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RESEARCH ARTICLE

A Prospective Observational Study on Drug Utilization Evaluation of Atorvastatin in Tertiary Care Hospital

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ABSTRACT:

OBJECTIVES: Our objectives are to study the rational use of Atorvastatin in patients in a tertiary care hospital. **METHODOLOGY:** It was a prospective and observational study which was undertaken in hospital such as various departments, ESI hospital, Ayanavaram for a period of 6 months. A total of 110 patients were included in the study and were followed for the drug utilization evaluation of the study. This study criterion was carried out in In-patients of age greater than 35 years of either gender who are prescribed with HMG-COA reductase inhibitor Atorvastatin. **RESULTS:** The Drug was found to be prescribed more in males [56%] compared to females [44%]. In the lipid profile study, all the different parameters like Total cholesterol: HDL ratio, HDL: LDL ratio and Triglycerides: HDL ratio was analyzed. Drug interactions were analyzed and reported. **CONCLUSION:** We conclude that the drug use was found to be rational. Interventions for improving more accurate use of Atorvastatin should be implemented. Further studies from time to time are essential in drug utilization pattern and standard treatment guidelines to be circulated among practicing physicians.

KEYWORDS: Rational use, Body Mass Index, Lipid profile, Atorvastatin.

INTRODUCTION:

Hyperlipidemia is one of the major risk factor which is related with Atherosclerosis and Atherosclerosis induced conditions, such as Ischemic heart disease, cerebrovascular disease, coronary heart disease and peripheral vascular disease[1]. The World Health Organization (WHO) in 1997 defined drug utilization as the marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences[2].

Drug utilization review (DUR) is defined as an authorized, structured, ongoing review of prescribing, dispensing and use of medication. DUR encompasses a drug review against predetermined criteria that results in changes a drug therapy when there criteria are not met. It involves a comprehensive review of patients' prescription and medication data before, during and after dispensing to ensure appropriate medication decision-making and positive patients outcomes. As a quality assurance measure, DUR programs provide corrective action, prescriber feedback and further evaluations.

Classification of DUR:

- Prospective –evaluation of a patient's drug therapy before medication is dispensed.
- Concurrent – ongoing monitoring of drug therapy during the course of treatment.

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- Retrospective- review of drug therapy after the patient has received the medication[3].

Sources of drug utilization data:
- Medical Practitioner Records
- Pharmacy Records
- Health Surveys
- Computerized databases.

Types of drug use information:
- Drug based information
- Patient information
- Problem based information
- Prescriber information[4].

Steps involved in conducting drug use study:
Step 1 – Identify drugs or therapeutic areas of practice for inclusion in the program
Step 2 – Study design
Step 3- Define Standard and Criteria
Step 4 – Design the data collection form
Step 5 – Data collection.
Step 6 – Evaluate results.
Step 7- Provide feedback of results.
Step 8- Develop and implement interventions
Step 9– Re-evaluate to determine if drug use has improved.
Step 10- Revise the DUE programme
Step 11 – Feedback results[5.]

Role of pharmacists in DUE[6]:
- Program development, supervision and coordination.
- Presentation of DUE results at meetings and conferences.
- Education of hospital staff about DUE.
- Promotion of goals and objectives of DUE.
- Publication of results in peer-reviewed journals.

The History of Statin Therapy: When and Why did they become so important?
- Cholesterol is essential for the functioning of all human organs.
- It is however, a contributing cause of coronary heart disease and cerebral vascular disease. This is known after nearly a century of investigation.
- Cholesterol was first isolated from gallstones in 1784, and it has fascinated scientists ever since. How and why could a normal product of liver metabolism cause so much trouble? Answering this question has been of such concern, that thirteen Nobel prizes have been awarded to scientists who devoted major parts of their careers to cholesterol research.
- In response to the established relationship between cholesterol and CAD/CVD, the pharmaceutical industry has been quite successfully developed a remarkably effective class of drugs- the statins, which lower cholesterol levels in blood and reduce the frequency of CAD/CVA[7].

Atorvastatin:
Atorvastatin is in a group of drugs called HMG CoA reductase inhibitors, or "statins". Atorvastatin reduces levels of "bad " cholesterol (low-density lipoprotein, or LDL) and triglycerides in blood, while increasing levels of "good" cholesterol (high –density lipoprotein, or HDL). Atorvastatin is used to treat high cholesterol, and to lower the risk of stroke, heart attack, or other heart complications in people with type 2 diabetes, coronary heart disease, or other risk factors.

Brand Name:
Lipitor/Storvas/Tonact/Atorlip/Aztor/Atorvas.

Indications:
Hyperlipidemia, Hypercholesterolemia, Homozygous familial hypercholesterolemia, Elevated serum triglyceride, Type III familial hyperlipoproteinemia[8].

Dosage:
Initial Dose: 10, 20 or 40 mg orally once a day. The 40 mg starting dose is recommended for patients who require a reduction in LDL cholesterol of more than 45%.

Maintenance Dose: 10 to 80 mg orally once a day [8].

Mechanism of action :
Reduces production of cholesterol in body by inhibiting enzyme HMG- CoA reductase that catalyzes early rate-limiting step in cholesterol synthesis; increases HDL; reduces LDL, VLDL, and triglycerides.

Adverse drug reactions:
Headache; Insomnia; Rash; Asthenia; Dizziness; Myalgia; Rhabdomyolysis; Pharyngitis; Sinusitis; Arthralgia[9].

Pregnancy Category: X
Contraindications:
Active liver disease or unexplained persistent elevation of serum transaminases, pregnancy, lactation[10].

OBJECTIVES:
- To evaluate the drug utilization patterns of Atorvastatin were prescribed for various diseases.
- To evaluate the rational use of Atorvastatin.
- To minimize the drug error.

METHODOLOGY:

It was a prospective and observational study which was undertaken in hospital such as various departments, ESI hospital, Ayanavaram for a period of 6 months. A total of 110 patients were included in the study and were followed for the drug utilization evaluation of the study. This study criterion was carried out in In-patients of age greater than 35 years of either gender who are prescribed with HMG-COA reduction inhibitor Atorvastatin.

INCLUSION CRITERIA:

- Males and Non Pregnant female patients aged between 35 – 75 years.
- Patients with or without history of hyper tension/ diabetes / cardiovascular diseases.
- Patients who presented with signs and symptoms of cardiovascular diseases.

EXCLUSION CRITERIA:

- Patients aged below 35.
- Terminally ill patients.
- Pregnant and Lactating women.

RESULTS:

1. GENDER DISTRIBUTION:

Table No-1 Gender distribution

S. No	GENDER	NO.OF PATIENTS	PERCENTAGE %
1	MALE	62	56
2	FEMALE	48	44

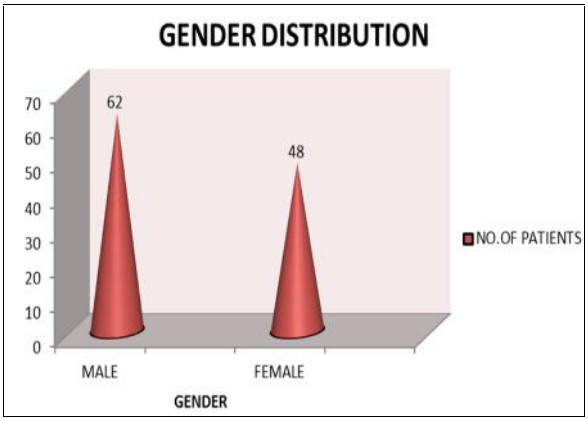

Figure no 1 Gender distribution

Table 1 and Figure 1 Indicates Out of 110 patients 62 were Male and 48 were Female.

2. AGE DISTRIBUTION:

Table no-2 Age distribution

S.NO	AGE	NO. OF PATIENTS	PERCENTAGE %
1	36-45	12	11
2	46-55	40	36
3	56-65	32	29
4	66-75	20	18
5	>75	6	5

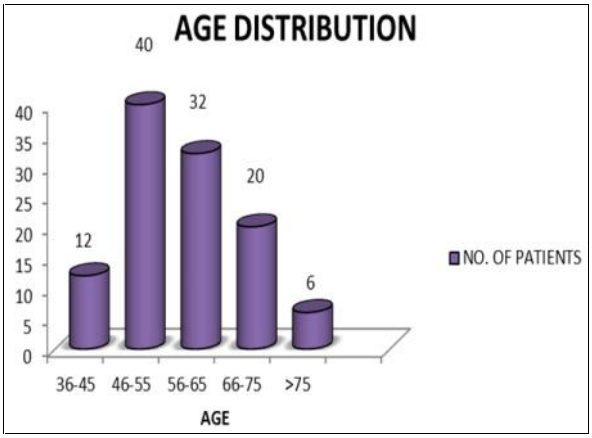

Figure no : 2 Age distribution

Table 2 and Figure 2 representing Age distribution among study population (110 Patients).

3. LIPID PROFILE SEGREGATION

Table No 3 Lipid profile segregation

S. No	PARAMETERS	HIGH RISK	AVERAGE RISK	LOW RISK
1	SR CHOLESTEROL: HDL [<5]	9	60	41
2	HDL:LDL [>3]	16	80	14
3	TRIGLICERIDES: HDL [<4]	44	50	16

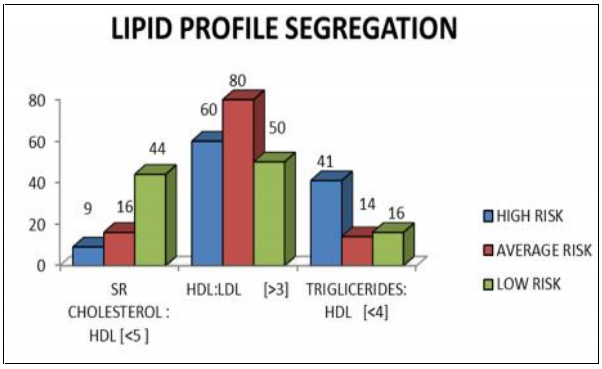

Figure No 3 Lipid profile segregation

Table 4 and Figure 4 Indicates the number of patients with High, Average, Low risk of getting Cardiovascular Diseases.

4. BMI Segregation:

Table No : 4 BMI Segregation

Sl No	CATEGORIES	NO OF PATIENTS	PERCENTAGE %
1	UNDERWEIGHT (<18.5)	0	0
2	NORMALWEIGHT(18.5-25)	15	13
3	OVERWEIGHT (25-30)	35	32
4	OBESE(>30)	60	55

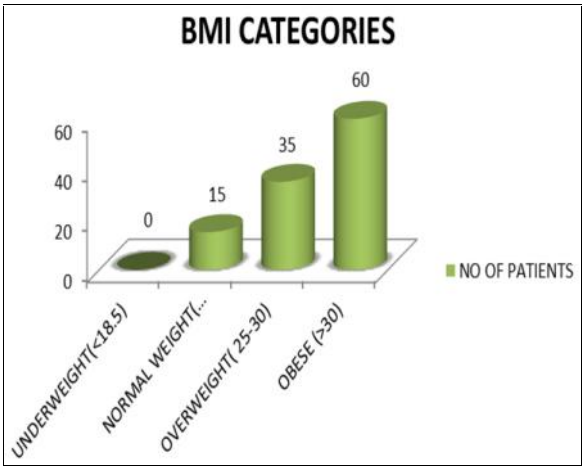

Figure No: 4 BMI segregation

Table 4 and Figure 4 representing Underweight 0%, Normal weight 13%, Overweight 32%, Obese 55% based on BMI segregation.

5. Social habits:

Table No: 5 (A) Smoking Habit

S. NO	SOCIAL HABITS	NO OF PATIENTS	PERCENTAGE %
1	SMOKER	28	25
2	NON-SMOKER	82	75

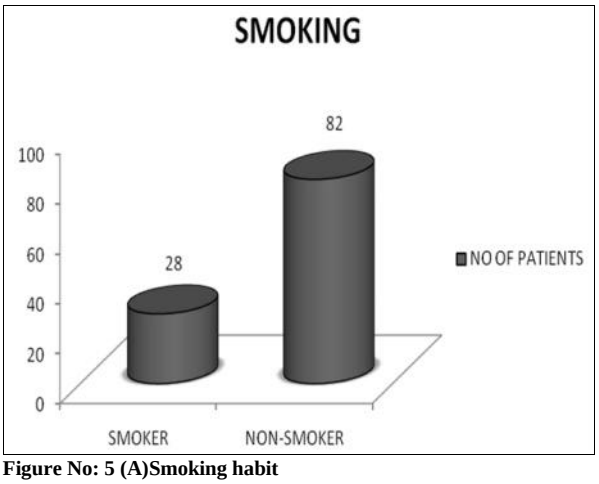

Figure No: 5 (A)Smoking habit

Among the study Population (110 Patients) 28 Patients are smokers and 82 Patients are non smokers as represented in Table 5(a) and Figure 5(a).

Table No: 5 (B) Alcohol Habit

SL NO	SOCIAL HABIT	NO OF PATIENTS	PERCENTAGE %
1	ALCOHOLIC	22	20
2	NON-ALCOHOLIC	88	80

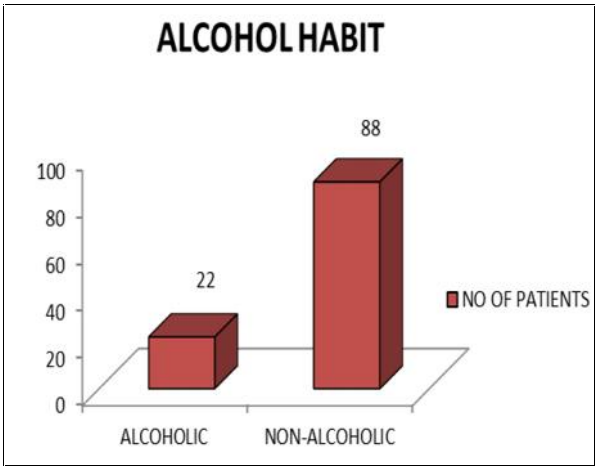

Figure No: 5 (b) Alcohol habits

Among the study population (110 Patients) 22 patients are Alcoholic and 88 Patients are Non-Alcoholic as represented in Table 5(b) and Figure (5b).

6. Based on comorbidities

Table No: 6 Based On Comorbidities

S.NO	COMORBIDITIES	NO.OF PATIENTS	PERCENTAGE %
1	HYPERTENSION	24	22
2	TYPE II DM	16	15
3	ISCHEMIC HEART DISEASE	15	14
4	CORONARY ARTERY DISEASE	10	9
5	OTHERS	23	21
6	NIL	22	20

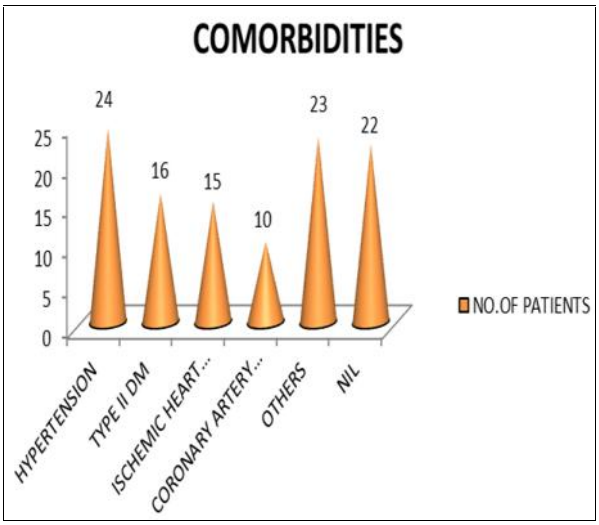

Figure No : 6 Based on comorbidities

Table 6 and Figure 6 represent the comorbid conditions underlying with the study population of 110 patients.

7. Therapeutic class of drugs used during hospital stay.

Table No: 7 Therapeutic class of drugs used during hospital stay

S. NO	THERAPEUTIC CLASS OF DRUGS	NO.OF PATIENTS	PERCENTAGE %
1	ANTI HYPERTENSIVES	91	83
2	GI AGENTS	69	63
3	ORAL DIABETIC DRUGS	80	73
4	INSULIN	37	34
5	ANALGESICS	17	15
6	ANTIBIOTICS	37	34
7	VITAMINS	56	51
8	CARDIOVASCULAR AGENTS	63	57

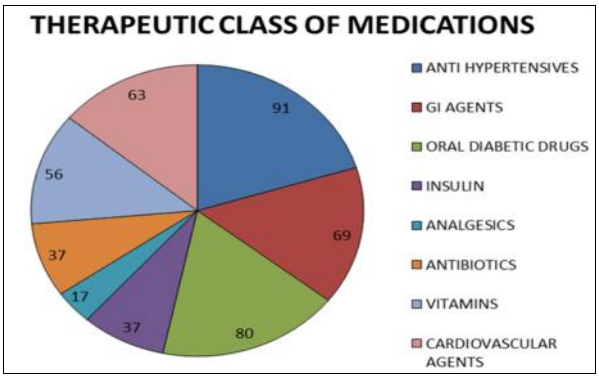

Figure no:7 Therapeutic class of drugs used during hospital stay

Table 7 and Figure 7 representing the Therapeutic class of Drugs which are used by the study Population during Hospital stay.

8.Drug interactions found with atorvastatin

TABLE NO:8 DRUG INTERACTION WITH ATORVASTATIN

S. No	Drug interaction	No of Prescriptions	Percentage %
1	OMEPRAZOLE	31	28
2	NIFEDIPINE	5	5
3	SPIRINO LACTONE	10	9
4	DIGOXIN	2	2
5	LIRAGLUTIDE	12	11
6	NO INTERACTIONS	50	45

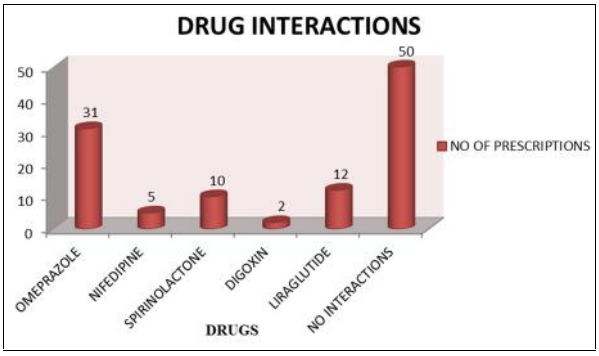

Figure No: 8 Drug interaction with atorvastatin

Table 8 and Figure 8 shows the Drug interaction with atorvastatin found in the prescription during hospital stay.

9. Indications for statins:

TABLE NO: 9 INDICATIONS FOR STATINS

S. NO	INDICATIONS FOR STATINS	NO OF PATIENTS	PERCENTAGE %
1	PRIMARY AND SECONDARY PROPHYLAXIS OF CVD	76	69
2	DIAGNOSIS	34	31

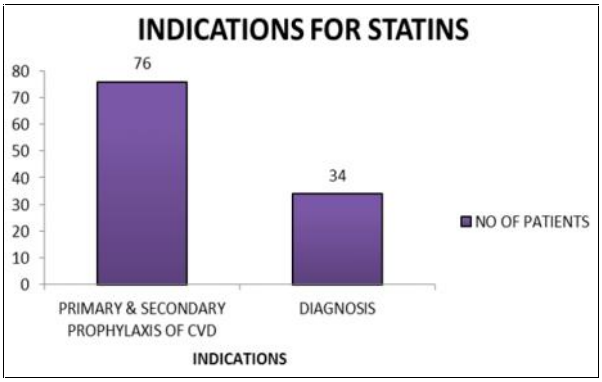

Figure no: 9 Indications for statins

Among the study population (110 Patients) 76 Patients are treated with atorvastatin for Primary and secondary prevention of Cardiovascular Diseases and 34 Patients are treated for their Diagnostic Conditions and was represented in Table 8 and Figure 8.

DISCUSSION:

This study provides the data and usage of Atorvastatin in various departments of tertiary care hospitals. Atorvastatin prescribed patients were identified mostly in general medicine department based on diseased condition. In my study the male [56%] population prescribed with atorvastatin was found to be more than female [44%][(11)]. This finding is similar to the study conducted by Kamlesh P. Patel et.al, which showed the male pre dominance [55.33%] compared to female [44.67%]. In our study the age groups prescribed more with Atorvastatin were 46-56 years [36%] followed by 56-65 years [29%]. In my study BMI segregation is studied and analyzed from that obese patients (55%) are found more among the study population, followed by overweight patients (32%). In my study Lipid profile is segregated and was analyzed. Most of the patients assessed to have average risk of developing cardiovascular diseases by monitoring Total Cholesterol: HDL ratio, HDL: LDL ratio, Triglycerides: HDL ratio. In our study [25%] of patients were smokers and [75%] of patients were non-smokers. Followed by [20%] of patients were alcoholic whereas [80%] of patients were

non-alcoholic. In my study, the other class of drugs prescribed during hospital stay also included oral diabetic drugs [73%], followed by antihypertensive drugs [83%], gastro intestinal agents [63%], Analgesics [15%], Cardiovascular agents [57%], Insulin [34%], Antibiotics [34%], Vitamins [51%].In our study Comorbid conditions such as DM [15%], HTN[22%], IHD[14%], CAD [9%],Other Comorbidities such as Thyroid, Alcoholic Liver disease, CVA [21%] is seen. In our study drug interaction with Atorvastatin is found in prescriptions among Omeprazole, Liraglutide, Spirinolactome, Digoxin, Nifedipine. Co-administration of Atorvastatin with omeprazole increases the blood levels and effects of Atorvastatin. This can increase the risk of side effects such as liver damage and a rare but serious condition called Rhabdomyolysis that involves the breakdown of skeletal muscle tissue. In some cases Rhabdomyolysis can cause kidney damage and even death. You may need a dose adjustment or more frequent monitoring by doctor to safely use both medications. Another moderate Interaction is found with the Co-administration of Digoxin with Atorvastatin. Combining these drugs together causes the Alterations in P-glycoprotein transport by which Atorvastatin increases digoxin concentrations. Digoxin is known to undergo intestinal secretion, mediated by p-glycoprotein. Atorvastatin is a CYP3A4 substrate. The Interaction between Atorvastatin and Digoxin is a result of Inhibition of P-Glycoprotein. Mediated secretion in the intestine, leading to an increase in the extent of Absorption. Liraglutide will decrease the level of Atorvastatin by other. Based on pharmacokinetics studies Liraglutide decreased Atorvastatin C_{max} by 38% and median T_{max} delayed from 1 hour to 3 hour with Liraglutide and AUC did not change. Nifedipine and Spironolactone will increase the level or effect of Atorvastatin by affecting hepatic / intestinal enzyme CYP3A4 metabolism. Major Comorbid condition is Hypertension [22%] is seen. This finding is similar to the study conducted by Kamlesh P. Patel et.al, Hypertension [49%] followed by Diabetes mellitus[28%]. In my study majority of the patients are prescribed with Atorvastatin for Primary and Secondary prevention of cardiovascular diseases [69%] [Prophylaxis] and also prescribed based on diagnosis [31%][(12)]. This finding is similar to the study conducted by Praveen KG et al, Primary and secondary prevention of cardiovascular diseases (62%) and diseased condition (38%). Atorvastatin is prescribed rationally according to guidelines of National Cholesterol Educational Program [NCEP Guidelines] and American Diabetic Association [ADA guidelines].

CONCLUSION:

As this study was focused on the drug utilization of Atorvastatin, the drug is prescribed rationally according to guidelines of National Cholesterol Education Program [NCEP] and American Diabetic Association Guidelines [ADA]. Atorvastatin is very commonly prescribed for the patient's with diabetes mellitus, Hypertension, Ischemic Heart disease and as Prophylaxis of cardiovascular diseases. The utilization of Atorvastatin is higher and was recommended as the most effective therapy for hyperlipidemia. This is a Preliminary Study, hence further studies are required for the broader evaluation of Atorvastatin and the rational use of the drug was ensured.

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