequently [15].

Of the study population, it was observed that most commonly used dual therapy drugs are Aspirin + enoxaparin in 8 cases (17.02%) Furosemide + Ivabradine in 6 cases (12.76%) and Ramipril + hydrochlorothiazide in 5 cases (10.63%) were in

Boggula N et al. studies show that out of 120 cases furosemide + spironolactone given in 11 cases (57.894%), Clopidogrel + atorvastatin in 3 cases (15.789%) and ethiophylline + theophylline given in 2 cases (10.253%). Triple therapy used in our study population including enoxaparin + aspirin + nebivolol in 10 cases (20%), aspirin + Rosuvastatin + Clopidogrel in 9 cases (18%) and Carvedilol + spiranolactone + Rosuvastatin in 7 patients (14%). The commonly used infusions were Noradrenaline in 5 cases and Dobutamine for 2 cases in various doses. Similar studies are conducted by Boggula N et al. includes, commonly used infusion were Dobutamine in 9 cases [20, 21] and Noradrenaline for 8 cases in various doses as monotherapy for CVD [18, 22, 23].

Better health care service will have a positive impact on health care system. Many studies were conducted to judge the value addition of the drug therapy management into the patient care in critical field, but CVD patient were rarely focused as the chance of readmission in hospital and number of day hospitalization is found more in cardiac ill patients. So this study secondarily focused on analysis of prevalence and prescription pattern of drug in cardiovascular disease patients in tertiary care hospital [18, 24, 25].

CONCLUSION

Of the study, indicated that DRPs are common among medical ward patients. It is concluded that there is an alarming rate of prevalence and incidence of drug interactions which is much higher in patients receiving combination of drugs, polypharmacy or suffering from co-morbidity of disease such as diabetes, hypertension, CKD and neurological disorders, which requires prolonging and multi treatments and the risk of drug interaction will increase as they are treated with multi therapies. It is well required that cardiovascular disease patients are suffering due to higher risk of drug interaction as they receive a combination of therapies for cardiovascular complication as well and hence the rate of occurrence of DI is rapidly increased. As medication experts, pharmacists are a vital part of treatment, especially when an ADR occurs. Treating an ADR consist mainly of supportive therapy with symptoms management. Furthermore, additional steps require determining the cause of the patient's symptoms and whether they can be attributed to the use of a drug. In comparison to the tablet form of drug with triple or multi treatments, the percentage of drug prescribed in monotherapy, injectable, and infusion was low. Irrational prescribing can be pre-

vented if treatment guidelines are consistently followed and prescriptions are written properly. Drug safety issues, such as DDI and ADRs, were linked to drugs given for patients with CVDs, as were drug selection issues, such as indication without medication, drug without indication, contraindication, drug duplication, and polypharmacy. Clinical pharmacy services in cardiology wards should be improved and maintained, which could lead to more rational drug prescribing and better patient outcomes.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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