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Evaluation of Statin Prescribing Guidelines, Practices, Safety, Efficacy, and Pharmacoeconomic Study of Chronic Statin Therapy

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Abstract

Hyperlipidemia is a medical health condition, defined as increased total cholesterol, low-density lipoprotein cholesterol or triglycerides and low high-density lipoprotein cholesterol or a combination of such abnormalities. Statins are the most commonly used drugs in the present scenario in cardiovascular diseases for dyslipidemia condition. However, recent studies have shown a wide range of interventions regarding its use in patients receiving statin therapy. This study aims to evaluate various parameters that contribute in the choice of statin therapy which includes the prescribing habits of statins in accordance with the guidelines, safety, efficacy; prevalence of adverse drug reaction associated with statins and cost effectiveness analysis of statin tablets of different brands which are varying in their price. A hospital-based prospective study was conducted in Cardiology Department of Aster Prime Hospital, Hyderabad. A total of 170 cases were collected in case collection forms. Data in relation to age, gender, investigations done to obtain final diagnosis, and type of statin therapy opted based on the diagnosis made were collected. The results of the study are validated statistically using SPSS software which incorporates mean, standard deviation method, t test, and Chi-square test. Results obtained illustrate that Rosuvastatin was associated with less adverse effects and is considered to be more cost saving, safe, and efficacious when compared with Atorvastatin. It is crucial to find an effective and an equally safe treatment of statins to reduce the further risk of comorbidities associated with hyperlipidemia.

Keywords: Adverse drug reaction, Atorvastatin, Cost-effectiveness, Hyperlipidemia, Rosuvastatin

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Introduction

The foremost cause of death worldwide is cardiovascular diseases (CVD).[1,2] of nearly 235 per 100,000 populations death rates.[3,4] In the enormous majority of patients, CVD is especially endorsed to atherosclerosis. In the development of atherosclerotic CVD (ASCVD) involves a variety of biological processes, high plasma cholesterol levels are thought to play a key causative role.[4,5] Therefore, the ideal treatment of hypercholesterolemia-induced cardiovascular-associated diseases, which embraces ASCVD, includes the use of statins, which are greatly effective in reducing the cholesterol levels.[4,6] Hyperlipoproteinemia describes an increased concentration of the lipoprotein macromolecules that transmitted lipids in the plasma. Plasma lipids abnormalities may lead to predisposition to coronary, cerebrovascular, and peripheral vascular arterial disease.[7]

The countries consuming a Western type of diet generally consuming higher Total Cholesterol and Low Density Lipoprotein (LDL)-Cholesterol levels differ from those where even consumption of saturated fat is low.[8] In the Prospective Cardiovascular Munster study, an enormous empiric study, mild hypertriglyceridemia (triglycerides >200 mg/dL) was more prevalent in men (18.6%) starting at age 30 years than in ladies (4.2%) beginning at age 60 years. Triglycerides increase gradually in men till regarding age 50 years and so decline slightly. In women, they still increase with age.[9] Primary hyperlipidemia usually occurs as a result of genetic problems, that is, mutation within receptor protein and secondary hyperlipidemia arises as a result of alternative underlining diseases such as myxoedema, diabetes, nephritic syndrome, and chronic alcoholism, with use of medications such as corticosteroids, oral contraceptives, and beta blocker.[9]

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Statins, a class of cholesterol-lowering medications that inhibit 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase are effective in key prevention of CVS diseases and the 2013 ACC-AHA guidelines recommended the use of statins to treat more people, save additional lives, and charge less.[10]

Statin medications appear to be safe for use in the vast majority of patients. However, patients with multiple medical comorbidities are at highest risk of adverse effects from long-term statin. Myalgia is the most common side effect of statin use, with a range of 1–10%.[11] In patients with intolerance to statin, it advises to alter the dose, switch to a unique medicinal drug, or implement alternate-drug regimen.[12]

Pharmacoeconomic analysis identifies, measures, and compares the prices and consequences of medicinal products and services. The research methods such as cost-minimization analysis (CMA),

cost-effectiveness analysis (CEA), cost-benefit analysis (CBA), cost-of-illness, cost-utility, and cost-consequences are included in pharmacoeconomics analysis to improve the quality of human life.[13]

Hence, the main aim of the present work is to carry out a prospective observational study, to evaluate various parameters that contribute in the choice of statin therapy which includes the prescribing habits of statins in accordance with the guidelines, safety, efficacy, and comparison of altered marketed statin drugs of same doses with variable costs by appropriate statistical test thus as to apply the CMA or CEA of pharmacoeconomics to the statin drugs, to conclude the relation between the cost and effectiveness.

Materials and Methods

Site of Study

The study was conducted in the Cardiology Department in Aster Prime Hospital, Ameerpet, Hyderabad, Telangana, India.

Ethics Approval

The study was carried out with the approval of the Institutional Ethical Committee with an Ethics approval number AP/EC/2019/06.

Study Design

A prospective study was carried out to study the use of hypolipidemic drugs called Statins in patients with hyperlipidemia.

Study Duration

The study is carried out for 6 months, that is, from September 2019 to February 2020 in the Cardiology Department.

Sample Size

The present study was carried out on 170 patients who have CVD with hyperlipidemia.

Study Procedure

The following data were collected:

1. Details of the patients such as age, gender, height, weight, body mass index, and diet.
2. Chief complaints, history of present illness, medical history, and past medications
3. Patient's Diagnosis, Comorbid conditions, Investigations done for obtaining Final diagnosis and Plan of care.
4. Current medications (drugs prescribed, brand/generic, dose, route, frequency, and duration).
5. Patient case collection form, treatment charts, and laboratory reports.
6. Software used: SPSS Version 17.

Sources of Data

Patient data collection form, medication history form, treatment chart, and laboratory reports.

Selection Criteria

Inclusion criteria

Patients who were diagnosed with hyperlipidemia, prescribed with statins and having a family history of hyperlipidemia of both genders were included in the study.

Exclusion criteria

Pediatrics, pregnant, and lactating women were excluded from the study.

Method of Study

This is a prospective observational study carried out for 6 months in the Cardiology Department of Aster Prime Hospital, Hyderabad. A minimum of 170 cases of hyperlipidemia along with comorbidities were collected. A suitable data collection form was designed to collect demographic details of patients. Data about age, gender, diagnosis, lab reports, and statin therapy (a drug prescribed, brand/generic, dose, route, frequency, and duration) were collected and lab monitoring parameters were routinely followed and the study involved SPSS Software version 17.

Results

Gender Distribution

Out of 170 patients, 110 (64.7%) were male and 60 (35.2%) were female. In our study, it was found that hyperlipidemic patients were more prevalent in males than females. This is depicted in Figure 1.

Age Distribution

A total of 170 patients were grouped according to their age taking 10 as the class interval. Patients were grouped under age groups 21–30 years (3 patients), 31–40 (13 patients), 41–50 (27 patients), 51–60 (49 patients), 61–70 (48 patients), 70–80 (27 patients), and 81–90 (3 patients). The majority of the patients were of the age group of 51–60 years (29%) and the

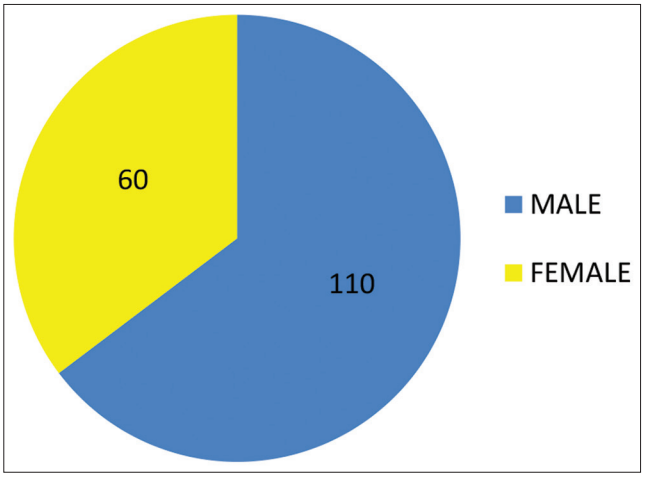

Figure 1: Patient's gender

least was in 21–30 years (1.76%) and 81–90 years (1.76%). This is depicted in Figure 2.

Distribution of Study Population Based on Disease Condition

Evaluation of patient characteristics data showed that out of 170 patients, 53% were indicating for CAD + MI + Hyperlipidemia, 25% were indicating for Angina + Hyperlipidemia, 15% were indicating for newly detected hyperlipidemia, and 7% were indicating for CVA Stroke + Hyperlipidemia. This is depicted in Figure 3 and Table 4.

Distribution of Study Population Based on Social History

The distribution of the study population based on social history was assessed. The common of the male patients were smokers with 31% (n = 52) and female patients were alcoholics with 17% (n = 29). The P-value was calculated using the Chi-square test which is equal to 0.0001 and a significant difference was found between the genders in the social history. This is depicted in Figure 4.

Distribution of Statin Use

Different type of statins was prescribed in the treatment of the patients suffering from hyperlipidemia which are categorized based on the number of patients using them. This is depicted in Table 5. The majority of the patients were prescribed with ATORVASTATIN (45%) and least with a combination of ATORVASTATIN + CLOPIDOGREL (8%). This is depicted in Figure 5.

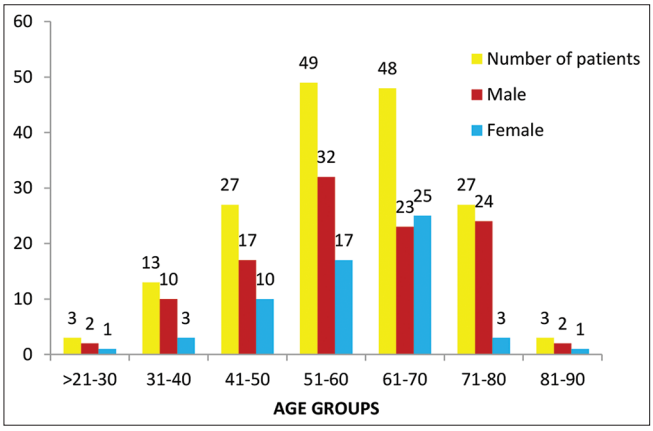

Figure 2: Demography of age groups

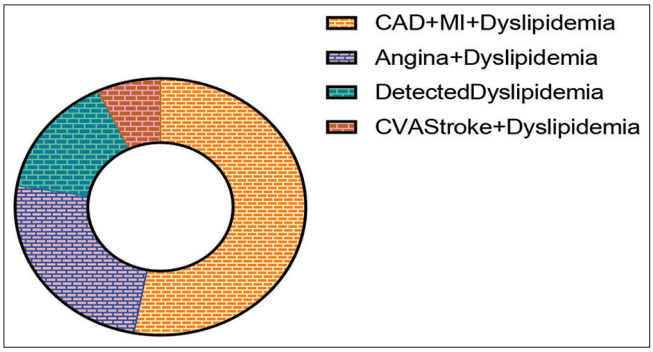

Figure 3: Distribution of study population based on disease condition

Proportion of Adverse Drug Reaction (ADR)

The proportion of ADR in a total of eight patients with different statins used was assessed. The major ADR found was Myopathy in 4.7% of the population. The P-value was calculated using the Chi-square test which is equal to 0.2093, that is, >0.05 which indicates no statistically significant difference was found. This is depicted in Table 8 and Figure 6.

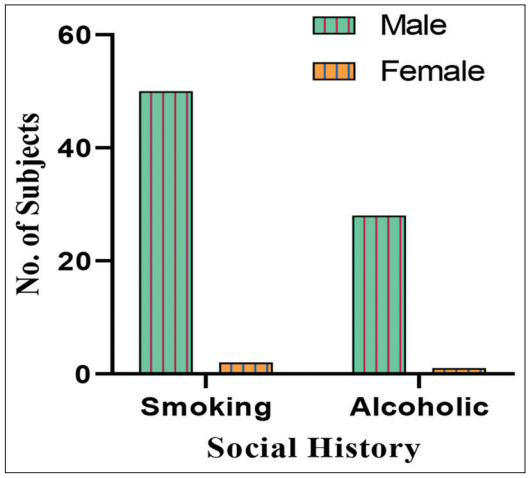

Figure 4: Distribution of study population based on social history

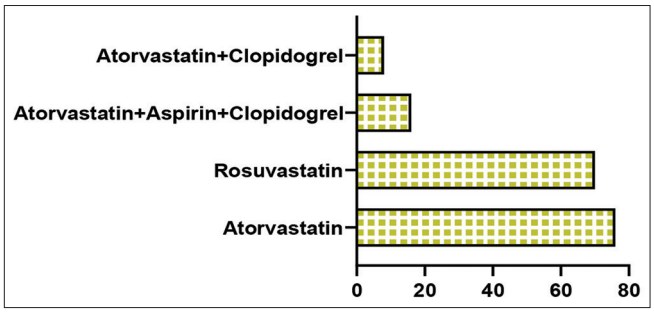

Figure 5: Distribution of statin use

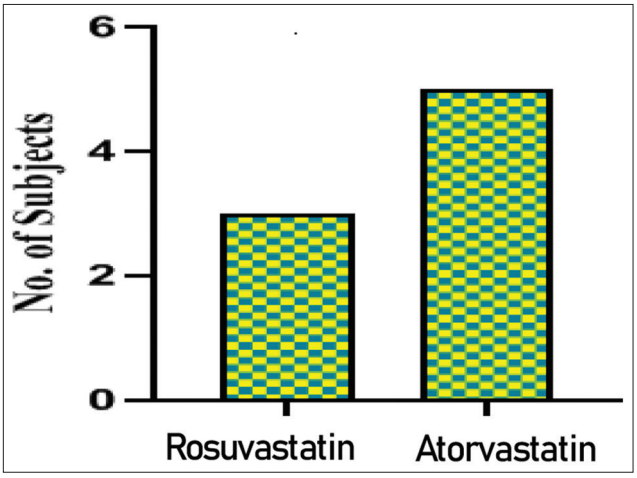

Figure 6: Proportion of adverse drug reaction

Table 1: Comparison of statin prescribing international guidelines

Guidelines	*Low Intensity Statins*	*Medium Intensity Statins*	*High Intensity Statins*
ACC/AHA-2013 (American College of Cardiology/American Heart Association)	≤30% LDL-C reduction Atorvastatin-20–40 mg Lovastatin-20 mg Simvastatin -10 mg Pravastatin-10–20 mg	30–49% LDL-C reduction Atorvastatin-10–20 mg Rosuvastatin -5–10 mg Simvastatin -20–40 mg Pravastatin -40 mg Fluvastatin -40 mg	≥50% LDL-C reduction Atorvastatin-80 mg Rosuvastatin-20–40 mg
ESC/EAS-2016 (European Society for Cardiology/European Atherosclerosis Society Guidelines)	20–30% LDL-C reduction Fluvastatin-40 mg Pravastatin-20–40 mg Lovastatin-10–20 mg Simvastatin-10 mg	31–40% LDL-C reduction Atorvastatin-10 mg	≥40% LDL-C reduction Atorvastatin-40 mg Rosuvastatin-40 mg Pitastatin-2–4 mg
NICE (National Institute for Health and Care Excellence)	20–30% LDL-C reduction Atorvastatin-20 mg Fluvastatin-20 mg Pravastatin-20–40 mg	31–40% LDL-C reduction Atorvastatin-10 mg Rosuvastatin-5 mg Simvastatin-20–40 mg	≥40% LDL-C reduction Atorvastatin-20–80 mg Rosuvastatin -10–40 mg Simvastatin-80 mg
PoLA -2016 (Polish Lipid Association)	<50% LDL-C reduction Atorvastatin -10–20 mg Rosuvastatin -5–10 mg	Minimum 50% LDL-C reduction Atorvastatin -20–40 mg Rosuvastatin -10–20 mg	50–60% LDL-C reduction Atorvastatin -40–80 mg Rosuvastatin -20–40 mg

Table 2: Distribution of study population based on social history

S. No	*Social History*	*Gender*		*Total*		*P value*
		Male	*Female*	*N*	*%*	
1	Smoking	50	2	52	31	<0.0001
2	Alcoholic	28	1	29	17	<0.0001

P value calculated by Chi-square test. Statistically significant difference was found in the social history between the genders

Table 3: Gender wise age distribution

Gender	*Minimum*	*Maximum*	*Mean±SD*	*P value*
Male	21	89	58.80±13.42	0.0612
Female	34	91	58.53±10.39	

P value calculated by Independent *t*-test. Statistically significant difference was not found in the age between the genders.

Table 4: Distribution of study population based on diagnosis

S. No	*Condition*	*n*	*%*
1	CAD+MI+Dyslipidemia	90	53
2	Angina+Dyslipidemia	42	25
3	Detected Dyslipidemia	26	15
4	CVA Stroke+Dyslipidemia	12	7

TABLE 5: Distribution of statin use

S. No	*Drug*	*n*	*%*
1	Atorvastatin	76	45
2	Rosuvastatin	70	41
3	Atorvastatin+Aspirin+Clopidogrel	16	9
4	Atorvastatin+Clopidogrel	8	5

CMA

- The CMA between different brands of Atorvastatin was assessed. The brand of TONACT provided the least percentage of saving (0%) followed by ATORVA(17%), ATORLIP (28%), ATOCOR (44%), and the brand LIPVAS showed highest cost minimization of 50% by 108 rupees. This is depicted in Table 9a.
- The CMA between different brands of Rosuvastatin was assessed. The brand of ARVAST provided the least percentage of saving (0%), followed by CRESTOR (3%), CREVAST (6%), ZYROVA (11%), NOVASTAT (26%), and the brand ROZAT showed highest cost minimization of 53% by 122 rupees. This is depicted in Table 9b.

Table 6: Effect of statin on LDL-C

Drug	*Minimum*	*Maximum*	*Mean±SD*	*P value*
Atorvastatin	17	260	143.4±43.71	0.5359
Rosuvastatin	38	195	147.6±33.30	

P value calculated by Independent *t*-test. Statistically significant difference was not found

Table 7: Effect of statin on HDL

Drug	*Minimum*	*Maximum*	*Mean ± SD*	*P value*
Atorvastatin	06	70	39.32±10.42	0.1464
Rosuvastatin	15	69	41.94±11.86	

P value calculated by Independent *t*-test. Statistically significant difference was not found

Table 8: Proportion of ADR

ADR	*Atorvastatin*	*Rosuvastatin*	*Total*	*%*	*P value*
Muscle weakness	3	5	8	4.7	0.2093

P value calculated by Chi-square test. Statistically significant difference was not found

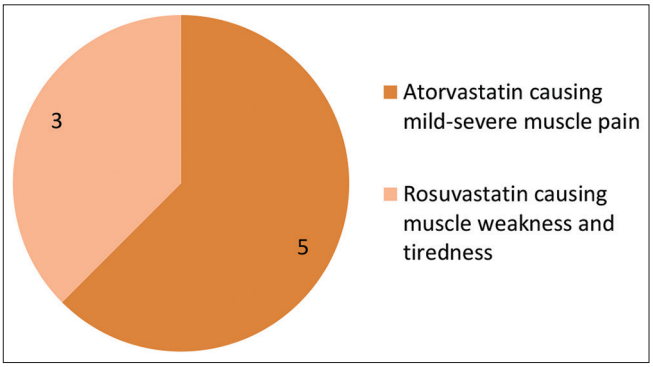

Figure 7: Incidence of adverse drug reaction

Table 9: Cost minimization analysis

Brands	*Units*	*Per Unit Price*	*Total Price*	*Saving Per Drug*	*% Saving*
		(a) Atorvastatin			
LIPVAS	10	11.0	110	108	50%
ATOCOR	10	12.1	121	97	44%
ATORLIP	10	15.8	158	60	28%
ATORVA	10	18.2	182	36	17%
TONACT	10	21.8	218	0	0%
		(b) Rosuvastatin			
ROZAT	10	10.8	108	122	53%
NOVASTAT	10	17.0	170	60	26%
ZYROVA	10	20.5	205	25	11%
CREVAST	10	21.6	216	14	6%
CRESTOR	10	22.4	224	6	3%
ARVAST	10	23.0	230	0	0%
		(c) Atorvastatin+Aspirin+Clopidogrel			
NOKLOT-CV	10	3.6	36	29	45%
ATORVA GOLD	10	4.3	43	22	34%
ECOSPRIN GOLD	10	6.0	60	5	8%
DEPLATT-CV	10	6.5	65	0	0%
		(d) Atorvastatin+Clopidogrel			
ATORFIT-CV	10	12.0	120	77	39%
CLOPITORVA	10	19.7	197	0	0%

- SThe CMA between combination therapies of statins was assessed. The brand of CLOPITORVA provided the least percentage of saving (0%) followed by the brand ATORFIT-CV showed the highest cost minimization of 39% by 77 rupees. This is depicted in Table 9d.

Discussion

The study was carried out at Aster Prime Hospital in Hyderabad. All the patients of hyperlipidemia of both genders under age group 21–91 years on statin drug treatment are included in the study. The demographics, clinical characteristics, diagnosis, and treatment were obtained from case files and documented in predefined suitable data collection forms.

1. Data of 170 patients of hyperlipidemia and its comorbidities were collected and the results were calculated using SPSS version 17. Out of 170 patients, 110 patients were males with 64.7% and 60 patients were females with 35.2%. $P < 0.05$ is considered significant since the Confidence interval is 95%. This is depicted in Figure 1. Evaluation of statin prescribing guidelines has showed the difference between the different guidelines and the effective approach to adapt the lipid lowering therapies based on the evidence and recommendation of guidelines. This is depicted in Table 1. In the present study of 170 patients, 31% ($n = 52$) were smokers and 17% ($n = 29$) were alcoholic. (Statistically significant difference was found in the social history between the genders). This is depicted in Table 2. The patient distribution data according to age group is illustrated in Figure 2. Evaluation of patient characteristics showed that the distribution of study population based on disease condition. This is depicted in Figure 3. The ages of the patients in our study for males are with Mean ± SD: 58.80 ± 13.42 and females with Mean ± SD: 58.53 ± 10.39. Statistically significant difference was not found in the age between the genders. This is depicted in Table 3. Evaluation of patient's treatment chart showed that out of 170 patients, 45% ($n = 76$) were prescribed with Atorvastatin, 41% ($n = 70$) were prescribed with Rosuvastatin, 9% ($n = 16$) were prescribed with a combination of Atorvastatin + Aspirin + Clopidogrel, and 55 ($n = 8$) were prescribed with a combination of Atorvastatin+ Clopidogrel. This is depicted in Table 5. The efficacy of statin on LDL and high density lipoprotein (HDL) were assessed and *P*-value was calculated using Independent t test, statistically significant difference was not found. These are depicted in Tables 6 and 7.
2. The incidence of ADR (i.e. Myopathy) was observed in 8 out of 170 patients after treatment with statins. Among which Atorvastatin showed ADR in five patients out of 8 and Rosuvastatin showed ADR in three patients out of 8. The ADR which was observed to be the highest in the patients treated with Atorvastatin for hyperlipidemia. This is illustrated in Figure 7.
3. The study found that drugs of Atorvastatin, the brand of TONACT provided least percentage of saving (0%), followed by ATORVA (17%), ATORLIP (28%), ATOCOR (44%), and the brand LIPVAS showed highest cost minimization of 50% by 108 rupees. This is depicted in Table 9a. For drugs of Rosuvastatin, the brand of ARVAST provided least percentage of saving (0%), followed by CRESTOR (3%), CREVAST (6%), ZYROVA (11%), NOVASTAT (26%), and the brand ROZAT showed the highest cost minimization of 53% by 122 rupees. This is depicted in Table 9b. For combination drugs of Atorvastatin + Aspirin + Clopidogrel, the brand of DEPLATT-CV provided least percentage of saving (0%), followed by ECOSPRIN GOLD (8%), ATORVA GOLD (34%), and the Brand NOKLOT-CV showed the highest cost minimization of 45% by 29 rupees. This is depicted in Table 9c. For combination drugs of Atorvastatin + Clopidogrel, the brand of CLOPITORVA provided least percentage of saving (0%) followed by the brand ATORFIT-CV showed the highest cost minimization of 39% by 77 rupees. This is depicted in Table 9d.

Conclusion

In our study, we evaluated the utilization of statin prescribing drugs and conclude the safety, efficacy of statin on lipoproteins and cost effectiveness of statin therapy. For optimal use of available statin

prescribing drugs, there are several guidelines published that should be endorsed in the daily clinical practice. Statin prescribed for hyperlipidemic patients in our hospital was appropriate and was in accordance with the NICE GUIDELINES 2014. Statins are usually thought to be safe. However, as with any medication statins may have negative effects in some patients. ADRs from statins, for example, MYOPATHY is dose related. We explore the statin therapy within the light of latest proof and supply clinician with support concerning statin's safety. Treatment with Rosuvastatin-10 mg costs 53% of saving compared with Atorvastatin -10 mg cost 50% of saving. Hence, Rosuvastatin has showed less adverse effects, more percentage of cost saving and highest efficacies in lowering LDL-C levels in hyperlipidemic patients compared to Atorvastatin.

Acknowledgment

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