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A STUDY ON PRESCRIBING PATTERN OF CARDIOVASCULAR DRUGS & POTENTIAL DRUG - DRUG INTERACTIONS IN AN INPATIENT CARDIOLOGY UNIT OF A CARDIAC - CARE HOSPITAL AT TIRUPATHI.

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ABSTRACT

Cardiovascular disorders (CVD's) are estimated to be the leading cause of mortality worldwide. A prospective observational study was carried out at inpatient department of cardiology in tertiary care hospital, Tirupathi from December 2012 – May 2013 during regular ward rounds. A survey of prescribing patterns was undertaken among inpatients admitted with cardiovascular disease. The demographic details and treatment data of the 180 inpatients were collected in a specially designed proforma. The average age of study population was found to be 59.06 ± 1.8 years. Subjects of age groups > 40 (92.77 %) were found to be more susceptible to CVD and majority of them were males 46.66 %. Average number of cardiovascular drugs per patient was 5.58. 57.05 % of the drugs prescribed were from the Indian 2011 list of essential drugs. Polypharmacy was observed in 68.33 % (123) prescriptions. The prescription rate of antiplatelet, anticoagulant and fibrinolytics were 22.46 %, followed by 20.07 % of antianginal drugs. The prescribing frequency of antianginal drugs 88.57 % during discharge time was higher. 390 potential drug - drug interactions were screened. Medication adherences were more in male patients 56.12 % among the 86.66 % of follow up patients. This preliminary study reveals a lot of scope for CVD prevalence studies in India and used for implementation of an alert guidelines.

KEYWORDS: Cardiovascular diseases (CVD), cardiovascular drugs, Prescription pattern, drug - drug interactions & medication adherence.

INTRODUCTION

Cardiovascular disease (CVD) is a group of general category diseases that affects the heart and the circulatory system. CVD is caused by disorders of the heart, blood vessels that includes coronary heart diseases (CHD), congestive heart failure (CHF), stroke, Hypertension (HTN), peripheral artery disease (PAD) and rheumatic heart disease (RHD)[1]. Throughout the world high morbidity and mortality is associated with CVD[2]. The important risk factors for CVD are industrialization, urbanization and associated lifestyle changes leads to increased prevalence of obesity, Type - II Diabetes mellitus (DM) and metabolic syndrome[3]. According to world health organization (WHO 2009), almost 20 million people may meet death due to CVD by 2015[4]. Now a day's globally almost 80 % of CVD related deaths occur in low and middle income nations, which cover most countries in Asia[5]. The leading cause of death in India is CVD[6], India will notice a large number of people between 35 and 64 years die of CVD over the next 30 years as well as an increasing level of morbidity due to CVD[7]. In developing countries like India the quality of life can be improved by enhancing the standards of medical care at all levels of health care system[8]. For promoting well - being and human health drugs play a crucial role, but for this desired effect they have to be safe and efficacious and have to be used rationally and in addition to the burden of CVD, errors identified in the prescription are common and raised due to ignorance or lack of knowledge about the disease, Pharmacotherapeutic management of CVD patient[9]. Prescription by a clinician consider as a reflection of his attitude towards the disease and role of drug in the treatment. Prescribing pattern studies deduce to monitor, evaluate and insinuate modifications in the practioners prescription habits, so as to make patient care rational and cost effective[10, 11, 12]. Rational drug prescribing is related to the use of least number of drugs to obtain the possible effect in the right time[13]. Measurement of prescription pattern in health care systems not only describes drug use pattern but also helps in in the identification of polypharmacy and the problems

associated with it like drug related problems, Polypharmacy is a significant problem with cardiovascular inpatients admitted for a prolonged period of time[14]. In the drug related problems drug interactions is the major problem and drug interaction is defined as when the effect of one drug is changed by the presence of another drug, food or by some environmental chemical agent[15]. Drug interactions create a significant challenge to health care providers and may affect mortality, morbidity and a quality life of patients[16]. Previously treatment pattern of cardiovascular drugs was examined in different countries but the studies on inpatient in tertiary care setups specifically in Andhra Pradesh is lacking and incomplete, thus we propose to study the prescribing pattern of cardiovascular drugs and associated drug interactions in our hospital.

MATERIALS AND METHODS

A prospective observational study was carried out from December 2012 - May 2013 at was cardiac inpatient department of Sri Venkata Sai Hrudayalaya, Tirupathi. The study was conducted with the approval of the human ethical committee, Sri Padmavathi School of Pharmacy, Tiruchanoor **(IHEC SPSP/M. PHARM (PP)/2012/01).** Patients who have been diagnosed with CVD as per Newyork Hear Association (NYHA) guidelines and hospitalized for the treatment were included. Total sample size was 180. During the study, patient's case records were observed and the data was recorded in the designed Patient data recording form. Patient characteristics such as age, sex, diagnosis and duration of hospitalization were recorded. All the data has to be collected to overview the prevalence of cardiovascular disease patients with presence or absence of co - morbidities. Prescription pattern data of the study participants include average number of drugs per prescription, average number of cardiovascular drugs per prescription, number of drugs received by the patients during their hospital stay and at the time of discharge, percentage of drugs from the national essential drug list of INDIA (2011 and percentage of drugs prescribing with generic names. Drugs were classified into different groups according to the ATC classification of WHO's collaborating Centre for Drugs Statistics methodology for the prescription pattern analysis[17]. Potential drug - drug interactions were screened by using text books and journal references and the drug interaction facts software version 4.0. The screened interaction is then classified based on severity and the level of scientific evidence[18]. We also identified the medication adherence in the patients by using Morisky medication adherence scale. Patient characteristics and other relevant data were computed using MS Excel and SPSS statistical package. The results were presented as percentage and mean ± Standard deviation (SD). Here we have to apply Chi-square test for data by using Graph Pad Prism Version 6.01 software to calculate P value. We considered Null hypothesis & Alternate hypothesis for statistical purpose. (P value should be < 0.05.)

RESULTS

The gender/age specific prevalence of CVDs increased with age, Prevalence of CVD were more 29.44 % (53) in (60 - 69) age group, followed by 20.55 % (37) in > 70 years and 25 % (45) in (50 - 59) year age group. Remaining age specific prevalence were 17.77 % (32), 5 % (9) and 2.22 % (4) in (40 - 49), < 30 and (30 - 39) age groups respectively. Female patients were found to be more 52.83 % (28) in the age group of (60 - 69) than the male patients 47.16 % (25), followed by 62.5 % (20) in the age group of (40 - 49) than the male patients 37.5 % (12), but the male patients were found to be more 59.45 % (22) than the female patients 40.50 % (15) in the age group of ≥ 70 years (figure - 1).

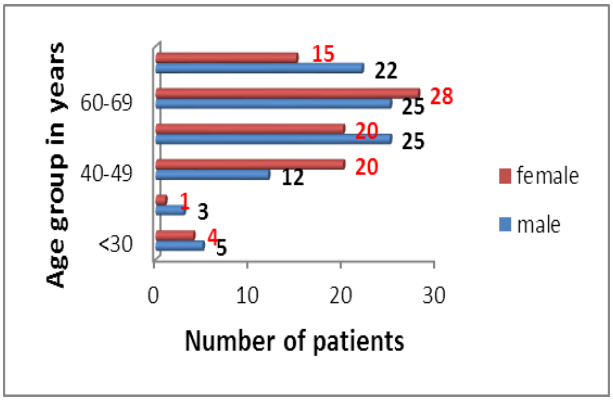

Figure 1- Gender and age distribution of Inpatients

We observed that the distribution of comorbidities in the study population. Patients without comorbidities were found to be 53.33 % (96), 1 comorbidity was 39.44 % (71), 2 comorbidities were observed in 6.11 % (11), 3 comorbidities were found in 1.11 % (2). Finally our results suggest that the more comorbidity were 46.66 % (84) observed in the study population (Table - 1).

Table No .1: Distribution of Comorbidities in the study population

Comorbidities	No. of patients	Percentage (%)
One	71	39.44
Two	11	6.11
Three	2	1.11
Without comorbidities	96	53.33

We observed the presence of comorbidities in 43 male patients 51.19 % (43) out of 93 and in female patients 41 out of 87. The both gender has comorbidities more or less equals (46.23 % Vs 47.12 %). In male patients CKD is more 13.09 % (11), followed by APD & CKD 5.95 % (5), CKD & COPD 2.38 % (2) and CKD, COPD & APD 2.38 % (2) than the female groups 3.57 % (3), 3.57 % (3), 1.19 % (1), 0 % (0) respectively. But APD 33.88 % (28), hypothyroidism 7.14 % (6) is more in female than the male 27.38 % (23), 0 % (0) respectively (Table - 2).

Table No. 2: Distribution of Co morbidities according to the gender of the Patients

Comorbidities	Male (93)	Female (87)	Total
	No. of Patients (%)	No. of Patients (%)	No. of Patients (%)
APD	23 (27.38)	28 (33.33)	51 (60.71)
CKD	11 (13.09)	3 (3.57)	14 (16.66)
APD + CKD	5 (5.95)	3 (3.57)	8 (9.52)
CKD + COPD	2 (2.38)	1 (1.19)	3 (3.57)
CKD + COPD + APD	2 (2.38)	0	2 (2.38)
Hypothyroidism	0	6 (7.14)	6 (7.14)
Total	43 (51.19)	41 (48.80)	84 (100)
Gender percentage of comorbidities	43/93 (46.23)	41/87 (47.12)	84/180 (46.66)

Average duration of hospitalization was 5.33 days (ranges from 3 to 12 days) .We classified the duration of hospital stay into 2 groups like ≤ 6 days and > 6 days by taking the average of the total stay of the all patients. The majority of the patients were hospitalized for a time period below ≤ 6 days 82.22 % (148) and 17.77 % (32) were hospitalized for a time period of > 6 days (Figure - 2).

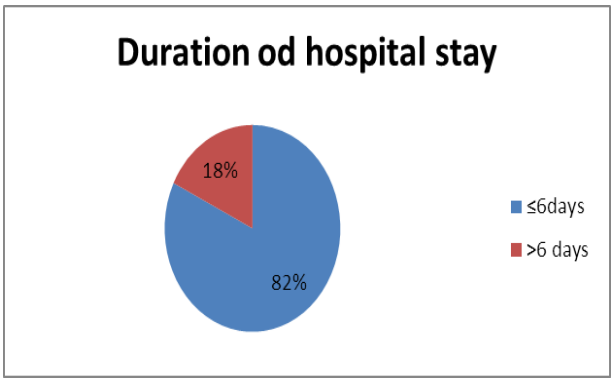

Figure 2 - Duration of hospital stay

Data of 180 patients were analyzed. Total number of drugs prescribed during hospitalization was 2918. The average number of drugs per patient was 16.21.Out of the total number of 2918 drugs prescribed, 34.47 % (1006) were cardiovascular drugs. The average number of cardiovascular drugs during hospitalization was 5.58. The frequency of parental preparations in our study was 39.41 % (1150), out of these cardiovascular parenteral preparations were 34.99 % (352). A total number of 1006 cardiovascular medications prescribed, 92.34 % (929) of drugs were non – combinational cardiovascular drugs and 7.65 % (77) were fixed dose category wise combinational drugs. Out of the total 1006 cardiovascular drugs 57.05 % (574) were from essential drug list of INDIA (2011) and 42.94 % (432) were out of essential drug list (Table - 3).

Table No. 3: Details of drug therapy in cardiovascular disease patients

SL. No.	Details of drug therapy during hospitalization	Number (%)
1.	Total number of prescriptions analyzed	180
2.	Total number of drugs prescribed	2918
3.	Average number of drugs per patient	16.21
4.	Number of injections out of total number of drugs prescribed	1150 (39.41)
5.	Total number of Cardiovascular drugs out of total number of drugs prescribed	1006 (34.47)
6.	Average number of Cardiovascular drugs per hospital duration	5.58
7.	Total number of injections Cardiovascular drugs	352 (34.99)
8.	Single (non –combinational)cardiovascular drug therapy	929 (92.34)
9.	Fixed dose combinational cardiovascular drug therapy	77 (7.65)
10.	Cardiovascular drugs from the essential drug list	574 (57.05)
11.	Cardiovascular drugs out of essential drug list	432 (42.94)

The prescriptions contained 2 drugs 7.22 % (13), with 3 drugs 11.11 % (20), with 4 drugs 13.33 % (24). We observed the Polypharmacy in which 68.33 % (123) prescriptions contained 5 or more drugs (Figure – 3).

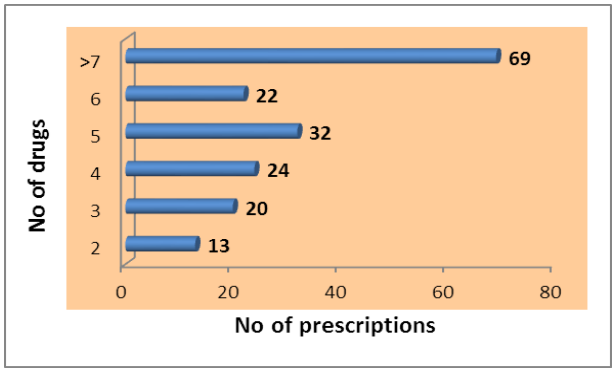

Figure 3 - Distribution of Cardiovascular drug therapy

Drugs from the cardiovascular system constitute 34.47 % (1006) of the prescribed drugs followed by Anti - infective for systemic use 24.50 % (715), Alimentary tract and metabolism 18.50 % (540), Nervous system 7.64 % (223) and blood forming organs 6.44 % (188). Distribution of drugs from other systems includes Respiratory system 4.79 % (140) and very less accounted for the Dermatological preparations 0.06 % (2). Drug distribution in the CVD patients indicates the disease condition with concominent illness, apart from the cardiovascular drugs, anti-infective for systemic use and Alimentary tract and metabolism prescribed in 180 patients. This indicates the DM, Systemic infection, APD are more. Apart from 180 patients drugs for respiratory system, blood and blood forming agents were distributed in 120 patients, thus it indicates the concominent illness of respiratory problems and others (Table - 4).

Table No. 4: Distribution of drugs in different categories based on ATC Classification prescribed in CVD patients

ATC CODE	Anatomical therapeutic chemical groups	Medications (n=2918) n (%)	Patients (n=180) n (%)
A	**Alimentary tract and metabolism** Drugs used in Diabetes Others [a]	**540 (18.50)** 161 (5.51) 379 (12.98)	**180 (100)** 71 (39.44) 180 (100)
B	**Blood and blood forming organs**	188 (6.44)	120 (66.66)
C	**Cardiovascular system**	1006 (34.47)	180 (100)
D	**Dermatological**	2 (0.06)	1 (0.55)
G	**Genito-urinary system and sex hormones**	10 (0.34)	17 (9.44)
H	**Systemic hormonal preparations, excl. sex hormones and insulin's**	10 (0.34)	10 (5.55)
J	**Anti-infective for systemic use**	715 (24.50)	180 (100)
M	**Musculo-skeletal system**	52 (1.78)	27 (15)
N	**Nervous system** Analgesics and antipyretics Other Nervous system drugs	**223 (7.64)** 180 (6.16) 43 (1.47)	**150 (83.33)** 107 (59.44) 43 (23.88)
R	**Respiratory system**	140 (4.79)	120 (66.66)
S	**Sensory organs**	12 (0.41)	12 (6.66)
V	**Various others**[b]	20 (0.68)	19 (10.55)

a- drugs used in the treatment of alimentary tract diseases and metabolism disorders
b- various drugs include vitamins and other drugs used apart from the above categories

We observed the distribution pattern of cardiovascular drug therapy. Among these 22.46 % (226) were Antiplatelet, anticoagulants and Fibrinolytics followed by 20.07 % (202) of Anti anginal drugs, 14.61 % (147) of Diuretics, 12.12% (122) Antiarrhythmic drugs, and 8.34 % (108) of Dyslipidemic agents 6.06 % (61) of cardiac glycoside. We also observed the remaining drugs in less percentages including 5.56 % (56) of β-blockers, 3.77 % (38) of ACE inhibitors/direct renin Inhibitors, 3.47 % (35) of Angiotensin II antagonist, 1.78 % (18) was Calcium channel blockers, 0.49 % (5) was α - blockers and others include 1.19 % (12) (Table - 5).

Table No .5: Distribution pattern of overall cardiovascular drug therapy

SL. NO.	Drugs Category	No. of drugs	Percentage (%)
1.	Antiplatelet, anticoagulants & Fibrinolytics	226	22.46
2.	Antianginal drugs	202	20.07
3.	Diuretics	147	14.61
4.	Antiarrhythmic drugs	122	12.12
5.	Dyslipidemic agents	84	8.34
6.	Cardiac glycosides	61	6.06

7.	β - blockers	56	5.56
8.	ACE inhibitors/direct renin Inhibitors	38	3.77
9.	Angiotensin II antagonist	35	3.47
10.	Calcium channel blockers[c]	18	1.78
11.	α - blockers	5	0.49
12.	Others	12	1.19
13.	Total	1006	100

c - except Amiodarone & diltiazem.

We observed the fixed dose combinations of the cardiovascular drug therapy. Out of total number of 77 prescriptions, 49.25 % (31) were Angiotensin II antagonist and β - blockers (Olmesartan, Medoxomil and Metoprolol), followed by 23.37 % (18) were Antiplatelets and Dyslipidaemic agents (Atorvastatin and Clopidogrel), 18.88 % (14) were accounted for the Calcium channel blockers and β - blockers, among these 10.38 % (8) were Amlodipine and Nebivolol and 7.79 % (6) were Amlodepine and Metoprolol. Angiotensin II antagonist and Diuretics were accounted for 11.68 % (9) among these 6.49 % (5) were Olmesartan Medoxomil and Hydrochlorothiazide and 5.19 % (4) were Telmisartan and Hydrochlorothiazide. Angiotensin II antagonist and Calcium channel blockers were distributed in fewer prescriptions 6.49 % (5) and these were Amlodepine and Olmesartan (Table - 6).

Table No. 6: Fixed dose combinations of cardiovascular drug therapy

SL. NO.	Drug combinations	No. of prescriptions	Percentage (%)
A.	**Angiotensin II antagonist & β-blockers** Olmesartan Medoxomil & Metoprolol	31	40.25
B.	**Antiplatelets & Dyslipidaemic agents** Atorvastatin & Clopidogrel	18	23.37
C.	**Calcium channel blockers & β - blockers** Amlodipine & Nebivolol Amlodepine & Metoprolol	**14** 8 6	**18.88** 10.38 7.79
D.	**Angiotensin II antagonist&Diuretics** Olmesartan Medoxomil&Hydrochlorthiazide Telmisartan & Hydrochlorothiazide	**9** 5 4	**11.68** 6.49 5.19
E.	**Angiotensin II antagonist & Calcium channel blockers** Amlodepine & Olmesartan	5	6.49
	Total	77	100

In our study 53.33 % (121) were Antiplatelet therapy. Among these 22.12 % (50) were Clopidogrel and Aspirin, 13.27 % (30) were Clopidogrel, 11.50 % (26) were Aspirin, 3.53 % (8) were Prasugrel and very less were Tirofiban 1.76 % (4) and Eptifibatide 1.32 % (3). In our study 46.46 % (105) were Anticoagulants, among the anticoagulants 40.26 % (96) received Enoxaparin sodium, 2.21 % (5) was Heparin and 1.76 % (4) was Acenocoumarol. In our study we also observed that the 0.88 % (2) was Fibrinolytics such as Streptokinase (Table - 7).

Table No. 7: Antiplatelet, anticoagulants & Fibrinolytics drug therapy

Drug name	No. of drugs	Percentage (%)
Antiplatelet	**121**	**53.53**
Clopidogrel +Aspirin	50	22.12
Clopidogrel	30	13.27
Aspirin	26	11.50
Prasugrel	8	3.53
Tirofiban	4	1.76
Eptifibatide	3	1.32
Anticoagulants	**105**	**46.46**
Enoxaparin sodium	96	40.26
Heparin	5	2.21
Acenocoumarol	4	1.76
Fibrinolytics	**2**	**0.88**
Streptokinase	2	0.88
Total	**226**	**100**

We observed the Antianginal drug therapy in the CVD patients. 41.08 % (83) were nitroglycerine, 29.70 % (60) were Isosorbide dinitrate, 15.84 % (32) were Isosorbide mono nitrate and 12.87 % (26) were Nikorandil. Very less accounted for the Diltiazem 0.49 % (1) (Table - 8).

Table No. 8: Antianginal drug therapy

Drug name	No. of drugs	Percentage (%)
Nitroglycerine	83	41.08
Isosorbide dinitrate	60	29.70
Isosorbide mono nitrate	32	15.84
Nikorandil	26	12.87
Diltiazem	1	0.49
Total	202	100

Distribution of Diuretics therapy in the CVD patients was 15.82 % (147). Among these 65.30 % (96) were Furosemide, 23.12 % (34) were Torsemide, 10.20 % (15) were Trimetazidine and 1.36 % (2) were Metolazine (Figure - 4).

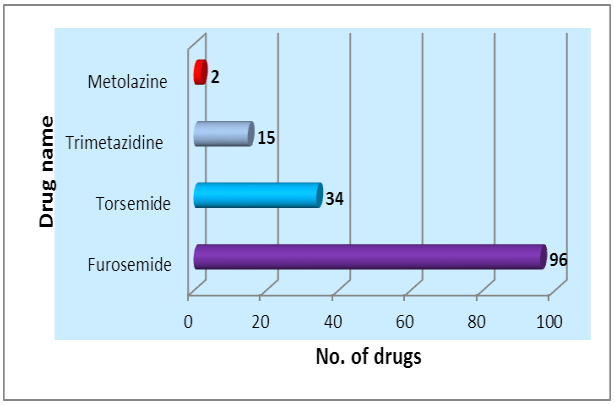

Figure 4 - Diuretics therapy

In our study a total number of 9.04 % (84) Dyslipidemic drugs were prescribed. The most commonly prescribed drug was Atorvastatin 79.76 % (67), followed by Atorvastatin and Ezetimide 9.52 % (8), Rosuvastatin 5.95 % (5) and very less prescriptions with Rosuvastatin and Fenofibrate 2.38 % (2) and Fenofibrate 1.19 % (1) (Figure - 5).

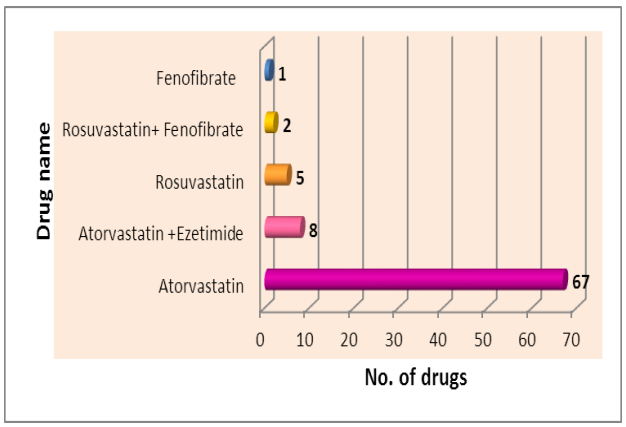

Figure 5 - Dyslipidemic drug therapy

The results shows the total number of prescriptions with β - blockers 56, 51.35 % (31) prescriptions are carvedilol as a 1st choice followed by Metoprolol 23.21 % (13) and Nebivolol 21.42 % (12) (Table - 9).

Table No. 9: β - Blockers drug therapy

Drug name	No. of drugs	Percentage (%)
Carvedilol	31	55.35
Metoprolol	13	23.21
Nebivolol	12	21.42
Total	56	100

In our study a total number of 3.76 % (35) Angiotensin II antagonist drugs, 80 % (28) were Olmesartan Medoxomil, 17.14% (6) were Losartan and 2.85 % (1) were Telmisartan (Figure - 6).

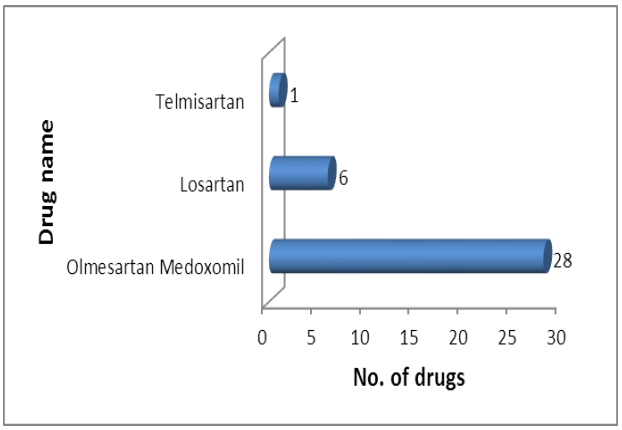

Figure 6 - Angiotensin II antagonist drug therapy

In our study 12.12 % (122) were Amiodarone (Antiarrhythmic), 6.06 % (61) were Digoxin (Cardiac glycosides), 3.77 % (38) were Perindopril (ACE inhibitors/direct renin Inhibitors), 1.78 % (18) were Clinidipine (Calcium channel blockers), 0.49 % (5) Prazocin (α-blockers), 1.19 % (12) were dopamine (Table - 10).

Table No. 10: Other category of cardiovascular drug therapy

Drug name	No. of patients	Percentage (%)
Antiarrhythmic Amiodarone	122	12.12
Cardiac glycosides Digoxin	61	6.06
ACE inhibitors/direct renin Inhibitors Perindopril	38	3.77
Calcium channel blockers Clinidipine	18	1.78
α-blockers Prazocin	5	0.49
Dopamine	12	1.19

We observed that the prescribing frequency of drugs at discharge time include antianginal drugs 88.57 % (160) followed by antiplatelet 86.11 % (155), β - blockers 68.57 % (124), Dyslipidemic agents 57.14 % (103), ACE inhibitors 42.77 % (77), Calcium channel blockers 34.44 % (62), Diuretics 34.44 % (62), Cardiac glycosides 34.44 % (62), Angiotensin –II antagonist 25.55 % (46) and Anticoagulants 11.66 % (21) (Table - 11).

Table No. 11: Distribution of drugs at Discharge time

SL. NO.	Drugs category	Individual drug	Number of patients (%)
1.	**Antianginal drugs**		**160(88.88)**
		Nitroglycerine	82 (45.55)
		Isosorbide mononitrate	62 (34.44)
		Diltiazem	16 (8.88)
2.	**Antiplatelets**		**155 (86.11)**
		Clopidogrel +Aspirin	78 (43.33)
		Clopidogrel	36 (20)
		Prasugrel	16 (8.88)
		Aspirin	25 (13.88)
3.	**β - blockers**		**124 (68.88)**
		Metoprolol	103 (57.22)
		Carvedilol	21 (11.66)
4.	**Dyslipidemic agents**	Atorvastatin	**103 (57.22)**
5.	**ACE inhibitors**	Perindopril	**77 (42.77)**
6.	**Calcium channel blockers**		**62 (34.44)**
		Amlodepine	42 (23.33)
		Clinidipine	20 (11.11)
7.	**Diuretics**		**62 (34.44)**
		Torsemide	30 (16.66)
		Hydrochlorthiazide	17 (9.44)
		Metolazine	15 (8.33)
8.	**Cardiac glycosides**	Digoxin	**62 (34.44)**
9.	**Angiotensin –II antagonist**		**46 (25.55)**
		Losartan	10 (5.55)
		Olmesartan	36 (20)
10.	**Anticoagulants**	Acenocoumarol	**21 (11.66)**

Potential drug – drug interactions identified from the Prescriptions were listed in the above table. The most frequently occurred were those with Atorvastatin - Clopidogrel (89) with moderate severity and Pharmacokinetic Mechanism, ACE inhibitors - Aspirin (74) with moderate severity and Pharmacokinetic Mechanism and enoxaparin – eptifibatide (17) with moderate severity and Unknown mechanism and Aspirin & Nebivolol (8) with minor severity (Table - 12).

Table No. 12: Distribution of ten most potential drug - drug interactions

SL. NO.	Drug pair	Level of severity	Mechanism	Frequency
1.	Atorvastatin - Clopidogrel	Moderate	Pharmacokinetic	89
2.	ACE inhibitors - Aspirin	Moderate	pharmacodynamic	74
3.	Digoxin - Atorvastatin	Moderate	Unknown	40
4.	Digoxin - Furosemide	Moderate	Pharmacokinetic	35
5.	Aspirin - Enoxaparin	Moderate	pharmacodynamic	18
6.	Insulin – Timolol	Moderate	Unknown	18
7.	Enoxaparin + Eptifibatide	Major	Unknown	17
8.	Enoxaparin + Clopidogrel	Major	pharmacodynamic	14
9.	Clopidogrel + Prasugrel	Major	pharmacodynamic	10
10.	Aspirin + Nebivolol	Minor	Unknown	8

Out of the total number of 390 potential drug – drug interactions 46.15 % (180) constitutes moderate, followed by 30.76 % (120) major and 23.07 % (90) minor severity (Table - 13).

Table No. 13: Severity of potential drug – drug interactions

Severity of potential DI (390)	Number of interactions (%)
Major	120 (30.76)
Moderate	180 (46.15)
Minor	90 (23.07)

Follow up is important to detect disease progression in earlier stage that might require escalation of treatment. We observed that the among the 180 patients 86.11 % (155) patients were came for the follow up and remaining patients were not follow up patients 13.88 % (25) (Table - 14).

Table No. 14: Follow up of the Patients

Follow up	No. of patients (%)
Patients who came for follow up	155 (86.66)
Patients who doesn't came for follow up	25 (13.88)

We observed that Medium medication adherence 61.29 % (95) was found to be more than the High medication adherence 21.93 % (34) and Low medication adherence 6.45 % (26). The medication adherences were found to be more in male 56.12 % (87) patients than the female 43.87 % (68) patients. Medium medication adherences were found to be more in male 41.93 % (65) patients than the female 19.35 % (30) patients. The low adherence in male 6.45 % (10), female 10.32 % (16) and high adherence in male was 7.74 % (12), female 43.87 % (68) (Table - 15).

Table No. 15: Medication adherence among the follow up patients

Adherence level	No. of patients			P value (< 0.05)
	M	F	TOTAL	
Low adherence	10 (6.45)	16 (10.32)	26 (16.77)	0.0005^{S}
Medium adherence	65 (41.93)	30 (19.35)	95 (61.29)	
High adherence	12 (7.74)	22 (14.19)	34 (21.93)	
Total	87 (56.12)	68 (43.87)	155 (100)	

DISCUSSION

Total 180 patients data was collected and analysed. Present study showed that the predominance of male 51.66 % with early onset of cardiovascular diseases than female 48.33 %. Heart diseases progresses with the advancing age, there is a greater prevalence, which increases with the higher age. When categorized age-wise, maximum number of patients (29.44 %) were from the age group 60-69 years, followed by (20.55 %) in more than 70 years of age. There were significantly lower number of patients in the younger ages, (2.22 %) in the age group 30-39 and (5 %) in the age group <30 which is comparable to studies by ***Cheah Whye Lian et al.,*** **and** ***Mitu Baskota et al .,*** *which* shows (38.6 %) in more than 60 years and (45 %) in 46-65 years[19, 20].

Our study shows the majority of the patients 53.33 % were without any comorbidity 46.66 % were presented with comorbidities. The commonest co-morbid condition seen in this group of patients was APD 60.71 %, followed by CKD 16.66 % and CKD & COPD 11.90 % of the patients which is contrasted to ***Ravi P Shankar et al.,*** study shows the commonest co-morbid condition was chronic obstructive pulmonary disease (COPD) seen in 10.85 % of the patients[8].

The average length of hospitalization reported in present study was 5.33 days (ranges from3 to 12 days). In our study length of hospital stay ≤ 6 days were more (82.22 %) than the > 6 days (17.77 %), which shows the similarity with ***Ravi P et al.,*** in which average duration of hospitalization was 6.41 days and 55.81 % of patients were hospitalized for a time period < 6 days[8].

Many new potent, effective and expensive drugs have been introduced in the recent decade which has led to a steady increase and often misuse of drugs. In our study the prescribing prevalence has been expressed as the total number of prescriptions for a particular drug/drug category and also as the prescribing frequency. Prescribing prevalence studies are helpful to determine the prevailing morbidity patterns. Average number of drugs per patient during hospitalization was 5.58 indicates the polypharmacy and in most cases it was unavoidable, which are lower than ***Ashok Kumar et al.,*** study (6.58)[16]. 57.05 % of the drugs prescribed from the essential drug list of the India 2011 and 42.94 % drugs out of the essential drug list which shows the similarity with other studies ***Ashok Kumar et al.,*** shows 48.21 % from essential drug list[16] and ***Ravi P et al.,*** shows 60.33 % from essential drug list[8]. This is a matter of concern, however, a large number of drugs which are commonly used for cardiovascular disorders are not represented in India essential drug list and revision of the drug lists should be taken up as a matter of priority.

The frequency of use of injectable preparations in our study was 34.99 %. With the expenditure on disposable syringes and needles adding to the costs of drug treatment and the increase in rate of HIV positive cases,

this is becoming all the more important. The rate is much higher when compared to the rate reported from a study ***Ravi P et al.,*** where 7. 89 % of the patients received injectable preparations[8].

In our study we observed that the 92.34 % of drugs were single drugs and 7.65 % drugs were fixed dose combinational drugs which are similar to ***Ashok Kumar et al.,*** study (88 vs. 12 %). This may be attributed to cost of the drug, patients compliance and good response and less incidence of adverse events[16].

Our study describes the distribution of drugs based on ATC[21]. Drugs from the Cardiovascular system constitutes 34.47 % in total population, followed by Anti-infectives for systemic use 24.50 %, Alimentary tract and metabolism 18.50 % in total population and Nervous system 7.64 % in 83.33 % of patients which shows the disease severity with other comorbidities in study population ,our study was similar with other studies by ***Ashok Kumar et al.,*** shows Drugs from the alimentary tract and metabolism constitute 39.89 % of the prescribed drug followed by cardiovascular drugs 20.0 % and anti-infective for systemic use is 12.1 %[16].

In our study 22.46 % were Antiplatelets, anticoagulants and Fibrinolytics followed by 20.07 % of Antianginal drugs, 14.61 % of Diuretics, 12.12 % of Antiarrhythmic drugs and 8.34 % of Dyslipidemic agents. We also observed the remaining drugs in less percentages including 6.06 % of cardiac glycosides, 5.56 % of β-blockers, 3.77 % of ACE inhibitors/direct renin Inhibitors, 3.47 % of Angiotensin II antagonist, 1.19 % of Dopamine, 1.78 % was Calcium channel blockers, 0.49 % was α-blockers, which was contrasted with ***Ravi P et al.,*** study shows 34.88 % of patients received a calcium channel blocker, 28.68 % received an ACE inhibitor, 30.23 % received diuretics and only 12.3 % received a B blocker[8] and shows the similarity with ***Kamath A et al.,*** study shows 98.15 % of Antiplatelets[22].

In our study, the high prescribing frequency of the Antiplatelets and Antianginal drugs, diuretics, Dyslipidemic drugs reflects the high prevalence of coronary artery diseases.

Prescribing frequency of combinational cardiovascular drug therapy include 49.25 % were Angiotensin II antagonist and β-blockers (Olmesartan Medoxomil and Metoprolol), followed by 23.37 % were Antiplatelets and Dyslipidaemic agents (Atorvastatin and Clopidogrel). 18.88 % were accounted for the Calcium channel blockers and β-blockers, among these 10.38 % were Amlodepine and Nebivolol and 7.79 % were Amlodepine and Metoprolol. Angiotensin II antagonist and Diuretics were accounted for 11.68 % among these 6.49 % were Olmesartan Medoxomil and Hydrochlorothiazide and 5.19 % were Telmisartan and Hydrochlorothiazide. Angiotensin II antagonist and Calcium channel blockers were distributed in less prescription 6.49 % and these were Amlodepine and Olmesartan which was contrasted by studies ***Mitu Baskota et al.,*** Diuretics and Digoxin (54.8 %), followed by ACE - I and Diuretics with 35.5 %[19].

In our study among the Antiplatelets 41.32 % of the patients received dual Antiplatelets therapy (Aspirin and clopidogrel) which shows similarity with ***Kamath A et al.,*** study 90 % of the dual Antiplatelets therapy[73]. The association of physicians of India recommends that all patients with MI, including those with ST Segement elevation myocardial infarction (STEMI), should receive dual Antiplatelets therapy[74]. Aspirin inhibits platelet activation through TXA_2 pathway, clopidogrel inhibits platelet activation by a different mechanism different from aspirin and the combination therapy with aspirin may offer benefits over either drug used alone[22].

The use of Thrombolytic agents in our study was lower (0.88 %) than that reported in the Clinical Trial of Reviparin and the Metabolic Modulation in the Acute Myocardial Infarction Treatment Evaluation (CREATE) registry, where the use of Thrombolytics in tertiary care hospitals was 59.1 %[23]. Which is associated with more side effects and requires proper monitoring and also ours being a tertiary hospital, many patients were referred from other centers. So, the number of patients presenting after the time period for thrombolysis were high.

Among the Antianginal drugs 41.08 % of Nitroglycerine which is less cost than other drugs and Diltiazem prescribing frequency was less 0.49 %.

Among the Diuretics therapy furosemide was most prescribed drug 65.30 % due to its low cost when compared with other drugs. In antiarrhythmic drugs category Amiodarone 3.08 % was most commonly prescribed drug which shows similarity with ***Diane et al.,*** study 5 % of Amiodarone was prescribed[24].

In Dyslipidemic drug therapy Atorvastatin was most commonly prescribed drug 79.76 % which is lower when compared with ***Diane et al.,*** study 40.1 %. Most of the prescriptions contained Atorvastatin and Ezetimide combination of drug (9.52 %). Many patients require HMG - COA reductase inhibitors/Fibric acid derivatives. Because statin monotherapy may not be sufficient to manage the total lipid abnormalities of patient with the metabolic syndrome or Insulin resistant. Hence, combination therapy may frequently be necessary to reduce CAD risk in these patients[24].

More than 6.06 % of patients receiving Digoxin which similar with ***Diane et al.,*** study shows 5.1 % of Digoxin[24]. β - blockers drug therapy in our study shows Carvedilol in 55.35 %, metoprolol 23.21 % and Nebivolol 21.42 %. Olmesartan Medoxomil was 80 %, 17.14 % of losartan and 2.58 % of telmisartan in Angiotensin II antagonist drug therapy. ACE Inhibitors

include Perindopril in 3.77 %, Calcium channel blockers include clinidipine in 1.78 %. α - blockers in our study Prazocin 0.49 % was less than the ***Diane et al.,*** study shows 5.2 %[24].

The prescribing frequency of drugs during discharge time include Antiplatelets 85.71 %, Antianginal 88.57 % , β - blockers 68.57 %, Dyslipidemic drugs 57.14 %, ACE inhibitors 42.85 % and 34.28 % of calcium channel blockers, Diuretics and Cardiac glycosides which shows similarity with ***Kamath A et al.,*** The prescription rate of Antiplatelets agents, beta blockers, ACE inhibitors, ARBs and hypolipidaemics on discharge was 98.15 %, 66.30 %, 65.19 %, 3.33 %, 91.85 %, respectively[22] and similar to ***Andreas Spiess et al.,*** study showed the 64 % Antiplatelets, 42 % β – blockers[25].

More than 60 % of the patients received β-blockers on discharge, which might be due to initiation of the drug therapy following stabilization of cardiovascular events.

Our analysis shows the 86.66 % patients were came for the follow up and remaining patients were non follow up patients 13.88 %, our analysis was similar to the previous findings ***Sanjeev Saksena et al.,*** in which follow up of the patients were more 80 %[26]. Follow up is important to detect disease progression in earlier stage that might require escalation of the treatment.

We also extended our study to determine the drug - drug interactions. But the entire drug – drug interactions are potential. In our study most of the interactions were moderate 46.15 %, 30.76 % major and 23.07 % minor which is comparable to studies by ***Cristiano Moura et al.,*** in which moderate drug interactions were 78 % more when compared to other drug interactions like major drug interactions 22 %[27]. Patients with cardiovascular diseases are particularly vulnerable to DDIs due to their advanced age, polypharmacy and the influence of heart disease on drug metabolism. The DDI potential for a particular cardiovascular drug varies with the individual, the disease being treated, and the extent of exposure to other drugs[28].

In fact, some of the drug combinations are used for therapeutic benefit in clinical practice and others are introduced internationally to despite the increased risk of DDIs. Among these drug classes, heparin and aspirin (37.54 %), Clopidogrel and heparin (12.5 %), Clopidogrel and torsemide (12.5 %) and heparin and Warfarin (9.09%) were the most commonly observed drug pairs resulting in DDIs which is similar to ***UV Mateti et al.,*** study[29].

Medication non – adherence is of great concern to clinicians, health care system and other stakeholders because studies show that non-adherence is highly prevalent and is associated with adverse clinical outcomes and higher cost of care[30]. In our study we find out the gender difference in adherence, one possible reason for the finding of gender difference in adherence may be that the opportunity to observe more female patients in our study. In our study women were slightly less adherent than men (56.12 $v_{s.}$ 43.87 %, p=0.0005) which is similar to ***Brady B et al.,*** study (87.3 $v_{s.}$ 89.8 %, p=0.002)[30]. Adherence is complex, in which gender may be one of the factors that influence how someone takes medicines, there may be different barriers for women such as care taker issues, forgetfulness, and more complex conditions due to aging was contrast to previously published studies ***Elizabeth halt et al.,*** showing there is no gender difference[31].

Our study has several strengths. First it was conducted in the inpatients which provide more clinical data. Second there is less availability of prior studies on cardiovascular drugs utilization pattern in inpatients in India and we also extended our study to determine the medication adherence which was the major factor in treatment outcome in chronic diseases such as cardiovascular diseases.

There are some limitations to our study. First it was a single center study with limited sample size and limited period of time. Unfortunately, collection of over the counter medications (OTC) used by patients and their duration of use were not included as these are one of the major risk for cardiovascular diseases prevalence.

We are actively involved in the pharmacist interventions such as Educational pharmaceutical care by providing information to the patients regarding disease and healthy life style using specially designed patient information leaflets. The present study could serve as a frame work for further studies to investigate the scope for educational interventions for improving prescribing practices.

CONCLUSION

The present study concluded that most of the drugs were prescribed rationally according to the standard treatment guidelines. The potential drug interactions were more in the cardiovascular drugs prescriptions and medium medication adherence was mostly observed in the patients which determine the success of treatment.

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Abbreviations: CKD - Chronic kidney disease, COPD – Chronic obstructive pulmonary disease, APD - active peptic ulcer disease.

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