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A Prospective Observational Study on Drug Utilization Evaluation of Statins in Cardiovascular Disorders at Tertiary Care Hospitals

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ABSTRACT
BACKGROUND: A prospective DUE Study on usage of statins in cardiovascular disorders, statins usage has been increased in recent trends for both prevention and curing cardiac diseases. The need of this research is to gain some insight into the role of rational use of statins and identifying adverse effects that require further evaluation.
METHODOLOGY: This study was conducted at private cardiac hospital. The records of all patients who meet the inclusion criteria were collected, screened and relevant data was extracted. Then the filed forms were evaluated for outcomes of the study.
RESULTS: A total of 170 Patients were enrolled in this study. The majority age group was found to be 61-70 yrs. Males were more prone to cardiovascular disorders when compared to females. CAD was observed at high incidence when compared to other cardiac diseases. Monotherapy was indicated for most of the patients and it is observed that Atorvastatin was prescribed commonly. Lipid profile parameters were evaluated and DRP's interpreted were ADR's, drug interactions. DISCUSSION: In our prospective observational study we intended to monitor the usage of statins in cardiovascular disorders.
CONCLUSION: Drug related problems were monitored and there is a need to minimize adverse effects and drug interactions. Prescription of brand names were commonly observed. The mostly prescribed statin was atorvastatin and monotherapy was highly preferred then the combinational therapy. The results of this study will help in decrease Drug Therapy Problems and improving therapeutic outcome of patients.
KEYWORDS: DUE, ADR, CAD, DRP's.

I. INTRODUCTION:

Drug use evaluation (DUE) is an ongoing, authorised and systematic quality improvement process, which is designed to: review drug use and/or prescribing patterns provide feedback of results to clinicians and other relevant groups develop criteria and standards which describe optimal drug use promote appropriate drug use through education and other interventions. DUE is a discipline that aims to understand how and why drugs are used as they are, so that drug use and health outcomes can be improved[1].

STATINS: Synonyms: HMG-Co A Reductase Inhibitors, Anti-Hyperlipidemic agents.

Statins, a class of cholesterol-lowering drugs first introduced in the late 1980s, have been extensively studied for their ability to reduce serum lipid levels. Numerous studies have confirmed that statins are effective in reducing serum lipid levels. Statins reduce mortality in those who are at the risk of cardiovascular disease[2].

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Most Common Cholesterol-Lowering Drugs[3]:

TYPE OF STATIN	GENERIC NAME	STARTING DOSE (mg)	MAXIMUM DOSE (mg)
LIPOPHILIC	Atorvastatin	10	80
	Fluvastatin	20	80
	Simvastatin	5	80
	Pitavastatin	1	4
	Lovastatin	10	40
HYDROPHILIC	Rosuvastatin	5	40
	Pravastatin	10	40

MECHANISM OF ACTION OF STATINS: Statins exert their major effect reduction of LDL levels through a mevalonic acid–like moiety that competitively inhibits HMG-CoA reductase. By reducing the conversion of HMG-CoA to mevalonate, statins inhibit an early and rate-limiting step in cholesterol biosynthesis. Statins affect blood cholesterol levels by inhibiting hepatic cholesterol synthesis, which results in increased expression of the LDL receptor gene. Some studies suggested that statins also can reduce LDL levels by enhancing the removal of LDL precursors (VLDL and IDL) and by decreasing hepatic VLDL production. The reduction in hepatic VLDL production induced by statins is thought to be mediated by reduced synthesis of cholesterol, a required component of VLDLs[4].

STATINS AND THEIR OVERVIEW: Statins are used therapeutically for treatment of Cardiovascular diseases. Some of the statins and their dosage forms are illustrated as below:

ATORVASTATIN[5]:
Brand Name: STORVAS
Indication and Dosage:
CardiovascularDisease Prevention: 10-80mg PO qDay
Primary Hypocholesteremia: Initial:10-20mg PO qDay & Maintenance:10-80mg PO qDay
Hypertriglyceridemia:
- Initial:10mgPOqDay
- Maintenance:10-80mgPOqDay

ROSUVASTATIN[6]:
Brand Name:ROSUVAS, ROZAVEL
IndicationandDosage:
Hypercholesterolemia: Tablets and capsules:10-20mg PO qDay; not to exceed 40mg/day
Slowing Progression of Atherosclerosis: Tablets and capsules:10-20mg POq Day; not to exceed 40mg/day
Stroke, Myocardial Infarction:
Tablets:10-20mg POq Day; not to exceed 40mg/day Dosage range 5-40mg/day

SIMVASTATIN[7]:
BrandName:ZOCOR
Indication and Dosge:
- **Hypercholesterolemia:**
- Usual dosage range: 5-40mgPOqDay
- Initial:10-20mg POq Day in the evening
- Patients at high CHD risk: Start 40mg/day

Prevention of Coronary Events: 5-40mg PO qDay in the evening.

FLUVASTATIN[8]:
Brand Name: LESCOLXL
IndicationandDosage:
- **Hypercholesterolemia & Mixed Dyslipidemia:**
- Start dose: 20-40mgPO
- Dose range:20-80mg PO
- If 80 mg/day needed, divide into 40mg PO q12

ADVERSE EFFECTS[9]:
MYOPATHY:
The major adverse effect associated with statin use is myopathy. Myopathy refers to a broad spectrum of muscle complaints, ranging from mild muscle soreness or weakness (myalgia) to life-threatening rhabdomyolysis. The risk of muscle adverse effects increases in proportion to statin dose and plasma concentrations. Consequently, factors inhibiting statin catabolism are associated with increased myopathy risk, including advanced age (especially > 80 years of age), hepatic or renal dysfunction, and untreated hypothyroidism. Measurements of creatinine kinase are not routinely necessary unless the patient also is taking a drug that enhances the risk of myopathy.

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HEPATOTOXICITY: Serious hepatotoxicity is rare and unpredictable, with a rate of about 1 case per million person-years of use. ACC/AHA guidelines recommend measuring ALT at baseline prior to initiation of statins.

OTHER RARE ADVERS EEFFECTS[10]:

ORGAN/SYSTEMS	STATIN INDUCED ADR'S
Nervous	Stroke, neuropathy, sleep disorders
GI tract	Nausea, Gastric ulcer, Abdominal pain
Skin	Alopecia, Rashes, Chronic urticaria
Others	Gynecomastia, Ocular hemorrhage

II. METHODOLOGY:

Study site:
This study was conducted at Tertiary care hospitals in Narasaraopet. The patients who visit this hospital are usually from in and around the district of Guntur.

Study design:
A study design is a specific plan or protocol for conducting the study. Study design used in the study is a hospital-based Prospective Observational Study.

Sample size:
A total of 170 patients from the in-patient of the department of cardiology those who fulfilled the exclusion and inclusion criteria were selected for the study.

Study period:
This study was conducted for a period of 6 months.

Study criteria:

Inclusion criteria:
1. The study population must be between the age group of 30 to 80 years.
2. The study population may be either male or female.
3. The patients must stay in the hospital for more than a day.
4. The Patients who are willing to participate.

Exclusion criteria:
1. Patients below the age of 30 years and above 80 years.
2. Uncooperative and non-responding patients must be excluded.
3. Outpatients should not be taken into the account.
4. Patients who are pregnant, breast feeding cannot be taken as study subjects.

Source of data:
The patient's demographical data, clinical data, therapeutics data and other relevant and necessary data were obtained every day from the medical records and other information sources are documented.

Parameters measured:
The parameters that are measured in this study are age, gender, body weight, complete blood count, lipid profile (if present in patient's record).

III. RESULTS:

AGE CATEGORIZATION IN STUDY POPULATION

S.No	AgeGroups(Yrs)	No.of Cases	Percentage(%)
1	30-40	15	8.82
2	41-50	38	22.31
3	51-60	45	26.44
4	61-70	47	27.64

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5	71-80	25	14.73

Table1:Categorization based on Age (n=170)

Table 1 : The data reveals that patients aging between 61-70years were found to be high followed by 51-60years.

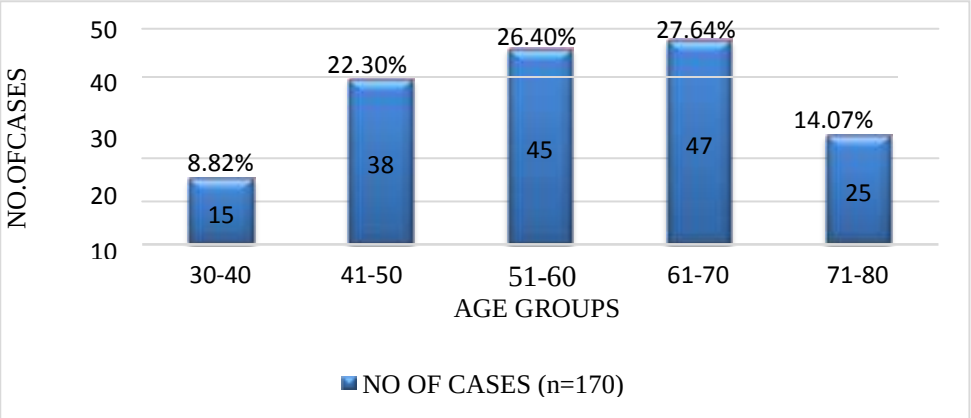

Figure 1: Categorization based on Age (n=170)

GENDER WISE CATEGORIZATION:

S.No	Gender	No. of Patients[n=170]	Percentage(%)
1	Males	114	67.05
2	Females	56	32.94

Table2 : Gender Wise Categorization

Table 2: The Gender Wise Categorization shows that males (n= 114) occupied more area compared to females (n= 56) population in the study.

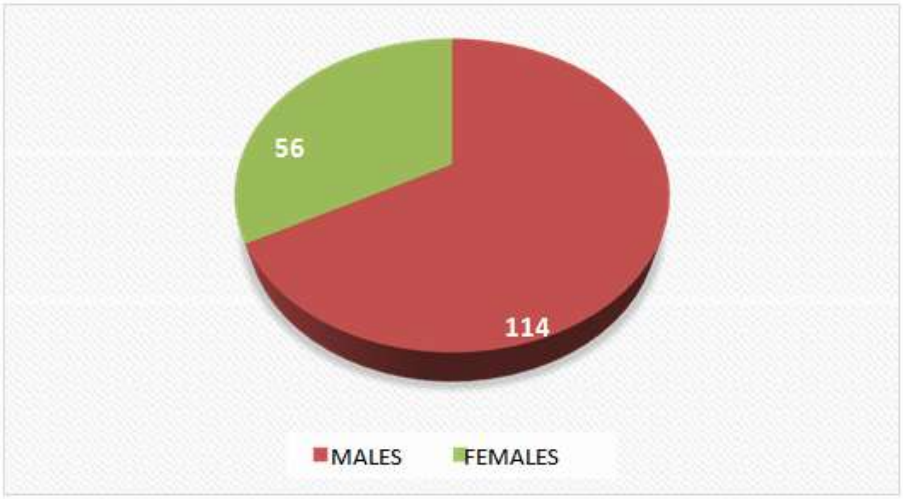

Figure2 : Gender Wise Categorization

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PREVALENCE OF DISEASES:

S.No	Disease	No. of Patients	Percentage(%)
1	CoronaryArteryDisease	52	30.58
2	MyocardialInfarction	54	31.76
3	AnginaPectoris	22	12.94
4	CongestiveHeart Failure	9	5.29
5	IschemicHeartFailure	10	5.88
6	Tricuspidvalvedisease	1	0.58
7	AtrialFibrillation	6	3.52
8	DilatedCardiacMyopathy	8	4.70
9	Atherosclerosis	1	0.58
10	Supraventriculartachycardia	2	1.17
11	PeripheralArteryDisease	2	1.17
12	Arrythmias	2	1.17

Table 3: Prevalence of Diseases

Table 3: The Prevalence of Diseases shows that MI (n=54, 31.76%) is the most commonly observed disease in the study population followed by CAD, angina pectoris, ischemic heart failure more commonly occurred.

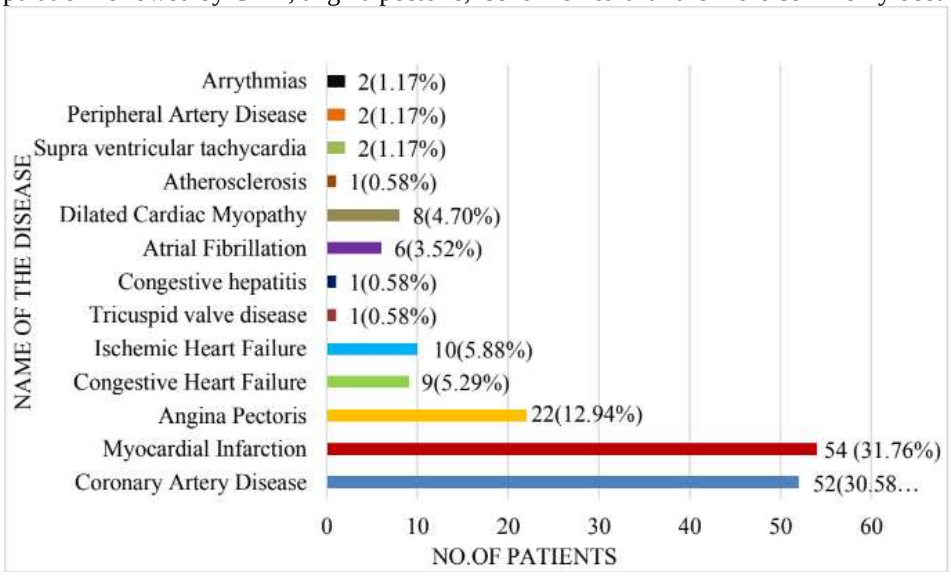

Figure 3: Prevalence of Diseases

BASED ON COMORBIDITIES:

S.No	Co-morbidCondition	No. ofPatients	Percentage(%)

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1	HTN+DM	32	18.82
2	HTN+CKD	01	0.58
3	DM+CKD	02	1.17
4	HTN+DM+CKD	03	1.76

Table 4:Based on Comorbidities

Table 4: From the collected data the co-morbid conditions associated with cardiovascular disorders are found to be HTN,DM,CKD of which HTN is 12.35%. The co-morbid condition of HTN+DM(n=32)is most commonly identified among a total of 79 co-morbid conditions.

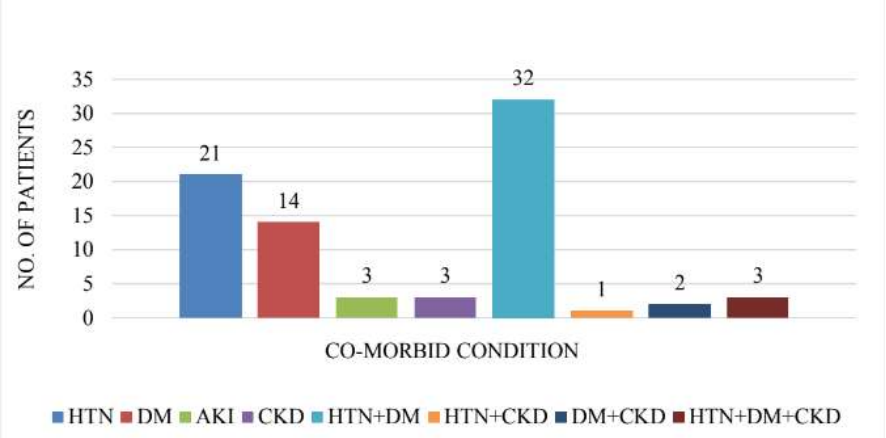

Figure4 :Based on Comorbidities

PRESCRIBING PATTERNS OF STATINS:

S.No	NameofStatinPrescribed	No.ofCases	Percentage(%)
1	Atorvastatin	124	72.94
2	Rosuvastatin	9	5.29
3	Simvastatin	1	0.58
4	Aspirin+Atorvastatin+Clopidogrel	3	1.76
5	Aspirin+Rosuvastatin+Clopidogrel	10	5.88
6	Aspirin+Atorvastatin	18	10.58
7	Rosuvastatin+Clopidogrel	2	1.17
8	AtorvastatinCalcium+Clopidogrel	3	1.76

Table 5: Prescribing patterns of statins

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Table 5: The most commonly prescribed statin in monotherapyis Atorvastatin 72.94% (n=124) and the least prescribed is Simvastatin 0.58%(n=1). In the combination therapy, Aspirin+Atorvastatin was prescribed for 18 patients (10.58%) and the least encountered combination is Rosuvastatin + Clopidogrel (n=2;1.17%).

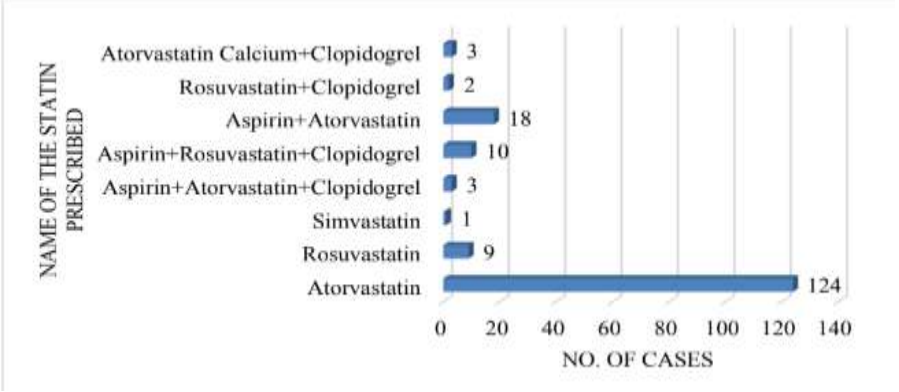

Figure 5 :Prescribing patterns of statins

LIPID PROFILE TEST:

S.No	LipidProfile	No. ofPatients	Percentage(%)
1	Patients with Lipid Profile advised	38	22.35
2	Patients who are not advised with Lipid Profile	132	77.64

Table 6 :Lipid ProfileTest

Table 6: The below table shows that out of 170 cases collected 38 patients (22.35%) wereadvised with Lipid Profile Test, while the remaining 132 patients (77.64%) were not advised with lipid profile test.

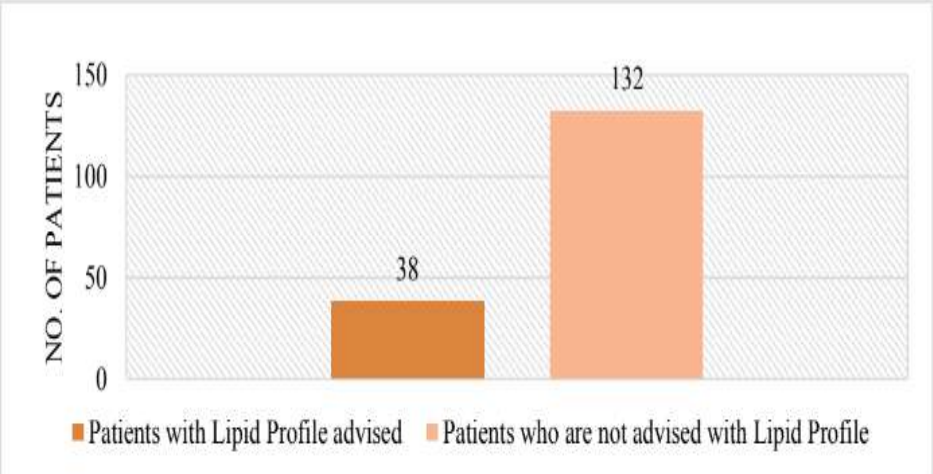

Figure 6 : Lipid Profile Test

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STATINS AND THEIR BRAND NAMES

S.No	BrandName	No. ofCases	Percentage(%)
1	ATORVAS(Atorvastatin)	46	27.05
2	STORVAS(Atorvastatin)	62	36.47
3	ECOSPRIN-AV (Aspirin+Atorvastatin)	18	11.17
4	LIPITOR(Atorvastatin)	8	4.70
5	ROSAVEL(Rosuvastatin)	6	3.52
6	ROSULIFEGOLD (Rosuvastatin+Aspirin+Clopidogrel)	8	4.70
7	STORVAS-CV (AtorvastatinCalcium+Clopidogrel)	3	1.76
8	ROSULIFE-CV (Rosuvastatin+Clopidogrel)	2	1.17
9	ATOCOR(Atorvastatin)	2	1.17
10	ROSUVA(Rosuvastatin)	3	1.76
11	ATOREC(Atorvastatin)	5	2.94
12	ZOCOR(Simvastatin)	1	0.58
13	DRATOR(Atorvastatin)	1	0.58
14	ROSAGOLD (Rosuvastatin+Aspirin+Clopidogrel)	2	1.17
15	AZTOGOLD (Atorvastatin+Aspirin+Clopidogrel)	1	0.58
16	ECOSPRINGOLD (Atorvastatin+Aspirin+Clopidogrel)	2	1.17

Table7: statins and their Brand names

Table 7: Among the brand names of statins reviewed the most commonly prescribed brand was found to be STORVAS (n=62;36.47%) followed by ATORVAS (n=46;27.05%) and the least prescribed brands was ZOCOR(n=1;0.58%).

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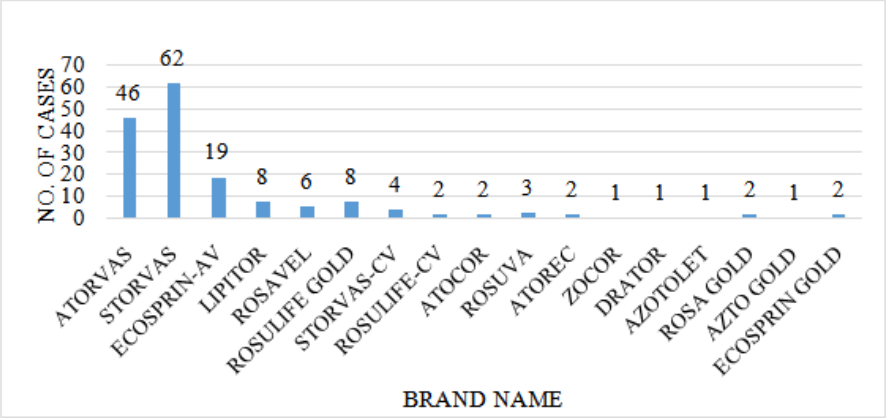

Figure 7 : Statins and their brand names

ADRs:

S.No	ADRs	No. of Patients	Percentage(%)
1	Myalgia	3	1.76
2	Insomnia	2	1.17
3	Diarrhoea	4	2.35
4	Nausea	8	4.70
5	Anorexia	8	4.70
6	Dizziness	3	1.76

Table8: Adverse effects reported

Table 8: The brief out line on ADRs reported shows that out of 28 subjects nausea, anorexia are the major complaints reported of n=8 (4.70%). Other ADRs such as Diarrhoea (n=4,2.35%), Myalgia and Dizziness (n=3,1.76%)were reported.

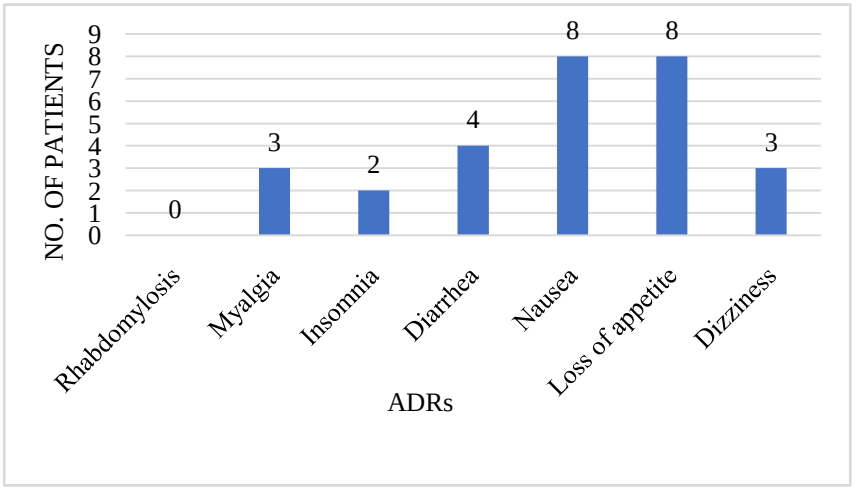

Figure 8: Adverse effects reported

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TYPE OF DRUG INTERACTIONS:

S.No	Drug InteractionType	No.of Patients	Percentage(%)
1	Synergism	30	17.64
2	Additive effect	3	1.76
3	Antagonism	4	2.35
4	Unknown mechanism	2	1.17

Table 9: Type of drug interactions

Table 9: Out of 170 cases collected drug interactions were identified in 39 subjects. The type of drug interactions identified were synergism (n=30,17.64%), antagonism(n=4,2.35%), additive effect (n=3,1.76%) and unknown mechanism (n=2,1.17%). The synergism type of interaction was found to be at higher rate while unknown mechanism at low rate.

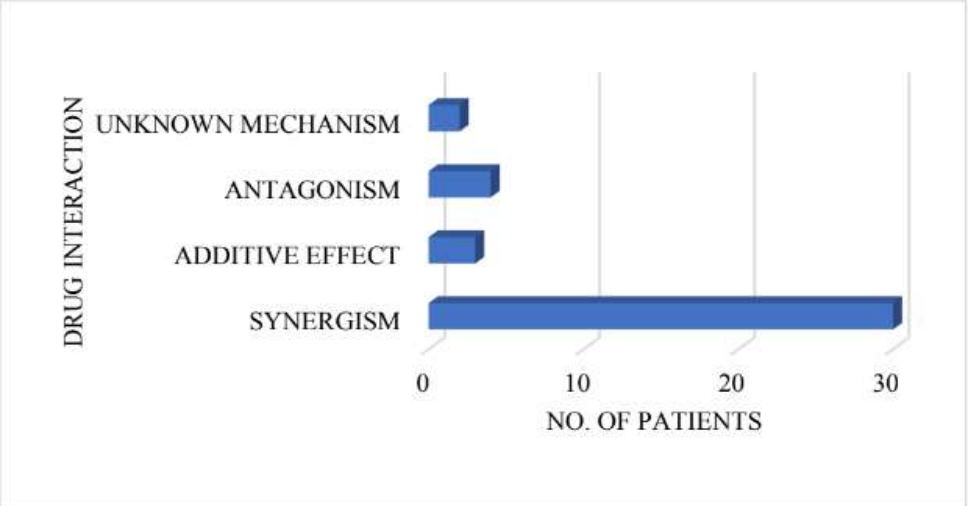

Figure9: Type of drug interactions

IV. DISCUSSION:

In our prospective observational study we collected patient's data that fulfilled inclusion and exclusion criteria were enrolled from various secondary care hospitals in Narasaraopeta. Our study was carried out for a time period of 6 months i.e., from October to March 2022. We collected patient's data like demographic details, reason for admission, past medical history, past medication history, present medications prescribed, type of statin therapy prescribed, their dose and frequency of administration. These details were collected from patient medical records and noted in designed data collection form. Parameters like patient's age, gender, body weight, complete blood count, lipid profile (if present in patient's record) were noted. In our study the a total of 170 samples were recorded and the age group of 61- 70 were recorded i.e, 27.64% and the male were higher than the women i.e, 67.05%. Out of 170 patients 54 of them were admitted due to MI shows the prevalence of the disease. The co-morbid condition of HTN, and the combination of HTN+DM are the most observed among the patients. The lipid profile was only recommended in 38 patients, of all the patients monotherapy was prescribed in 136 patients and the combination therapy was prescribed to 34 patients, and the atorvastatin was highly recommended i.e, 72.94% and the brand STORVAS is commonly

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used among 62 patients. ADR'S like anorexia and nausea was observed in 8 patients each and synergism type of drug interaction was observed in higher rate that is among 30 patients.

V. CONCLUSION:

Our study provides an insight on usage of statinsin cardiovascular disorders.In our study the sample size was estimated to be 170 patients. This study states that among total cases collected men (67.05%)are relatively higher in number than woman (32.94%) suffering from cardiovascular diseases. Predominance of male gender was observed. Age groups of 61-70 years were more prone to the disease followed by 51-60 age. Here the commonly found cardiovascular diseases are CAD, MI, Angina, CHF, AF, DCMP, TVD, SVT, PAD, Arrhythmias, Atherosclerosis, of these coronary artery disease is most common among all the patients followed by MI, Angina, CHF. Majority of patients received Atorvastatin(72.94%). Drug related problems were monitored and there is a need to minimize the adverse effects and drug interactions. Prescribing generic drugs will ensure the patients to get more affordable drugs and will also reduce hospital burden on the patient's. However, there is a need to sensitize the cardiologist and make them aware to adopt generic drugs, so as to ensure rational utilization of drugs.

The usage of statins was high in geriatric patients so there is a need to achieve appropriate use of statins to prevent the risk of exacerbations of the co-morbid conditions. The results of this study will help in rationalizing drug use by decreasing rate of adverse effects and interactions associated with them. Our study also helps in improving therapeutic outcome of the cardiac patients. As the sample size is small andsample distribution is also not even i.e. from few areas of district, further studies have to be conducted in more clinical setups and with large sample size for getting more accurate reports for decision making.

Finally this study concludes that the usage of statins in cardiovascular disorders have worked effectively for the patients which were used.

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