IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS)
e-ISSN:2278-3008, p-ISSN:2319-7676. Volume 13, Issue 1 Ver. III (Jan. – Feb. 2018), PP 45-53
www.iosrjournals.org

Analyzing the Impact of Statins Use in Type-2 Diabetes Mellitus Patients

Dr .C.Vani [1], B. Laxmi Narayana[2], P. Prashanthi[2], B. Karthik[2]

[1]*Assistant Professor, Pulla Reddy Institute Of Pharmacy, Dundigal, Sanga Reddy(D), Telangana, India*
[2]*Pharm-D Interns, Pulla Reddy Institute Of Pharmacy, Dundigal, Sanga Reddy(D), Telangana, India*
Corresponding author- Dr.C.Vani,

Abstract
Aim: *To analyze the impact of statins use in type-2 diabetes patients.*
Objective: *To improve the quality of life and to decrease the risk associated with cardiovascular events, to increase the patient compliance towards statin therapy and to increase the awareness among patients about statin therapy and lifestyle modifications. To identify the cost of different statins containing drug brands.*
Methodology: *A prospective observational study was conducted in secondary care centers and data was collected from medical case records,116 diabetic type 2 patients under treatment with stains were interviewed twice and their demographic data(age, gender, education) , statin information ,their serum lipid profile were recorded. In between three months after the initial visits, patients were assessed using questionnaires and also assessed cholesterol ratio. The Framingham Risk Score is a gender-specific algorithm used to estimate the 10-year cardiovascular risk of an individual.*
Results: *Among 150 cases we have found that 116 cases were referred follow up's respectively. From the results, statins have shown the impact in type-2 diabetes condition and the patients impacted by counseling, given by the clinical pharmacist. The cholesterol ratio (HDL, LDL, Total cholesterol) and risk of cardiovascular diseases was decreased which results in quality of life.*
Conclusion: *Impact of statin, as reflected by patient counseling and adherence, is significantly related to cholesterol goal achievement in patients with dyslipidemia. Questionnaires are used to identify patients who are adherent to statin therapy and quality of life.*
Keywords: *Adherence, lipid profile, quality of life, Statin, Type-2 diabetes,*

Date of Submission: 15-01-2018 Date of acceptance: 01-02-2018

I. Introduction

Statins, also known as HMG-CoA reductase inhibitors, are a class of lipid-lowering medications. Statins can competitively inhibit 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, resulting in an effective decrease of low-density lipoprotein (LDL) cholesterol levels, and their use has been proved to decrease major cardiovascular events in both primary and secondary prevention. [2] This is significant because most circulating cholesterol comes from internal manufacture rather than the diet. When the liver can no longer produce cholesterol, levels of cholesterol in the blood will fall. Cholesterol synthesis appears to occur mostly at night, [1] so statins with short half-lives are usually taken at night to maximize their effect. Studies have shown greater LDL and total cholesterol reductions in the short-acting simvastatin taken at night rather than the morning [3,4]. In diabetic patients, primary prevention with statins is recommended or should be considered in nearly all ≥40 years of age, with the intensity of therapy depending on the presence of other cardiovascular risk factors and end-organ damage [5, 6, 7]. Statin therapy should be added to lifestyle therapy, regardless of baseline lipid levels, for diabetic patients

- The primary goal is an LDL cholesterol <100 mg/dl (<2.6 mmol/l) (A); a lower LDL cholesterol goal of 70 mg/dl (1.8 mmol/l), using a high dose of a statin, is an option.
- Without CVD who are over the age of 40 years and have one or more other CVD risk factor. The primary goal is an LDL cholesterol <100 mg/dl (<2.6 mmol/l)
- Statin therapy should be considered in addition to lifestyle therapy if LDL cholesterol remains >100 mg/dl or in individuals with multiple CVD risk factors.

If drug-treated patients do not reach the above targets on maximal tolerated statin therapy, a reduction in LDL cholesterol of >40% from baseline is an alternative therapeutic goal.

1.1 **Link between Diabetes And Heart Disease**

The following statistics speak loud and clear that there is a strong correlation between cardiovascular disease (CVD) and diabetes.

- At least 68 percent of people age 65 or older with diabetes die from some form of heart disease; and 16% die of stroke.
- Adults with diabetes are two to four times more likely to die from heart disease than adults without diabetes.
- The American Heart Association considers diabetes to be one of the seven major controllable risk factors for cardiovascular disease.

Diabetes mellitus (DM) is a group of metabolic disorders in which there are high blood sugar levels over a prolonged period.[8] Symptoms of high blood sugar include frequent urination, increased thirst, and increased hunger. If left untreated, diabetes can cause many complications [9]. Acute complications can include diabetic ketoacidosis, hyperosmolar hyperglycemic state, or death [10]. Serious long-term complications include cardiovascular disease, stroke, chronic kidney disease, foot ulcers, and damage to the eyes [9].Over time, high blood glucose from diabetes can damage your blood vessels and the nerves that control your heart and blood vessels. The longer you have diabetes, the higher the chances that you will develop heart disease. People with diabetes tend to develop heart disease at a younger age than people without diabetes.

1.2 **Diabetes A Major Risk Factor**

A large body of epidemiological and pathological data documents that diabetes is an independent risk factor for CVD in both men and women [11,12,13] Women with diabetes seem to lose most of their inherent protection against developing CVD [11,14]. CVDs are listed as the cause of death in ≈65% of persons with diabetes [15]. Diabetes acts as an independent risk factor for several forms of CVD. To make matters worse, when patients with diabetes develop clinical CVD, they sustain a worse prognosis for survival than do CVD patients ‘without diabetes [16,17,18] . Diabetes is a prime risk factor for cardiovascular disease (CVD). Vascular disorders include retinopathy and nephropathy, peripheral vascular disease (PVD), stroke, and coronary artery disease (CAD). Diabetes also affects the heart muscle, causing both systolic and diastolic heart failure. The etiology of this excess cardiovascular morbidity and mortality is not completely clear. Evidence suggests that although hyperglycemia, the hallmark of diabetes, contributes to myocardial damage after ischemic events, it is clearly not the only factor, because both pre-diabetes and the presence of the metabolic syndrome, even in normo-glycemic patients, increase the risk of most types of CVD [19-22]. .

1.3 **Increased Risk Of Cvd In Diabetic Patients**

Diabetes is treatable, but even when glucose levels are under control it greatly increases the risk of heart disease and stroke. That's because people with diabetes, particularly type-2 diabetes, may have the following conditions that contribute to their risk for developing cardiovascular disease.

Smoking: If you have diabetes, it is important to stop smoking because both smoking and diabetes narrow blood vessels

High blood pressure*:* High blood pressure can strain your heart, damage blood vessels, and increase your risk of heart attack, stroke, eye problems, and kidney problems.

Abnormal cholesterol levels*:* Cholesterol is a type of fat produced by your liver and found in your blood. You have two kinds of cholesterol in your blood: LDL and HDL. LDL, often called “bad” cholesterol, can build up and clog your blood vessels. High levels of LDL cholesterol raise your risk of developing heart disease. Another type of blood fat, triglycerides also can raise your risk of heart disease when the levels are higher than recommended by your health care team.

Obesity and belly fat: Excess belly fat around your waist, even if you are not overweight, can raise your chances of developing heart disease. You have excess belly fat if your waist measures

- more than 40 inches and you are a man
- more than 35 inches and you are a woman

1.4 Risk Assessment

A risk factor is any attribute, characteristic or exposure of an individual that increases the likelihood of developing a disease or injury. Some examples of the more important risk factors are underweight, unsafe sex, high blood pressure, tobacco and alcohol consumption, and unsafe water, sanitation and hygiene. Risks for cardiovascular patients are calculated by the following scale.

Framingham risk score scale:

In our study we used Framingham risk score calculator because risk scores such as the Framingham Risk Score give an indication of the likely benefits of prevention, they are useful for both the individual patient

and for the clinician in helping decide whether lifestyle modification and preventive medical treatment, and for patient education, by identifying men and women at increased risk for future cardiovascular events.[23] Coronary heart disease (CHD) risk at 10 years in percent can be calculated with the help of the Framingham Risk Score. Individuals with low risk have 10% or less CHD risk at 10 years, with intermediate risk 10-20%, and with high risk 20% or more.

Patient Compliance And Medication Adherence:

The World Health Organization defines adherence as the degree to which the person's behavior corresponds with the agreed recommendations from a healthcare provider. Compliance is defined as the degree to which a patient correctly follows medical advice. There is no recognized gold-standard method to measure adherence. There are direct and indirect ways to measure adherence and a combination of these may be needed to accurately quantify adherence in actual practice. Direct methods include directly observing treatment, or measuring the concentration of the drug or metabolite or a biological marker added to the drug in blood or urine. However, these methods tend to be costly and burdensome [24,25]. Indirect methods include questionnaires, pill counts, prescription refill rates, measurement of physiological markers (e.g. LDL-C levels), filling out a medication diary and electronic medication monitoring [26,27].

II. Materials And Methods

We conducted a prospective observational study in patients with type 2 diabetes under treatment with statins. Participants enrolled in secondary care hospital. All patients received a 10min explanation of study protocol and patient compliance towards statin therapy and its significance was explained in simple language by clinical pharmacist. All patients who took statins were identified during 3 months and included to the study. Among enrolled patients who did not have documented LDL-c within 90 days after study inclusion or those who did not keep their scheduled visit 3 months after initial visit were excluded.Totally, 116 patients with diabetes and prescription of statins were included during 3 month sampling period. Clinical pharmacists interviewed patients and filled out demographic data (age, gender, education) and statin information (brand of statin) in data gathering form.In addition, data regarding cholesterol ratio over the same period were included. All patients were asked to return after initial visit to know their adherence and quality of life.

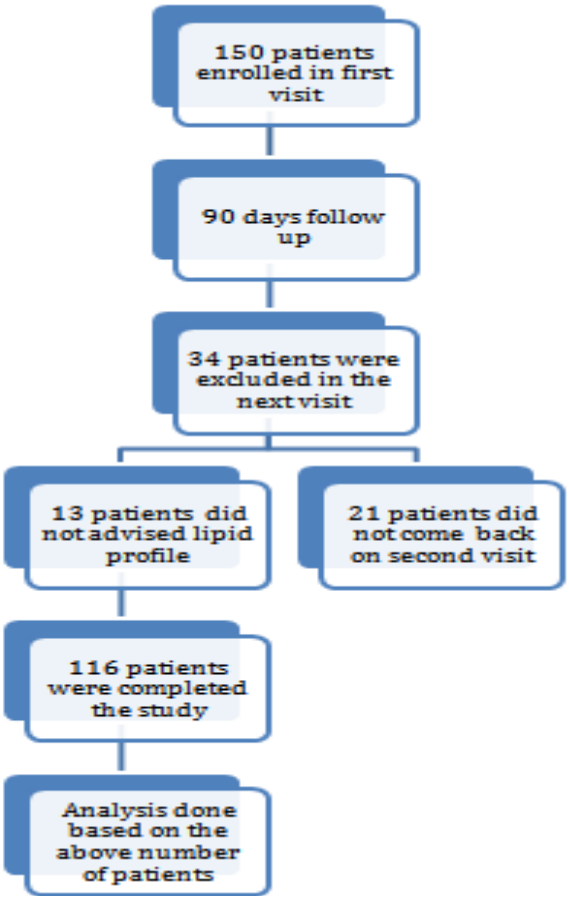


Figure 1: follow-up chart of the studied patients.

Statistical analysis:

Statistical analysis was performed by using Graph pad prism to determine student t-test. A 10 year risk score is calculated by using Framingham risk score.[23] The results are represented as mean, standard deviation and P-value with 95% confidence interval.

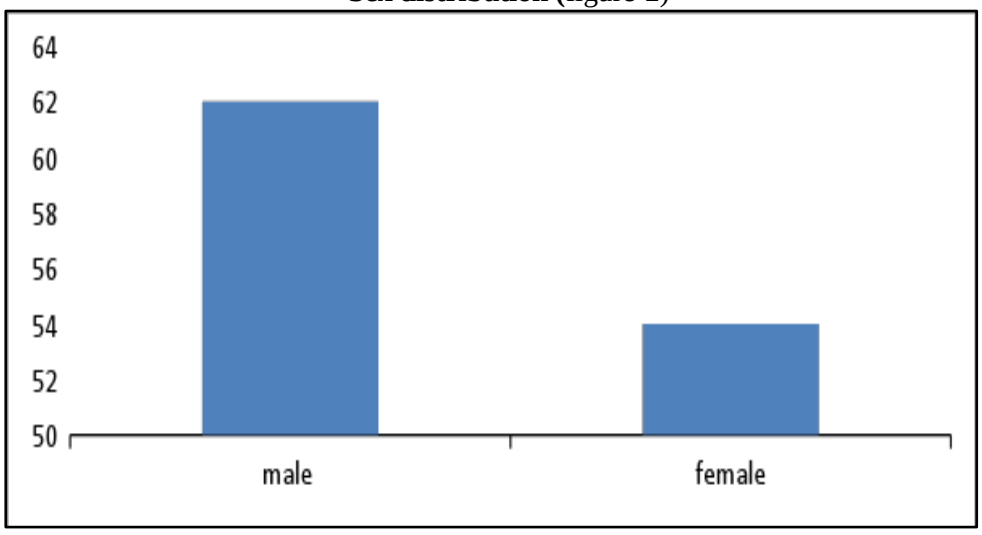
III. Results

Among 150 patients met inclusion criteria, 34 patients were excluded during the study and final analysis were conducted with data from 116 patients who completed the study. Atorvastatin were prescribed to 33 patients and rosuvastatin were prescribed to 32 patients, the combination with clopidogrel, aspirin, and fenofibrate was prescribed with statin. Atorvastatin combination drug were prescribed to 23 patients and rosuvastatin combination were prescribed to 28 patients (Figure-5). Average cost of prescribed statins were shown in (Figure 6) in which atorvastatin average cost were 55.14, atorvastatin combination average cost were 81.59, rosuvastatin average cost were 146.06, rosuvastatin average cost were 124.27Overall, the patients who followed diet and exercise along with statin therapy shown positive results.The study was carried out in patients between age group of 18-80 in which males were (53.4%) and females were (46.5%) (Table-1 and Figure 2). Out of which the patients of age group from 21-30 were (1.7%), 31-40 were (11.2%), 41-50 were (14.6%), 51-60 were (35.3%), 61-70 were (29.3%), 71-80 were 97.7%) (Table-1). The diabetic history of patients with denovo were (9.4%), 1-5 years were (21.5%), 6-10 years were (37.9%), 11-15 years were (19.8%), 16-20 years were (10.3%) and above 20 years were (0.8%) (Table-1 and Figure 4). Compared to initial visits the follow up results had shown the greater impact in which their life style modification were improved , cholesterol ratio was reduced and risk score were decreased which indicates quality of life was increased.(table 3) . The average cholesterol of all patients was assessed (table 5). Among 51 patients, 32 patients were reduced, 5 were stopped, and 14 were not reduced their social history (table 4).

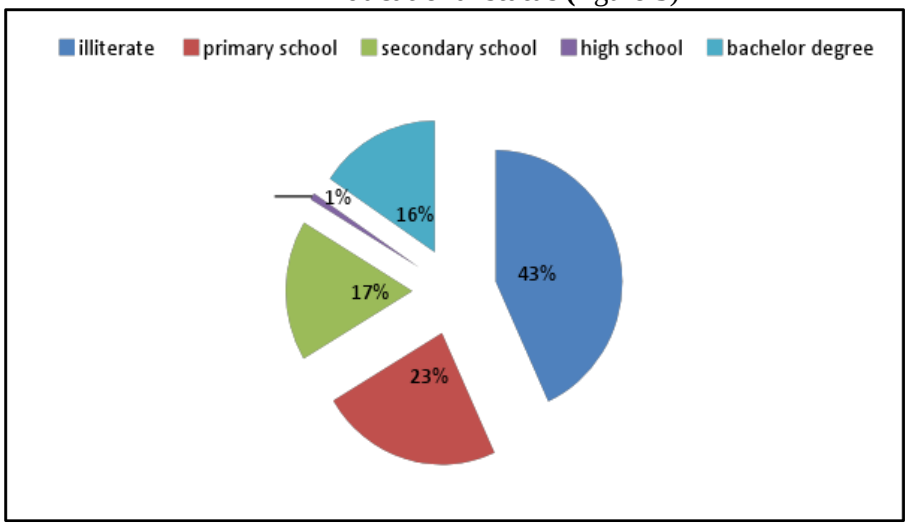
Table-1: demographic characteristics of the studied patients

CHARACTERISTIC	TOTAL	PERCENTAGE
Number of patients	116	100%
Gender		
Male	62	53.4%
Female	54	46.5%
Education		
Illiterate	50	43.1%
Primary school	27	23.2%
Secondary school	20	17.2%
High school diploma	1	0.8%
Bachelor degree	18	15.5%

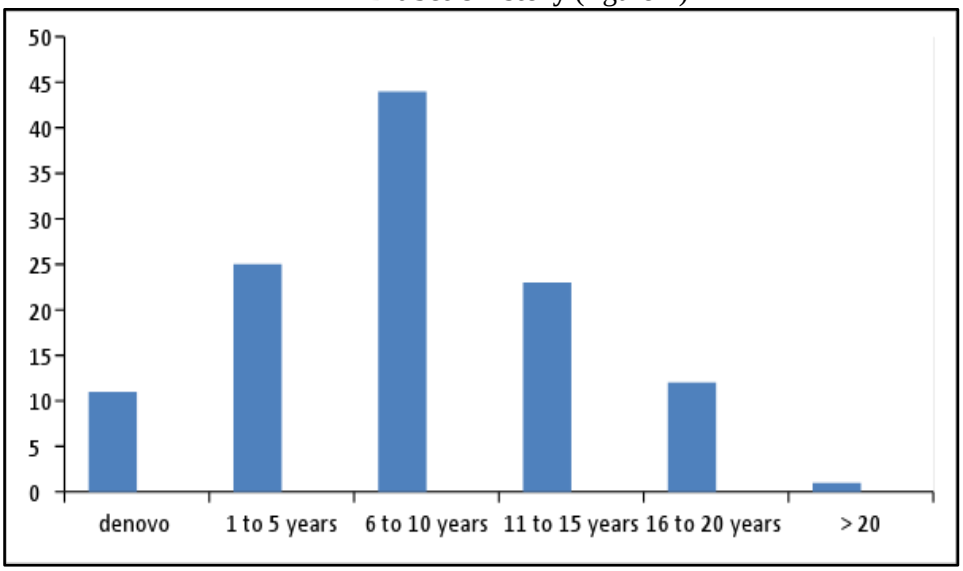
Sex distribution (figure-2)



Educational status (figure-3)



Diabetic history (figure-4)



Types of Statins (figure-5)

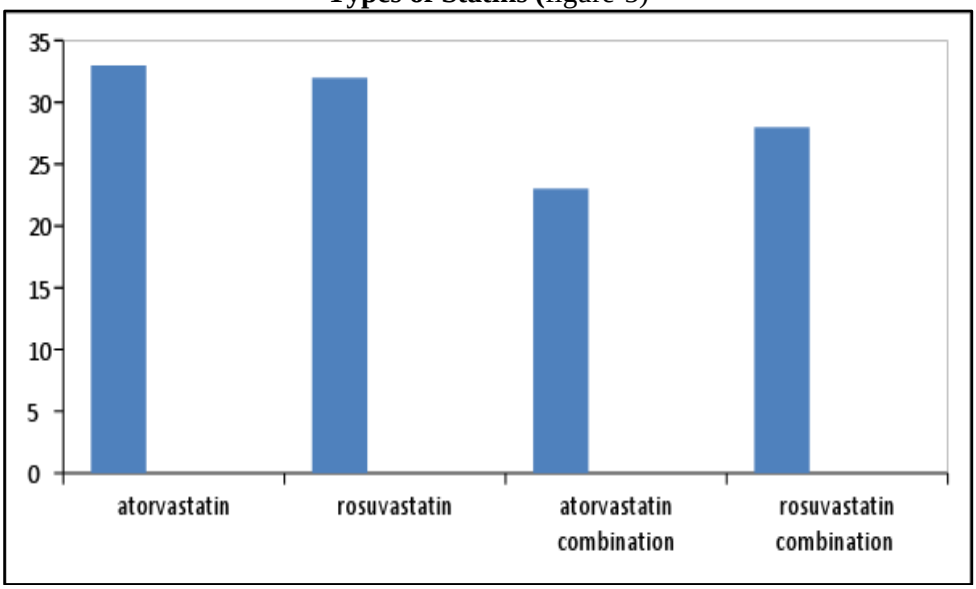
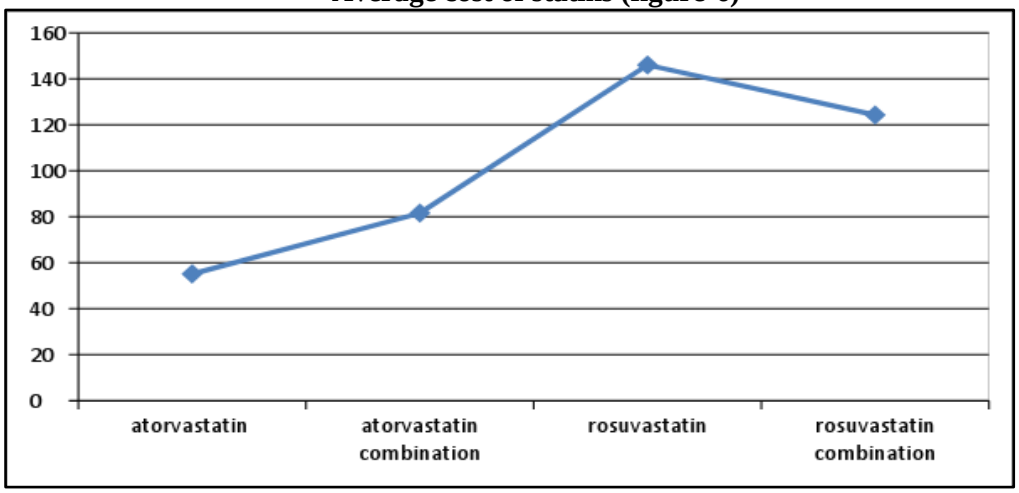


Table 2 Average Cost Of Statins		
Drugs	**Average Cost Of Different Brands**	**Number of drugs**
Atorvastatin	55.14	33
Atorvastatin Combination	81.59	23
Rosuvastatin	146.06	32
Rosuvastatin Combination	124.13	28

Average cost of statins (figure-6)



IV. Discussion

In spite of the importance of impact of statin therapy for achieving therapeutic goals, there are limited reports about impact of statin therapy and its associated factors.eduction in cholesterol ratio was shown to be associated with adherence to therapy and following diet and exercises. Through the questionnaires, the data about patient's adherence to statins was assessed. Our results revealed that according to the questionnaires and obtained data from the case records, three fourth of patients with diabetes were adherent to statin therapy. In addition, both questionnaire and case records agreed in defining adherent and impact of statin. Significant association between adherence and clinical outcomes were also found in similar studies [29,30,32]. In these studies, more than 60%of patients had good adherence to statin therapy especially during the first month of treatment [28-31].Small percentage of our study population had reached cholesterol ratio <4.4 in 98 patients. It is similar to conducted studies reported overall percent of patients with diabetes and dyslipidemia attained their cholesterol ratio less than 100mg/dl [29,33]. Initial findings show that in spite of importance of statin therapy to decrease risk of CHD, the major proportion of patients receiving statin therapy did not achieve cholesterol ratio. Inadequate adherence can be laid at many doors. Poly-pharmacy is common among patients with type 2 diabetes which implies to the prescription of oral hypoglycemic, antihypertensive and lipid lowering medications for an individual. It is also a growing barrier to adherence and attainment of therapeutic goal [34,35]. In addition, limited time spent during clinic visits contributes to inadequate attention to multiple aspects of this care [36].

Table 3: characteristics of statin therapy and associated factors

Characteristics	Females (n=54) (95% CI)			Males (n=62) (95%CI)		
	Baseline	Follow-up	p value	Baseline	Follow-up	p value
Diet						
Followed	19(3.16±2.56)	47(7.83±7.11)	<0.001	28(4.66±4.50)	51(8.5±6.09)	0.002
Not followed	35(5.83±5.94)	7(1.16±1.16)	<0.001	34(5.66±3.67)	11(1.83±1.83)	<0.001
Exercise						
Followed	14(2.33±2.06)	29(4.83±3.54)	0.006	25(4.16±3.06)	48(8±5.55)	<0.001
Not followed	40(6.66±6.37)	25(4.16±5.03)	0.085	37(6.16±4.30)	14(2.33±2.25)	<0.001
Cholesterol ratio						
Low	11(1.83±1.32)	44(7.5±6.38)	<0.001	24(4±2.75)	53(8.83±6.04)	<0.001

Average	41(6.16±6.49)	10(1.66±1.63)	<0.001	35(5.83±4.75) 9(1.5±1.37)	<0.001
Moderate	2(0.4±0.89)	0		3(0.5±0.83) 0	
High	0	0		- -	
Risk score					
<1	5(0.83±1.16)	7(1.16±1.94)	0.179	- 1(0.16±0.40)	
1 -5	30(5±5.29)	42(5.29)	0.222	5(0.83±1.16) 10(1.66±1.63)	0.281
6-10	11(1.83±2.13)	5(0.83±2.04)	0.396	9(1.5±2.34) 16(2.66±3.07)	0.3
11-15	8(1.33±2.42)	0		6(1±1.09) 12(2±2.09)	0.203
16-20	-	-		22(3.66±4.27) 16(2.66±3.01)	0.403
21-25	-	-		10(1.66±1.63) 7(1.16±1.60)	0.541
26-30	-	-		6(1±1.26) -	
>30	-	-		4(0.66±1.03) -	

Data are mean ± SD with confidence interval of 95%

Table 4: Characteristics of social history

Characteristics	Baseline	Follow-up		
		Reduced	Stops	Not reduced
Smokers	31(5.1±3.06)	20(3.33±1.63)	1(0.16±0.40)	10(1.66±1.75)
Alcoholics	20(3.33±2.73)	12(2±1.5)	4(0.66±0.81)	4(0.66±0.81)

Data are mean ± SD.

Table 5: cholesterol goal attainment

CHARACTERISTIC	BASELINE	FOLLOWUP
TOTAL CHOLESTEROL	198.19±38.02	170.4±29.94
HDL	38.95±6.07	47.61±7.49
LDL	135.09±29.42	117.81±21.49
CHOLESTEROL RATIO	5.06±1.1	3.61±0.81
SYSTOLIC BP	138.44±21.29	123.79±8.61
RISK SCORE	18±8.6	12.58±7.03

Data are mean ± SD. LDL= low density lipoprotein, SD= standard deviation, HDL= high density lipoprotein.

It is necessary to increase awareness of the most important causes of non-adherent [37]. Therefore the development of interventions such as asking questionnaires may be useful to improve adherence and to lower cholesterol ratio by explaining the importance of therapy and lifestyle modifications. Another previous study also demonstrated an improvement of health by decreased cholesterol ratio which decreases CHD and related outcomes in patients with type 2 diabetes by involving clinical pharmacist in the multidisciplinary team. However, more studies will be needed to evaluate the effects of different interventions [38]. Prescribing adequate amount of statins between physicians visits is another solution to improve adherence and quality of life. This makes patients sure of having enough available medications to use before physicians visit. After initial visit the patient adherence and impact of statin therapy were assessed.In addition, patient education and better interactions of patient and health care team will have the enormous effect on improving quality of life. Another factor could influence on quality of life was socioeconomic position including patients income. Although because of our local culture, we could not evaluate this factor but a recent cohort study showed a decreased quality of life with decreasing income in patients with established cardiovascular disease especially among men aged 40-64 years [38].There is controversy that increased medication adherence is associated with reduced

healthcare expenses particularly during the years immediately following the onset of diabetes. However, medication adherence can improve health care outcome [39, 40]. Therefore, education regarding statin therapy and life style modifications, adherence is necessary to improve quality of life particularly with low socio economic levels.Risk score was measured by using Framingham which is used to estimate 10 year cardiovascular risk. In our study we used Framingham risk score calculator because risk scores such as the Framingham Risk Score give an indication of the likely benefits of prevention, they are useful for both the individual patient and for the clinician in helping decide whether lifestyle modification and preventive medical treatment, and for patient education, by identifying men and women at increased risk for future cardiovascular events [23]. Coronary heart disease (CHD) risk at 10 years in percent can be calculated with the help of the Framingham Risk Score. Individuals with low risk have 10% or less CHD risk at 10 years, with intermediate risk 10-20%, and with high risk 20% or more.

V. Conclusion

Impact of statin seems to be a significant in health care system for diabetic patients. Emphasis should be put on health care delivery systems and policy organizations to improve health care providers and patient alliance and promote clinical programs to enhance medication adherence.In our study patients who participated in brief face to face counseling sessions with a clinical pharmacist at the beginning of statin therapy demonstrate greater medication adherence in follow up visits and improved their quality of life. Socio-economic burden is seen in patients with low income due to persistent medical advice.

Initially the male patients with social history had high risk of cardiovascular diseases, and may prone to strokes based on past social history, those are reduced their risk by improving adherence and quality of life through effective counseling.

Limitations:

Random selection of patients was done in study. In some patients due to socio-economic burden revisit is not seen. The results can be appropriate when it is done in large scale.

Acknowledgement

We are immensely thankful to Vijay Marie hospital, Relief Clinic, JNTU University, management and principal of Pulla Reddy Institute of Pharmacy, for their constant encouragement and support provided during the study.

References

[1]. Miettinen TA (March 1982). "Diurnal variation of cholesterol precursors squalene and methyl sterols in human plasma lipoproteins". Journal of Lipid Research. 23 (3): 466–73.
[2]. Cholesterol Treatment Trialists' (CTT) Collaboration. Baigent C, Blackwell L, Emberson J, et al. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170,000 participants in 26 randomised trials. Lancet. 2010;376(9753):1670–1681.
[3]. Saito Y, Yoshida S, Nakaya N, Hata Y, Goto Y (Jul–Aug 1991). "Comparison between morning and evening doses of simvastatin in hyperlipidemic subjects. A double-blind comparative study". Arterioscler Thromb. 11 (4): 816–26. doi:10.1161/01.ATV.11.4.816.
[4]. Wallace A, Chinn D, Rubin G (4 October 2003). "Taking simvastatin in the morning compared with in the evening: randomised controlled trial". British Medical Journal. 327 (7418): 788. doi:10.1136/bmj.327.7418.788.
[5]. Reiner Z, Catapano AL, De Backer G, Graham I, Taskinen MR, Wiklund O, et al. ESC/EAS guidelines for the management of dyslipidaemias. Eur Heart J. 2011;32:1769–1818. doi: 10.1093/eurheartj/ehr158.
[6]. Perk J, De Backer G, Gohlke H, Graham I, Reiner Z, Verschuren M, et al. European guidelines on cardiovascular disease prevention in clinical practice (version 2012) Eur Heart J. 2012;33:1635–1701. doi: 10.1093/eurheartj/ehs092.
Rydén L, Grant PJ, Anker SD, Berne C, Cosentino F, Danchin N, et al. ESC guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD: the task force on diabetes, pre-diabetes, and cardiovascular diseases of the European Society of Cardiology (ESC) and developed in collaboration with the European Association for the Study of Diabetes (EASD) Eur Heart J. 2013;34:3035–3087. doi: 10.1093/eurheartj/eht108.
[7]. About diabetes". World Health Organization. Archived from the original on 31 March 2014. Retrieved 4 April 2014.
[8]. Diabetes Fact sheet N°312". WHO. October 2013. Archived from the original on 26 August 2013. Retrieved 25 March 2014.
[9]. Kitabchi, AE; Umpierrez, GE; Miles, JM; Fisher, JN (July 2009). "Hyperglycemic crises in adult patients with diabetes". Diabetes Care. 32 (7): 1335–43. doi:10.2337/dc09-9032.
[10]. Wilson PW, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB. Prediction of coronary heart disease using risk factor categories. Circulation. 1998;97:1837–1847.
[11]. Wilson PW. Diabetes mellitus and coronary heart disease. Am J Kidney Dis. 1998;32:S89–S100.
[12]. McGill HC Jr, McMahan CA. Determinants of atherosclerosis in the young: Pathobiological Determinants of Atherosclerosis in Youth (PDAY) Research Group. Am J Cardiol. 1998;82:30T–36T.
[13]. Brezinka V, Padmos I. Coronary heart disease risk factors in women. Eur Heart J. 1994;15:1571–1584.
[14]. Geiss LS, Herman WH, Smith PJ, National Diabetes Data Group. Diabetes in America. Bethesda, Md: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 1995:233–257.
[15]. Stone PH, Muller JE, Hartwell T, York BJ, Rutherford JD, Parker CB, Turi ZG, Strauss HW, Willerson JT, Robertson T, et al, the MILIS Study Group. The effect of diabetes mellitus on prognosis and serial left ventricular function after acute myocardial infarction: contribution of both coronary disease and diastolic left ventricular dysfunction to the adverse prognosis. J Am Coll Cardiol. 1989;14:49–57.

[16]. Singer DE, Moulton AW, Nathan DM. Diabetic myocardial infarction: interaction of diabetes with other preinfarction risk factors. Diabetes. 1989;38:350–357.
[17]. Smith JW, Marcus FI, Serokman R. Prognosis of patients with diabetes mellitus after acute myocardial infarction. Am J Cardiol. 1984;54:718–721.
[18]. Muhlestein JB, Anderson JL, Horne BD, Lavasani F, Allen-Maycock CA, Bair TL, Pearson RR, Carlquist JF: Effect of fasting glucose levels on mortality rate in patients with and without diabetes mellitus and coronary artery disease undergoing percutaneous coronary intervention. Am Heart J146 : 351–358,2003
[19]. Thrainsdottir IS, Aspelund T, Thorgeirsson G, Gudnason V, Hardarson T, Malmberg K, Sigurdsson G, Rydén L: The association between glucose abnormalities and heart failure in the population-based Reykjavík Study. Diabetes Care 28:612 –616, 2005
[20]. Nielson C, Lange T: Blood glucose and heart failure in nondiabetic patients. Diabetes Care 28:607 –611,2005
[21]. The DECODE Study Group.: Glucose tolerance and mortality: comparison of WHO and American Diabetic Association diagnostic criteria. Lancet354 : 617–621,1999
[22]. Estimation of cardiovascular risk in an individual patient without known cardiovascular disease. Wilson PWF. In: UpToDate [Textbook of Medicine]. Basow, DS (Ed). Massachusetts Medical Society, and Wolters Kluwer publishers, The Netherlands. 2010.
[23]. EuroQol Group. EuroQol EQ-5D user guide. Rotterdam: Rotterdam Centre for Health Policy and Law, Erasmus University; 1996.
[24]. Chambers LW. The McMaster health index questionnaire (MHIQ): methodologic documentation and report of second generation of investigators. Hamilton, Ontario: McMaster University, Department of Clinical Epidemiology and Biostatistics; 1982.
[25]. Bell KJ, Kirby A, Hayen A, Irwig L, Glasziou P. Monitoring adherence to drug treatment by using change in cholesterol concentration: secondary analysis of trial data. BMJ. 2011;342:d12.
[26]. Osterberg L, Blaschke T. Adherence to medication. N Engl J Med. 2005;353(5):487–497.
[27]. Benner JS, Glynn RJ, Mogun H, Neumann PJ, Weinstein MC, Avorn J. Long-term persistence in use of statin therapy in elderly patients.JAMA 2002;288:455-61
[28]. Parris ES,Lawrence DB, Mohn LA, long LB. Adherence to statin therapy and LDL cholesterol goal attainment by patients with diabetes and dyslipidemia. Diabetes care 2005;28:595-9.
[29]. Pittman DG, Chen W, Bowlin SJ, Foody JM. Adherence to statins, subsequent healthcare costs, and cardiovascular hospitalizations. Am J Cardiol 2011;107:1662-6
[30]. Jackevicius CA, Mamdani M, Tu JV. Adherence with statin therapy in elderly patients with and without acute coronary syndromes. JAMA 2002;288:462-7.
[31]. Al-Hayek AA, Robert AA, Alzaid AA, Nusair HM, Zbaidi NS, AL-Eithan MH, et al. Association between diabetes self-care, mediaction adherence, anxiety, depression, and glycemic control in type 2 diabetes. Saudi Med J 2012;33:681-3.
[32]. Beaton SJ, Nag SS, Gunter MJ, Gleeson JM, Sajjan SS, Alexander CM. Adequacy of glycemic, lipid, and blood pressure management for patients with diabetes in a managed care setting. Diabetes Care 2004;27:694-8.
[33]. 3Hosokawa M, Hamasaki A, Nagashima K, Harashima S, Toyoda K, Fujita Y, et al. Lack of goal attatinment regarding the low-density lipoprotein cholesterol level in the management of type 2 diabetes mellitus. Intern Med 2013;52:2409-15
[34]. Kukarni SP, Alexander KP, Lytle B, Heiss G, Peterson ED. Long-term adherence with cardiovascular drug regimens. Am Heart J 2006;151:185-91
[35]. Woodard LD, Landrum CR, Urech TH, Wang D, Virani SS, Petersen LA. Impact of clinical complexity on the quality of diabetes care. Am J Manag Care 2012;18:508-14
[36]. Bates TR, Connaughton VM, Watts GF. Non-adherence to statin therapy: A major challenge for preventive cardiology. Expert Opin Pharmacother 2009;10:2973-85
[37]. Wallach-Kildemoes H, Andersen M, Diderichsen F, Lange T. Adherence to preventive statin therapy according to socioeconomic position. Eur J Clin Pharmacol 2013;69:1553-63
[38]. Cheng SH, Chen CC, Tseng CH. Does medication adherence lead to lower healthcare expenses for patients with diabetes? Am J Manag Care 2013;19:662-70.
[39]. Bitton A, Choudhry NK, Matlin OS, Swaton K, Shrank WH.The impact of medication adherence on coronary artery disease costs and outcomes. A systemic review. Am J Med 2013;126:357.e7-357.e27.

Dr .C.Vani,"Analyzing The Impact of Statins Use In Type-2 Diabetes Mellitus Patients." IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS) 13.1 (2018): 45-53.