Indian Journal of Pharmacy Practice | Association of Pharmaceutical Teachers of India

Drug Utilization and Evaluation of Hmg-co a Reductase Inhibitors in Tertiary Care Teaching Hospital

Praveen KG[1*], Arun K[2]

[1]Department of Pharmacy Practice, C.L. Baid Metha College of Pharmacy, Jyothi Nagar, IT high way, Thorapakkam, Chennai: 600 097

[2]Department of Pharmacy Practice, ISF College of Pharmacy, Ferozepur Road, Ghal Kalan, Moga, Punjab, Postal Code: 142001

Submitted: 04-10-2013 Accepted: 30-11-2013

ABSTRACT

A prospective study was conducted to evaluate the drug utilization of HMG-CoA reductase inhibitors (statins) in a tertiary care teaching hospital to ensure rational use, safety, prescribing pattern and economic strategy for 6 months, in which 440 patients prescribed with statins were recruited for the study and the data were collected and analyzed statistically. Statins were more prescribed in 60-70 years age group and it was prescribed mainly for primary and secondary prevention of cardiac and cerebro-vascular complications(62.87%) followed by dyslipidemia (29.38%) and hypertriglyceridemia (7.74%). Atorvastatin was more prescribed (85.42%) than Simvastatin (4.78%) and Rosuvastatin (9.79%). Drug-drug interactions were found with digoxin, verapamil and phenytoin. The DDD/12 bed days were found to be 82.32, 2.4, and 15 for the three statins respectively. the prescribed daily dose and the defined daily dose were as follows atorvastatin 19.33mg;20mg, Simvastatin 15.73mg;30mg, and for Rosuvastatin 15.73mg;10mg. The cost of the three statins according to the amount utilized was found to be 4918,302 and 887 rupees respectively. The dosages used for Atorvastatin were generally closer to the maintenance dose recommended by WHO. Whereas a slight difference seen in case of Simvastatin and Rosuvastatin. Though several brands available the least priced statins brands can be selected rather than costlier brands which cause a drastic increase in patient's drug compliance as well as economic status

INTRODUCTION

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.[1]

Drug use is a complex process. In any country a large number of socio-cultural factors contribute to the ways drugs are used. In India, these include national drug policy, illiteracy, poverty, use of multiple health care systems, drug advertising and promotion, sale of prescription drugs without prescription, competition in the medical and pharmaceutical market place and limited availability of independent, unbiased drug information. The complexity of drug use means that optimal benefits of drug therapy in patient care may not be achieved because of underuse, overuse or misuse of drugs. Inappropriate drug use may also lead to increased cost of medical care, antimicrobial resistance, adverse effects and patient mortality.[2]

Studies on the process of drug utilization focus on the factors related to the prescribing, dispensing, administering, and taking of medication, and its associated events, covering the medical and non-medical determinants of drug utilization, the effects of drug utilization, as well as studies of how drug utilization relates to the effects of drug use, beneficial or adverse. The therapeutic practice is expected to be primarily based on evidence provided by pre marketing clinical trials, but complementary data from post marketing period are needed to provide an adequate basis for improving drug therapy.[3]

In recent years pharmacists have been increasingly involved in many emerging areas of pharmacy in addition to drug therapy. Pharmacists are expected to share their knowledge in improving policy decision in hospitals. At drug therapy level, pharmacists may utilize their expertise in making choice of drugs include or exclude in the formulary based on pharmacoeconomics.[4]

In recent years studies on drug utilization have become a potential tool to be used in the evaluation of health systems. The interest in drug utilization studies began in the early 1960s and its importance has increased since then because of increase in marketing of new drugs, wide variation in the pattern of drug prescribing and consumption, growing concern about delayed adverse effects and the increasing concern regarding the cost of drugs.[5]

The role of clinical pharmacists is to ensure rational, effective and safe treatment for the patient in their care. This involves interacting with patient to identify the medicines they have been taking before they were admitted to hospital and educating patient on the use of their medicines when they leave the hospital. Pharmacists, by virtue of their expertise

Address for Correspondence:

Dr. G. Praveen Kumar, Department of Pharmacy Practice, C.L. Baid Metha College of Pharmacy, Jyothi Nagar, IT high way, Thorapakkam, Chennai : 600097

E-mail: praveen.pharmd@gmail.com

and their mission of ensuring optimal patient outcomes, should work in the process of medicine use improvement through DUE. [6]

Thus DUE plays a key role in helping the healthcare system to understand, interpret and improve the prescribing, administration and use of medications. The principal aim of DU research is to facilitate rational use of drugs, which implies the prescription of a well-documented drug in an optimal dose on the right indication, with correct information and at an affordable price. It also provides insight into the efficacy of drug use i.e. whether a certain drug therapy provides value for money. DU research can thus help to set priorities for the rational allocation of health care budgets.[7]

STATINS

Statins (atorvastatin, fluvastatin, pravastatin, rosuvastatin, and simvastatin) competitively inhibit 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, an enzyme involved in cholesterol synthesis, especially in the liver. Statins are more effective than other lipid-regulating drugs at lowering LDL-cholesterol concentration but they are less effective than the fibrates in reducing triglyceride concentration. However, statins reduce cardiovascular disease events and total mortality irrespective of the initial cholesterol concentration. Statins should be considered for all patients, including the elderly, with symptomatic cardiovascular disease such as those with coronary heart disease (including history of angina or acute myocardial infarction), occlusive arterial disease (including peripheral vascular disease, non-hemorrhagic stroke, or transient ischemic attacks).

In patients with diabetes mellitus, the risk of developing cardiovascular disease depends on the duration and complications of diabetes, age, and concomitant risk factors. Statin therapy should be considered for all patients over 40 years with diabetes mellitus (type 1cand 2). In younger patients with diabetes, treatment with a statin should be considered if there is target-organ damage, poor glycemic control (HbA_1C greater than 9%), low HDL-cholesterol and raised triglyceride concentration, hypertension, or a family history of premature cardiovascular disease. Statins are also used for the prevention of cardiovascular disease events in asymptomatic individuals who are at increased risk. Statin treatment should also be considered if the total cholesterol concentration to HDL-cholesterol ratio exceeds[7]

The recommendations of the NCEP for dyslipidemia control are aimed at decreasing or preventing cardiovascular disease attacks. In coronary heart disease (CHD) or in equivalent diseases, the target lipid levels are less than 100 mg/dl (2.6 mmol/l), which is called secondary prevention (NCEP, 2002). Patients with clinical CHD and the equivalent diseases have the following characteristics:

1. Clinical CHD: myocardial ischemia (angina), MI, coronary angioplasty, and/or stent placement, coronary bypass graft and prior unstable angina.
2. Carotid artery disease: stroke history, transient ischemic attack history, carotid stenosis > 50%.
3. Peripheral arterial disease
4. Abdominal aortic aneurysm.
5. Diabetes mellitus.

If the patient does not have any of the above coronary heart diseases or equivalents, then he or she must be considered for primary prevention. This prevention is influenced by total cholesterol and HDL, age, gender, hypertension, family history of CHD, smoking, etc. All of these are considered as risk factors for cardiovascular diseases.[8]

METHODOLOGY

Study design: A prospective study was done for 6 months in which patient's data was collected from the hospital. Duration of the study was for 6 months which includes 440 subjects and the study was done under a multi-specialty tertiary care teaching hospital. Patient's identification was kept confidential and their medication chart was just reviewed according to their clinical condition.

Inclusion and exclusion criteria: Patients who are prescribed with HMG-CoA reductase inhibitors above age of 18 years. Pregnant women and breast feeding mothers were excluded from the study.

A specially designed proforma was prepared to collect data which includes patient demographics (age, sex, past medical history, past medication history, personal habits, and socio-economic status), drug details (name of the drug, dosage form, frequency, route of administration, duration of treatment) and medication profile.

Subjects fulfilling the inclusion criteria were recruited from the hospital. The subject's demographical data, physical examination, past medical history and medication history were recorded in the proforma. The drugs were categorized according to the ATC (anatomical therapeutic chemical) classification system. The collected data from the above sources were analyzed for:

Dosing pattern: Recommended dosages and dosing schedule followed for the statins that were prescribed.

Prescribed daily dose (PDD): It is defined as the average dose prescribed according to a representative sample of prescriptions. The PDD can be determined from prescription studies and medical or pharmacy records. PDD is useful in determining the average daily amount of a drug that is actually prescribed for a specific indication.

Defined daily dose (DDD): The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults. It is useful in estimating the drug needs to provide a good therapeutic care to a patient.

Adverse drug reaction: Any response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, long therapy of disease or for the modification of physiological function.

Drug interaction: Drug interaction is a situation in which substances affect the activity of a drug i.e., the effect are increased or decreased or produce a new effect that neither produce its own effect (Drug-drug/Drug-food/Drug-disease interactions).

Cost effectiveness: Cost-effectiveness analysis thus measures the incremental cost of achieving an incremental health benefit expressed as a particular health outcome that varies according to the indication for the drug.

The statistical analysis was performed using SPSS version 16 software and the results were analyzed by t-test and non-parametric test.

RESULT

This prospective study involved 440 patients. Among the patients 265 (60.2%) patients were male and 175 (39.8%) patients were female (Table 1 & Figure 1). The maximum number of the patients was found in the 66-75 year age group which was followed by age group 56-65 years -37.13%, 46-55 years-19.36%, 36-45 years-11.39%, above 75 years-7.74% and 26-35 years-2.28% (Table 2& Figure 2). The specialty wise percentage of the patients prescribed with HMGCoAreductase inhibitors was highest in the cardiology department which accounts for 50.11% followed by neurology-21.87%, nephrology-10.25%, general medicine-7.52%, endocrine-4.33%, general surgery-2.05%, ortho-1.82%, urology-1.59%)and radiology- 0.46% (Table 3 & Figure 3). Statins prescribed in the population under study included atorvastatin, rosuvastatin and simvastatin of which the drugs were prescribed in 85.42%, 9.79% and 4.78% of the patients respectively (Table 4 & Figure 4).

Atorvastatin was prescribed in the hospital under different brand names which included Atorva (ZydusCadila)-29.8%, Tonact (Lupin)-24%, Storvas (Stancare)-10.67%, Tonact-TG (Lupin)-8.80%, Aztor (Sun Pharma)-4.8% , Atorlip(Cipla)-2.93%, Caat (Piramal Healthcare)-2.67%, Stator (Nicolas Piramal)-0.8%, S tatix (Biocon)-0.8%, Atorva-EZ (ZydusCadila)-0.53% (Table 5 & Figure 5).

Rosuvastatin was prescribed under brand names Rosuvas (Ranbaxy)-73.81% and Crestor (Astrazeneca)-26.19% (Table 6 & figure 6). Similarly Simvastatin was prescribed as Simvotin(Ranbaxy)-61.90%, Simcard (Cipla)-38.10%(Table 7& Figure 7).

Table 1: Gender Distribution

Gender	No. of Patients (n=440)	% of patients
Male	265	60.2%
Female	175	39.8%

Table 1: Shows the distribution of study population in which the male patients (60.2%) were found to be higher than the female patients (39.8%)

Fig. 1: Gender Distribution

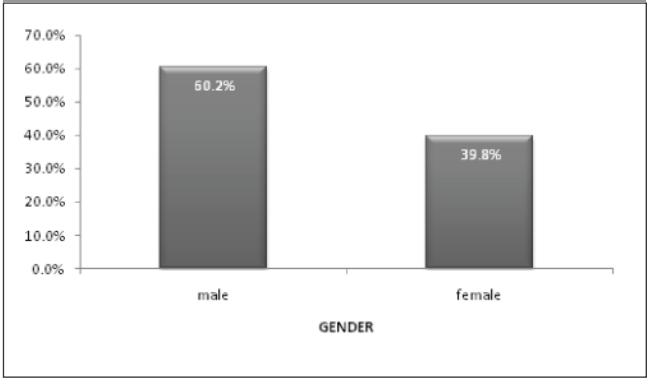


Table 2: Age Distribution

Age	No. of Patients (n=440)	% of patients
18-25	0	0.00%
26-35	10	2.28%
36-45	50	11.39%
46-55	85	19.36%
56-65	163	37.13%
66-75	260	59.23%
>75	35	7.74%

Table 2: shows distribution of patients among various age groups. The maximum numbers of patients were found to be in 66-75 age group(59.23%). (P-value< 0.05)

Fig. 2: Age Distribution

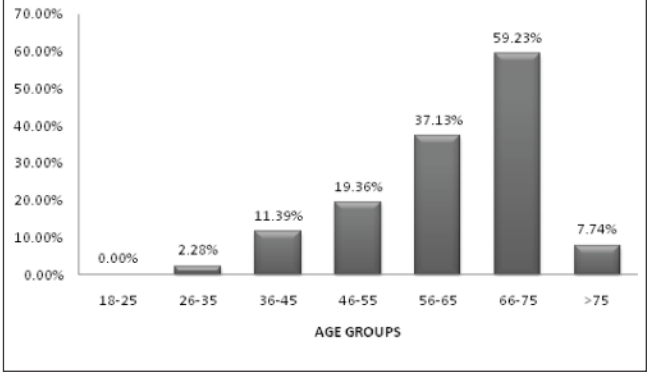


Table 3: Specialty Wise Distribution Of Statins

Department	No. of Patients (n=440)	% of patients
Cardiology	221	50.11%
Neurology	96	21.87%
Nephrology	45	10.25%
General medicine	33	7.52%
Endocrione	19	4.33%
General surgery	9	2.05%
Urology	7	1.59%
Ortho	8	1.82%
Radiology	2	0.46%

Table 3 indicates the number of patient prescribed specialty wise.
The highest numbers of patients of about 50.11% (221 patients) were found in cardiology. (P-value <0.05)

Fig. 3: Specialty Wise Distribution of Statins

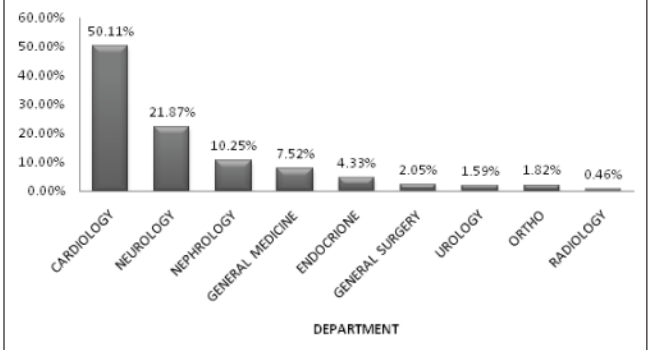


Table 4: Statins Prescribed in Study Population

Statins	No. of Patients (n=440)	% of patients
Atorvastatin	376	85.42%
Rosuvastatin	43	9.79%
Simvastatin	21	4.78%

Table 4 shows that among the statins prescribed in the study population atorvastatin was found to be the most common in 85.42% of patients followed by 9.79% of rosuvastatin and 4.78% of simvastatin. (P-value<0.05)

Figure 4: Statins Prescribed

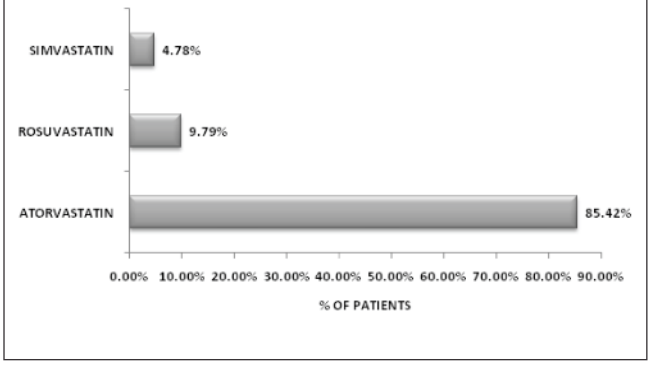


Table 5: Brand Wise Distribution of Atorvastatin

Brands	No. of Patients (n=440)	% of patients
Atorva(ZydusCadila)	113	29.87%
Tonact (Lupin)	90	24.00%
Xtor (Ipca)	52	13.87%
Storvas(Stancare)	40	10.67%
Tonact-TG(Lupin)	33	8.80%
Aztor(Sun Pharma)	18	4.80%
Atorlip(Cipla)	12	2.93%
Caat (Piramal Healthcare)	10	2.67%
Stator(Nicolas Piramal)	3	0.80%
Statix (Biocon)	3	0.80%
Atorva-EZ (ZydusCadila)	2	0.53%

TABLE 5 shows the study population among various brands of atorvastatin prescribed in which atorva (29.87%) and tonact (24.00%) were found to be commonest prescribed. (p-value<0.05)

Figure 5: Different Brands of Atorvastatin

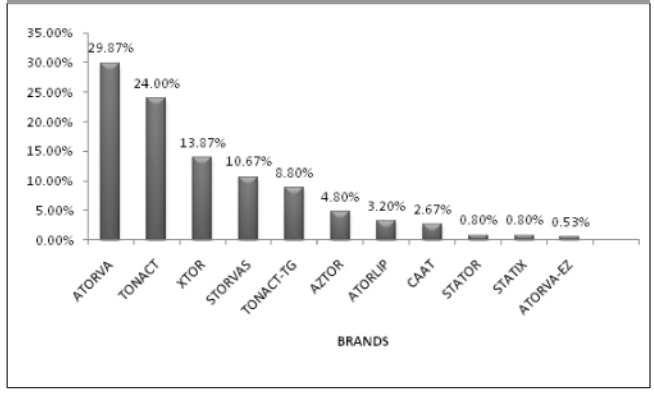


Table 6: Brand Wise Distibution of Rosuvastatin

Brand	No. of Patients (n=440)	% of patients
Crestor(AstraZeneca)	11	26.19%
Rosuvas(Ranbaxy)	31	73.81%

TABLE 6 shows the study population among various brands of Rosuvastatin prescribed in which rosuvas (73.81%) was found to be prescribed more.

Figure 6: Brand Wise Distribution of Rosuvastatin

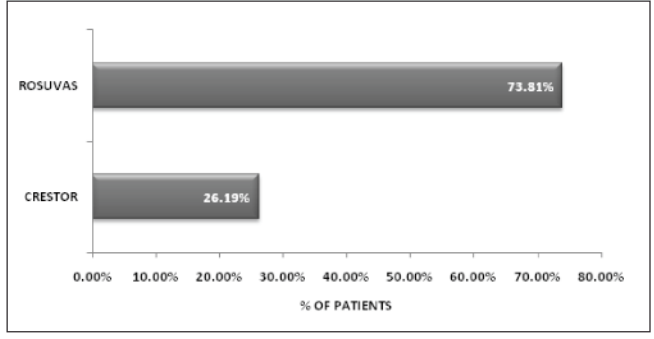


Table 7: Brand wise Distribution of Simvastatin

Brands	No. of Patients (n=440)	% of patients
Simcard (Cipla)	8	38.10%
Simvotin (Ranbaxy)	13	61.90%

TABLE 7 shows the study population among various brands of simvastatin prescribed in which simvotin (61.90%) was found to be prescribed more.

Fig. 7: Brand wise Distribution of Simvastatin

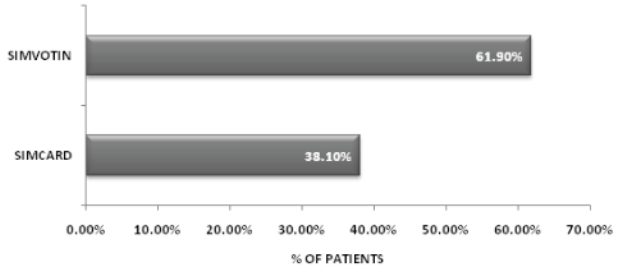
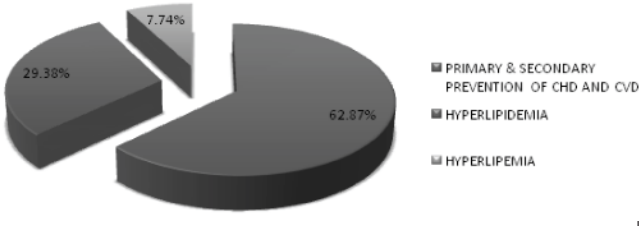


Table 8: Indications for Statins

Indication	No. of Patients (n=440)	% of patients
1^0 & 2^0 Prevention of CHD and CVD	277	62.87%
Hyperlipidemia	129	29.38%
Hyperlipemia	34	7.74%

TABLE 8 shows the various indications for which statins prescribed in which 62.87% was indicated for 1^0 & 2^0 prevention of CHD and CVD followed by 29.38% for hyperlipidemia and 7.74% for hyperlipemia. (P-value <0.05)

Fig. 8: Indication for Statins



Among the patients under study, statins were prescribed for primary and secondry prevention of CHD and CVD in 277 patients (62.87%), Hyperlipidemia in 129 patients (29.38%) and Hyperlipemia in 34 patients (7.74%) -table 8 and figure 8.

Statins were prescribed under the strengths of 10 mg, 20mg, 40 mg and 80 mg depending on the severity of the disease. Among 213 (48.52%) patients 10 mg atorvastatin was prescribed which was followed by 20 mg-70(15.95%) patients, 40 mg-91 (20.73%) and 80mg in 1(0.23%) patient.

Similarly in case of rosuvastatin, the drug was prescribed 10mg among 18 (4.10%) patients and 20 mg among 24 (5.47%) patients. Simvastatin 10 mg was prescribed among 12 (2.73%) patients followed by 20 mg among 12 (2.05%) patients (Table 9 and Figure 9). During the study a few possible drug-drug interactions were also observed. Major possible interactions caused by verapamil (calcium channel blocker) were observed in 10 (2.28%) prescription and moderate interactions caused by digoxin and phenytoin was seen in 84 (19.13%) prescriptions (Table 10, Figure 10) without causing any harm to the patients.Total defined daily dose (DDD) and cost of total defined daily dose (DD) of various dose strength of atorvastatin, simvastatin and rosuvastatin has been shown in table no. 11, 12 and 13 respectively.

Costs of prescribed brands of statins (per tablet) have been indicated in table no.14.

Table 15 indicates the use of ATC/DDD methodology as developed by WHO DUR group. The DDD/1000 /day was

Fig. 9: Doses Prescribed in study Population

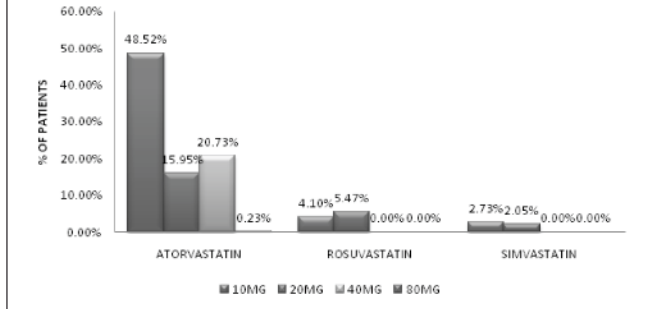


Table 9: Doses Prescribed in Study Population

Statin	Percentage of patients (10mg)	Percentage of patients (20mg)	Percentage of patients (40mg)	Percentage of patients (80mg)
Atorvastatin	213(48.52%)	70(15.95%)	91(20.73%)	1(0.23%)
Rosuvastatin	18(4.10%)	24(5.47%)	0(0.00%)	0(0.00%)
Simvastatin	12(2.73%)	9(2.05%)	0(0.00%)	0(0.00%)

In table 9 it was found that 10mg oral formulation of Atorvastatin (atorva-60 patients and tonact-47 patients) was prescribed highest followed by 20 and 40 mg formulations. Rosuvastatin and Simvastatin were least prescribed. (P-value <0.05)

Fig. 10: Drug-Drug Interactions

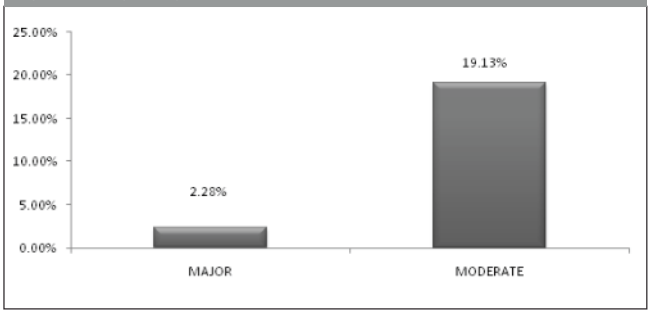


Table 10: Possible Drug-Drug Interactions

Interactions	No. of Patients (n=440)	% of patients
MAJOR(Verapamil)	10	2.28%
MODERATE(Digoxin, Phenytoin)	84	19.13%
TOTAL	94	21.41%

Drug-drug interactions were found in 94(21.41%) prescriptions has shown moderate interactions without causing harm to the patients.

Table 11: Defined Daily Dose of Statins (Atorvastatin)

Dose	DDD	Units	Total DDD	Total cost (Rs.)
10mg	0.5	213	106.5	2128.48
20mg	1	70	70.0	1071.03
40mg	2	91	182.0	1691.20
80mg	4	1	4.0	27.780
Total	**-**	**375**	**362.5**	**4918.49**

Table 12: Defined Daily Dose of Statins Simvastatin

Dose	DDD	Units	Total DDD	Total cost (Rs.)
10mg	0.333333	9	2.9997	94.5
20mg	0.666667	12	8.000004	208
Total	**-**	**21**	**10.9997**	**302.5**

Table 13: Defined Daily Dose of Statins Rosuvastatin

Dose	DDD	Units	Total DDD	Total cost (Rs.)
10mg	1	18	18	212.1
20mg	2	24	48	675.18
Total	**-**	**42**	**66**	**887.28**

Table 14: Cost (in Rs.) of Different Brands of Statinsprescribed (per Tablet)

Brand	10mg	20mg	40mg	80mg
Atorva	9.4	17.85	19	27.78
Tonact	10.6	12.02	17.4	-
Xtor	7.5	12	18	-
Storvas	9.33	18	-	-
Tonact-tg	13.83	-	-	-
Atorlip	8.55	-	-	-
Aztor	8.3	15.2	19.8	-
Caat	8.7	-	-	-
Stator	3.69	-	-	-
Statix	6.9	-	-	-
Atorva-ez	16	-	-	-
Simvotin	11	18.5	-	-
Simcard	9.43	15	-	-
Crestor	18	32	-	-
Rosuvas	11.55	26.54	-	-

found to be 6.88(82.59%) doses for atorvastatin, 0.2(2.40%) doses for Simvastatin and 1.25(15%) for Rosuvastatin. The DDD/12 bed days were found to be 82.32, 2.4, and 15 for the three statins respectively. the prescribed daily dose and the defined daily dose were as follows atorvastatin 19.33mg;20mg, Simvastatin 15.73mg;30mg, and for Rosuvastatin 15.73mg;10mg. The cost of the three statins according to the amount utilized was found to be 4918,302 and 887 rupees respectively.

DISCUSSION

The role of a pharmacist in clinical settings has undergone a revolutionary change. Today a pharmacist is not confined to the task of dispensing medicines only, but shoulders the responsibility in the mission of providing drug therapy to a patient in order to alleviate/cure illness. Pharmacists are trained to provide specialist services- health screening, diabetes care, immunizations, patient education on disease and medicines, nutrition, anticoagulation, chemotherapy and many more. Pharmacists are trained in the basic principles of drug education. This includes acquiring and understanding

Table 15: Drug Utilization Metrics

STATIN	SATC code	Total No. of Patients (n= 440)	Precribed strength (mg)	DDD (mg)	Total DDDs	DDD/1000 inhabitants Day	DDD/12 bed days	PDD (mg)	Cost (Rs.)
ATORVA STATIN	C10AA05	376	10,20,40,80	20	362.5	6.86	82.32	19.33	4918.49
SIMVA STATIN	C10AA01	21	10,20	30	10.99	0.2	2.40	15.73	302.5
ROSUVA STATIN	C10AA07	43	10,20	10	66	1.25	15.00	15.73	887.28

drug information, focus on drug use problems, drug utilization reviews, verbal skills in patients counseling, etc.,. These skills are acquired with the objective of providing optimal patient care.

As statins are heavily used in this large corporate 1765 bedded hospital, this short term study was done to give an insight of utilization of statins in our hospital. Several studies have shown the incidence of an increase in usage of statins.[7, 9, 10, 11, 12, 13, 14]

Patient who were prescribed statins have the presence of established hyperlipidemia, stroke, diabetes, cardiovascular disorders, which indicates the essential need for statin therapy as per national cholesterol education program (NCEP) adult treatment panel (ATP) III[8].

Our study has generated data on optimal use of statins and we find that statins have been prescribed from age ranging 26 to 85 years with most patients in the 60 – 70 age group. Prescribing for statins has shown a gradual increase with an increase in the age of the patients and declined with age >75 years, indicating the prevalence of high morbidity in the 60 – 70 age group.

Atorvastatin (atorva, tonact) was the most prescribed statin in the study and though 10 mg was prescribed to more number of patients (48.52%) the PDD (prescribed daily dose) in the total population of 440 patients was found to be 19.33mg. WHO[2] has recommended a DDD of 20mg and our usage is in accordance. Prescription data on the utilization of statins is expressed as DDD/1000 patients/day. It is only an average assumed maintenance dose but the prescribed daily dose differs from the defined daily dose as it is based on individual patient characteristics. This indicates our cautious use of statins.

The DDD/12 beds days were calculated according to WHO[2] recommended method and it was found to be 82.32 for Atorvastatin, 2.4 for simvastatin and 15 for Rosuvastatin. This indicates that 82.32% of statin users might receive a DDD of Atorvastatin in our hospital, but only 2.4% and 15% of statin users might receive simvastatin and Rosuvastatin respectively.

Though there are several equivalent statins the pricing for the different brands vary greatly, Simvastatin though low priced is less prescribed has Atorvastatin is preferred because of its better effectiveness and since Rosuvastatin is costlier it is less prescribed.

Similar studies also referred to support the study[15-42]

CONCLUSION

The study clearly indicates that HMG-CoA reductase inhibitors (statins) were used within locally and internationally accepted dosage ranges. The dosages used for Atorvastatin were generally closer to the maintenance dose recommended by WHO. Whereas, a slight difference seen in case of Simvastatin and Rosuvastatin.

REFERENCES

1. WHO Expert Committee. The Selection of Essential Drugs, Technical Report Series no. 615. Geneva: World Health Organization, 1977.
2. Einarson T. Pharmcoepidemiology. In: Parthasarathi G, Hansen KN, Nahata MC, editors. A Text book of Clinical Pharmacy Practiceessential concepts and skills. 1st ed., Hyderabad: Universities Press (India) Limited; 2008. p.405-23.
3. Gama Helena, Drug Utilization Studies-ARQUIVOS DE MEDICINA, 22(2/3):69-74.
4. Introduction to drug utilization research/WHO International Working Group for Drug Statistics Methodology, WHO Collaborating Centre for Drug Statistics Methodology, WHO Collaborating Centre for Drug Utilization Research and Clinical PharmacologicalServices; 21-3.
5. P D Sachdeva. Drug Utilization Studies- Scope and future perspectives; Intern Jour Pharmaceut Biolog Res 2010;1(1):11-7.
6. FolkeSjoqvist, Donald Birkett. Introduction to Drug Utilization Research- Drug Utilization 2003, ISBN 92 4 156234X (with the permission of the WHO Office of Publications -Mr. D.W. Bramley).Ch.10; 83- 4.
7. Jones, P. Comparative dose efficacy study of atorvastatin versus simvastatin, pravastatin, lovastatin, and fluvastatin in patients with hypercholesterolemia (The CURVES Study). The American Journal of Cardiology 1998 Mar 1;81(5):582-7.
8. Paola Deambrosis, Cristina Saramin, Gianni Terrazzani. Evaluation of the prescription and utilization patterns of statins in an Italian local health unit during the period 1994–2003. Eur J Clin Pharmacol 2007;63:197–203.
9. Edmundas K. Policy implications of rationalization of statin use in Lithuania, Intern Jour of Tech Assessment in Health Care 2009;25:3:419–24.
10. Truter, T. J van W. Kotze. A drug utilisation study investigating prescribed daily doses of hypolipidaemic agents. SAMJ 1996;86(11):1397-1401.
11. Suwansuksree N, Thamlikitkul V, Yamwong P. Drug use evaluation of statins at Siriraj Hospital. Basic Clin Pharmacol Toxicol 2005 Apr;96(4):289-94.
12. T. Walley, P. Folino-Gallo, P. Stephens. Trends in prescribing and utilization of statins and other lipid lowering drugs across Europe 1997–2003. *Br J Clin Pharmacol, 2005;*60(5):543–51.
13. Pasternak RC. ACC/AHA/NHLBI clinical advisory on the use and safety of statins. Journal of the Amer Col of Card 2002;40:567-72.
14. Joshua S. Benner; Robert J. Glynn; Helen Mogun. Long-term Persistence in Use of Statin Therapy in Elderly Patients. *JAMA* 2002;288(4):455-61.
15. IngeborgHartz, SolveigSakshaug, Kari Furu, Aspects of statin prescribing in Norwegian counties with high, average and low statin

consumption – an individual-level prescription database study, *BMC Clin Pharmacol* 2007.

16. G. Trifiro, M. Alacqua, S. Corrao. Lipid lowering drug use in Italian primary care effects of reimbursement criteria revision. Eur J Clin Pharmacol 2008;64:619-25.
17. Richard c. Pasternak, sidney c. Smith, c. Noel bairey-merz. ACC/AHA/NHLBI clinical advisory on the use and safety of statins. Jour of the Amer col of card 2002;40(3).
18. Yvan BL Tran, Tony Frial1, Paul SJ Miller. Statin's Cost-Effectiveness: a Canadian analysis of commonly prescribed generic and brand name statins. Can J Clin Pharmacol 2007;14(2):e205-e214.
19. Jeffrey J. Ellis, Steven R. Erickson, James G. Stevenson. Suboptimal Statin Adherence and Discontinuation in Primary and Secondary Prevention Populations J GEN INTERN MED 2004;19:638–45.
20. B. Jonsson, M. Johannesson, J. Kjekshus et al Cost-effectiveness of cholesterol lowering Results from the Scandinavian Simvastatin Survival Study (4S) *European Heart Journal* 1996;17:1001-100.
21. Maria J. Silveira, Anamariasegninikazanis, Matthew p. Shevrin. Statins in the last six months of life: a recognizable,Life-limiting condition does not decrease their use. Jour of palliative med 2008;11(5):688-93.
22. Gregg C. Fonarow, william J. French, lori S. Parsons. Use of Lipid-Lowering Medications at Discharge in Patients with Acute Myocardial Infarction. Circulation 2001;103:38-44.
23. Susan M. Abughosh, stephen J. Kogut, susan E. Andrade, persistence with lipid-lowering therapy: influence of the type of Lipid-lowering agent and drug benefit plan option in elderly patients. *J manag care pharm* 2004;10(5):404-11.
24. Grundy SM, Benjamin IJ, Burke GL. Diabetes and cardiovascular disease. a statement for healthcare professionals from the American Heart Association. *Circulation* 1999;100:1134–46.
25. Michael H. Davidson et al Safety Profiles for the HMG-CoA Reductase Inhibitors Treatment and Trust, Drugs 2001;61(2):197-206.
26. Peter L, Martin B, Thomas K. Cost-effectiveness of atorvastatin for the prevention of coronary and stroke events: an economic analysis of the Anglo-Scandinavian Cardiac Outcomes Trial—lipid-lowering arm (ASCOT-LLA). Eur J Cardiovasc Prev Rehabil 2005:30-5.
27. Smart J, Waiters L. Pharmacoeconomic assessment of the HMG-CoA reductase inhibitors SAMJ 1994;84(12):838-42.
28. Jones, P. Comparative dose efficacy study of atorvastatin versus simvastatin, pravastatin, lovastatin, and fluvastatin in patients with hypercholesterolemia (The CURVES Study). The Amer Jour of Card 1998 Mar 1;81(5):582-7.
29. Heiner K Berthold, IoannaGouni-Berthold, Michael Bohm, Patterns and predictors of statin prescription in patients with type 2 diabetes. *Cardiovasc Diabet* 2009;8:25.
30. Alan S. Go, Wendy Y. Lee, Jingrong Yang, Statin Therapy and Risks for Death and Hospitalization in Chronic Heart Failure. JAMA November 1 2006;296(17):2105-13.
31. SuleApikogluRabus Æ Fikret V. Izzettin, MesutSancar, Five-year follow-up of drug utilization for secondary prevention in coronary artery disease, Pharm World Sci 2008;30:753–8.
32. Susan A. Abookire, Andrew S. Karson, Julie Fiskio. Use and Monitoring of "Statin" Lipid-Lowering Drugs Compared With Guidelines. Arch Intern Med 2001;161:53-8.
33. Ryan P. Morrissey, George A. Diamond, Sanjay Kaul. Statins in Acute Coronary Syndromes. Jour of the Amer Col of Card 2009;54(15):1425–33.
34. VardaShalev, Gabriel Chodick, Haim Silber. Continuation of Statin Treatment And All-Cause Mortality. Arch Intern Med 2009;169(3):260-8.
35. Nanette K. Wenger, Sandra J. Lewis, David M. Herrington. Outcomes of Using High- or Low-Dose Atorvastatin in Patients 65 Years of Age or Older with Stable Coronary Heart Disease. Ann Intern Med 2007;147:1-9.
36. James shepherd. Intensive Lipid Lowering With Atorvastatin in Patients With Coronary Artery Disease, Diabetes, and Chronic Kidney Disease. Mayo Clin Proc August 2008;83(8):870-9.
37. Douglas G Manuel, Kelvin Kwong, Pete Tanuseputro. Effectiveness and efficiency of different guidelines on statin treatment for preventing deaths from coronary heart disease: modelling study. BMJ 2006;332(17):1419–22.
38. Ryan P. Morrissey, George A. Diamond, Sanjay Kaul. Statins in Acute Coronary Syndromes: Do the Guideline Recommendations Match the Evidence? J Am Coll Cardiol 2009;54;1425-33.
39. The Scandinavian Simvastatin Survival Study Group. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). Lancet 1994;344:1383-89.
40. Blasetto J. Efficacy of Rosuvastatin Compared with Other Statins at Selected Starting Doses in Hypercholesterolemia Patients and in Special Population Groups. Amer Jour of Cardiol 2003;91(suppl 1):3C-10C.
41. Karol E. Watson. Potential Clinical and Economic Impact of Statin Formulary Management, Jour of Managed Care Medicine ;9(4):18-22.
42. Peter H. Jones. Comparing HMG-CoA Reductase Inhibitors. Clin. Cardiol 2003;26(Suppl. 1):I15–I20.