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SEVERITY ASSESSMENT OF ADVERSE DRUG REACTION AND QUALITY OF LIFE OF DYSLIPIDEMIA PATIENTS ON ATORVASTATIN OR ROSUVASTATIN V/S CONTROLLED.

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ABSTRACT
Background: Adverse drug reaction and quality of life is most important in terms of patient health, by analyzing these two parameters there must be improvement in dyslipidemia patients. **Method**: Rosuvastatin and Atorvastatin were used for the study. A total no. of 60 patients with dyslipidemia was taken and age group of 30-90 years. Total patient were divided into two groups. Atorvastatin drug given to group I and Rosuvastatin to group II. Study was carried out for six months.Inclusion criteria: Dyslipidemia, Age above 18, both sexes, Patient having multiple risk factors for heart diseases. Exclusion Criteria: History of myalgia, Hyersensitive to Atorvastatin or Rosuvastatin, Pregnancy and lactation, Woman on oral contraceptives, patient with abnormal liver function and abnormal renal function. While taking patient history, Questionnaire for quality of life has been prepared as per W.H.O guidelines.SF-36 was followed for both groups. **Result**: From total 60 patients, 70% were male and 30% were female. Total percentage of adverse drug reaction in group I, mild (51.72), moderate (44.8), severe (3.45) and for group II, mild (6.89), moderate (86.2), severe (6.89) and overall adverse drug reactions in percentage by both drugs were 58.61 for mild, 13.1 moderate and 10.34 severe. Quality of life was better shown in group II (Rosuvastatin) than group I (Atorvastain) and adverse drug reaction was shown less in group I (Atorvastatin). **Conclusion:** In future, study can be done on the basis of molecular and biochemical mechanisms of myopathy and rhabdomyolysis by statins as well as on Atherogenic Dyslipidemia.

KEYWORDS: Quality of Life, Adverse Drug Reaction, Dyslipidemia.

INTRODUCTION
Dyslipidemia is a general term that refers to abnormal levels of lipids; a broad category of compounds that encompass everything from cholesterol to vitamins; in the body. The most common Dyslipidemia are high cholesterol called hypercholesterolemia or "hyperlipoproteinemia and high triglycerides hypertriglyceridemia. When high cholesterol and triglycerides occur together, the condition is also called combined hyperlipidemia. Low levels of cholesterol also called hypolipoproteinemia; usually for genetic reasons. Treatment for dyslipidemia depends on condition; but can include maintaining a healthy diet; moderate exercise and taking medications.[1]

Dyslipidemia is a disorder of lipoprotein metabolism; including lipoprotein over production. Dyslipidemias may be manifested by elevation of total cholesterol; the "bad" low-density lipoprotein (LDL) cholesterol and the triglyceride concentrations; and a decrease in the "good" high-density lipoprotein (HDL) cholesterol concentration in the blood.[2]

Dyslipidemia is elevation of plasma cholesterol, triglycerides (TGs); or both; or a low high-density lipoprotein level that contributes to the development of atherosclerosis. Causes may be primary (genetic) or secondary. Diagnosis is done by measuring plasma levels of total cholesterol; TGs; and lipoproteins. Treatments are dietary changes; exercise; and lipid-lowering drugs.[3]

There is no cutoff naturally between normal and abnormal lipid levels because lipid measurement is continuous. A linear relation may exist between lipid levels and cardiovascular risk; so many people with normal cholesterol levels benefit from achieving still

lower level. Consequently; there are no numeric definition of dyslipidemia; the term is applied to lipid levels for which treatment has proven beneficial and proof of benefit is strongest for lowering elevated low-density lipoprotein levels. In the overall population; evidence is less strong for a benefit from lowering elevated TG and increasing low high-density -lipoprotein (HDL) levels; in part because elevated TG and low HDL levels are more predictive of cardiovascular risk in women than in men.[3]

Dyslipidemia are disorders of lipoprotein metabolism; including lipoprotein overproduction and deficiency. They may manifest one or more of the following:

- Elevated total cholesterol
- Low-density lipoprotein cholesterol (LDL)
- Triglyceride levels
- High-density lipoprotein cholesterol level decreased.[4]

Dyslipidemia is closely associated with atherosclerosis and is a major causal factor in the development of ischemic diseases. Ischemic cardiovascular and cerebrovascular events are leading causes of morbidity and mortality.[4]

This has been recognised as the foundation for atherosclerosis as well as development of coronary disease. The risk of CAD in Indians is (3-4) time higher than White Americans, (6) times higher than Chinese.[5, 6]

Adverse drug reaction and quality of life is most important in terms of patient health, by analyzing these two parameters there must be improvement in Dyslipidemia patients.

By, severity assessment of adverse drug reaction as well as quality of life in coronary heart patients, mortality and morbidity rate also reduced.

Using, statin in Dyslipidemia patients shows a better result in terms of adverse drug reaction as well as quality of life.

Rosuvastatin and Atorvastatin were used for the study as Rosvastatin is a relatively new member of statins and its prescription is also on the rise. And Atorvastatin has been taken as a standard drug due to the fact that it is more frequently used and has been reported to be better drug in dyslipidemia.

The initial approach to a patient of dyslipidaemia is modifications in life style i.e. diet modification (low fat consumption); weight loss; physical activity; smoking cessation; aggressive control of diabetes and hypertension. If the changes do not suffice then pharmacotherapy has to be implemented.

The United States National Cholesterol Education Programme-Adult Treatment Panel has issued guidelines from time to time to manage dyslipidaemia so as to decrease the incidence of coronary artery disease. These guidelines based on prevalent dyslipidaemia picture in the population help to define the treatment goals in patients by setting the desired values for the various lipid profiles. The latest report of adult treatment panel ATP III focuses on primary prevention of Dyslipidaemia in persons with multiple risk factors.[27]

HMG-CoA reductase inhibitors (statins) are the mainstay in the management of Dyslipidemia and since they are widely prescribed; their safety remains issue for concern. Rosuvastatin has proven to be effective in improving serum lipid profiles. Recently, study confirmed the efficacy of this statin in primary prevention for older patients with multiple risk factors and evidence of inflammation.[49]

As with other statins; Rosuvastatin treatment is associated with relatively low rates of severe myopathy; rhabdomyolysis and renal failure.[49] The earliest benefit of statins is an improvement in endothelial function and a decrease in hospitalization for angina.

Statins also decrease smooth muscle cell proliferation and prevent vascular remodeling manifesting itself in carotid intima-media thickening.[50]

Six statins are currently available; and they are known by a variety of brand names: Atorvastatin (Lipitor); Fluvastatin (Lescol); Lovastatin (Mevacor; Altoprev); Pravastatin (Pravachol); Rosuvastatin (Crestor); and Simvastatin (Zocor). Although these drugs have been very successful in managing the cardiovascular health of many patients; there are also potential adverse effects that have been identified. The common adverse effects reported include muscle pain or weakness that can progress to rhabdomyolysis and mortality.[51]

Patients who received the more aggressive atorvastatin therapy experienced a 16% reduction in the hazard ratio for death or a major coronary event compared with the moderate therapy group.[52] The most recent findings supporting yet lower LDL-C goals for statin therapy especially for patients at higher risk for developing coronary problems were included in a 2004 update to NCEP's earlier guidelines.[53]

All of the statins are associated with the adverse effects of myopathy.[54, 55] Myopathy refers to any disease of muscles; acquired or inherited; with symptoms including muscle weakness primarily in the extremities.[56] Symptoms of myopathy may occur at any time after the initiation of statin therapy. Factors that may increase the risk of myopathy are age greater than 80 years.

All of these factors formed the base of present study in which severity assessment of adverse drug reaction as well as quality of life of Dyslipidemia patients has been done by using Atorvastatin and Rosuvastatin.

MATERIAL AND METHOD

The study was approved by Institutional Human Ethics Committee of Uttarakhand Technical University, Dehradun (Uttarakhand). Patients were enrolled in Synergy Institute of Medical Sciences, Dehradun (Uttarakhand).

Demographic Area

A literature review was undertaken to find out the various effects of statin on dyslipidemia occurring all over the globe. To get familiarized with dissertation, various literatures were studied. Thereafter, out patient data was collected from a multi-specialty Synergy hospital, Dehradun (Uttarakhand), India. The present study was carried out after taking permission from hospital authorities.

Data Source

This study based entirely on outdoor patient data who were receiving treatment from hospital at the time of study.

Sample Size

A total no. of 60 patients was taken for the study and age group 30-90 years of patient are enrolled. Copies of the prescription from the patients attending OPD at a tertiary care hospital was obtained.

Duration of Study

Patient was taking treatment from hospital and study was carried out over a period of six months.
End points: clinical efficacy, adverse drug reaction, quality of life, safety, tolerability, hospitalizations.

Inclusion Criteria

- Dyslipidemia
- Age above 18
- Both sexes
- Patient having multiple risk factors for heart diseases

Exclusion Criteria

- History of myalgia
- Hypersensitive to atorvastatin or rosuvastatin
- Pregnancy and lactation
- Women on oral contraceptives pills
- Patient with abnormal liver function and abnormal renal function

Project Design

The study was randomized, open label and parallel study. After enrollment of patient, history of patient was taken. Total 60 patients were divided into two groups of 30 patients each and assigned as group 1 and group 2.

- Group 1 received Atorvastatin and group 2 received Rosuvastatin.
- While taking patient history Questionnaire for quality of life has been prepared as per W.H.O guidelines.
- SF-36 was followed for both groups.
- Adverse drug reaction was also obtained in patient information sheet

Data Collection

The data has been taken in patient information sheet and patient health questionnaire was filled.
The patient information sheet providing following information (Appendix -1)

o Name
o Age
o Sex
o Weight
o BMI
o Diagnosis and treatment prescribed by the physician is recorded for each patient
o Adverse drug reaction

For quality of life, patient health questionnaire was followed as per W.H.O guidelines, SF-36 has been followed (Appendix-2).

Statistical Analysis

Analysis was carried out as per the study objectives. The data were analyzed using a Microsoft Excel spreadsheet. After the completion of the mean, standard deviation were calculated for both adverse drug reaction and for quality of life. Mann Whitney-U test and Wilcoxon W test was used to evaluate statistical significance within a group and "t" values are obtained.

o Total no. of patient enrolled in the study
o Percentage of both sexes enrolled in the study
o Average age and standard deviation of patient (year)
o Average weight and standard deviation of patient (kg)
o Average height and standard deviation of patient (feet, inches)
o Average BMI and standard deviation of patient (cm/kg)
o Overall mean and standard deviation of quality of life parameter
o Percentage of adverse drug reaction of both drugs

RESULT

Table No.1: Overall population sex categorization for adverse drug reaction and quality of life of Atorvastatin-

	Atorvastatin	
Gender	**No. of patient (N=30)**	**Total No. of patient (%)**
Male	**22**	**73.33**
Female	**8**	**26.66**

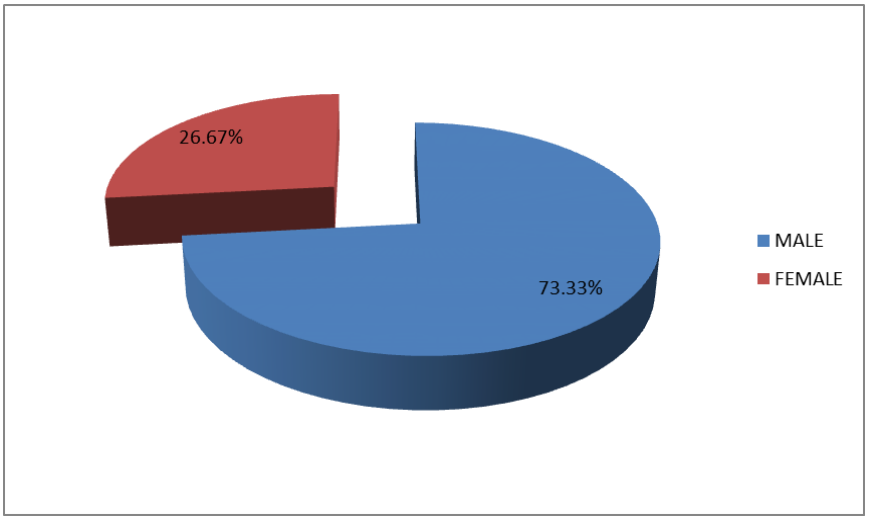

Fig No. 1: Sex categorized of study group in adverse drug reaction and quality of life of Atorvastatin

Table No.2: Overall population sex categorization for adverse drug reaction and quality of life of Rosuvastatin

	Rosuvastatin	
Gender	**No. of patient (N=30)**	**Total No. of patient (%)**
Male	**20**	**66.66**
Female	**10**	**33.33**

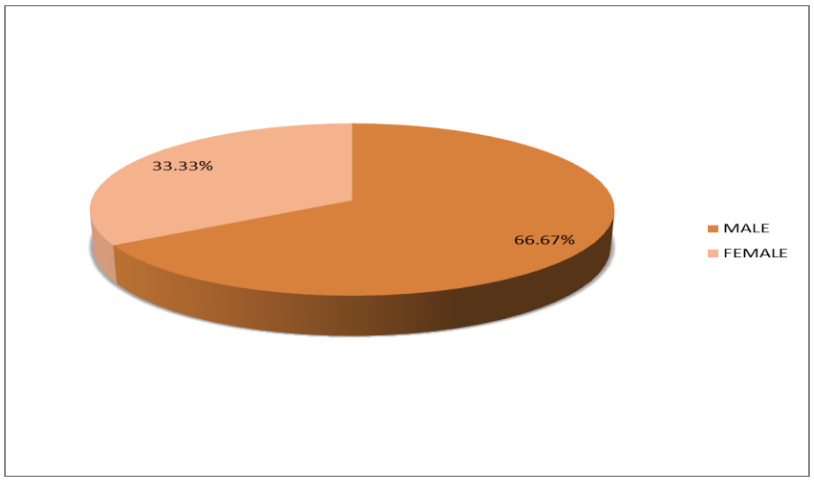

Fig No. 2: Sex categorized of study group in adverse drug reaction and quality of life of Rosuvastatin

1- Age group wise distribution of patient in OPD for adverse drug reaction and quality of life of both drugs.

The analysis shows that the distribution of the study population was greater for the overall population between the ages. The details of the distribution are given in Table (3, 4) and Fig (3, 4).

Table No. 3: Different age group of patient in OPD for adverse drug reaction and quality of life of Atorvastatin-

Age group	Total No. of patient	Percentage (%)
20-30	1	3.33
31-40	2	6.66
41-50	6	20
51-60	8	26.66
61-70	7	23.33
71-80	5	16.66
81-90	1	3.33

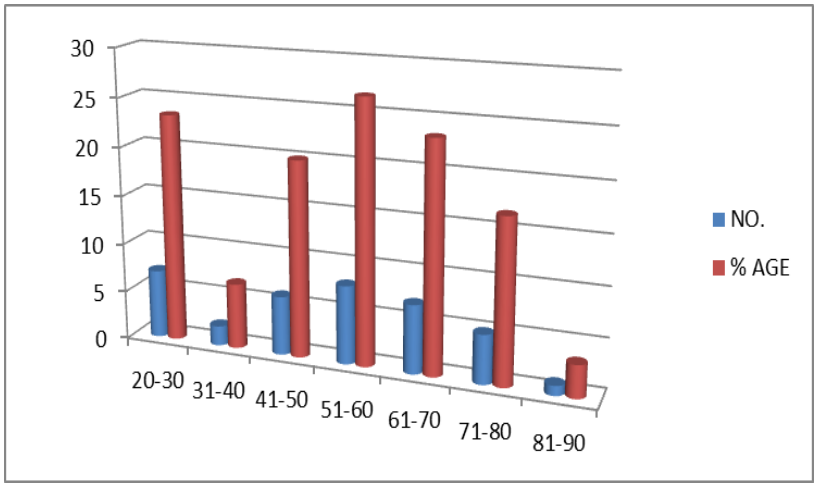

Fig No. 3: No. of patient in different age group in OPD for adverse drug reaction and quality of life of Atorvastatin

Table No. 4: Different age group of patient in OPD for adverse drug reaction and quality of life of Rosuvastatin-

Age group	Total No. of patient	Percentage (%)
30-40	2	6.66
41-50	11	36.66
51-60	10	33.33
61-70	6	20
71-80	1	3.33
81-90	1	3.33

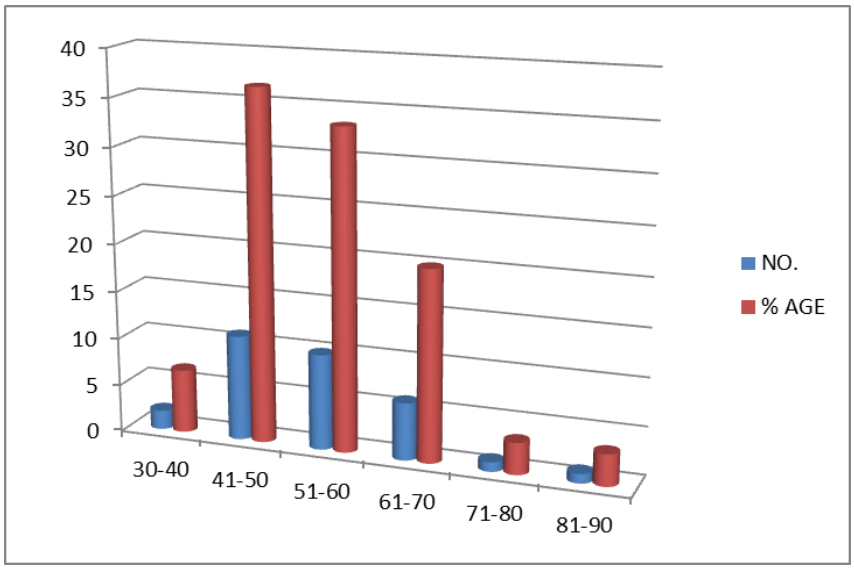

Fig No.4: No. of patient in different age group in OPD for adverse drug reaction and quality of life of Rosuvastatin-

2- Overall characterization of both drugs

The analysis is done in 60 patients, group 1 consist 30 patients and group 2 consist of 30 patients. For Atorvastatin age mean was 58.03 and standard deviation was 13.67, weight mean was 65.65 and standard deviation was 10.89, height mean was 5.45 and standard deviation 0.20, BMI mean was 24.24 and standard deviation was 38. Whereas, for Rosuvastatin age mean was 55.06 and standard deviation was 10.96, weight mean was 70.59 and standard deviation was 10.08, height mean was 5.44 and standard deviation was 0.25, BMI mean was 26.44 and standard deviation was3.67.Details are given in Table.5 and Fig No.5,6,7,8.

Table No.5: Overall drug characterization

CHARACTERISTICS		ATORVASTATIN (N %)	ROSUVASTATIN (N %)
AGE (YRS)		57.6 (13.8)	55.06 (11.15)
SEX (%)	M	73.33	66.66
	F	26.67	33.33
WEIGHT (Kg)		65.65 (11.08)	70.59 (10.08)
HEIGHT (FEET,INCHES)		5.45 (0.20)	5.44 (0.25)
B.M.I (cm/Kg)		24.24 (3.38)	26.44 (3.67)

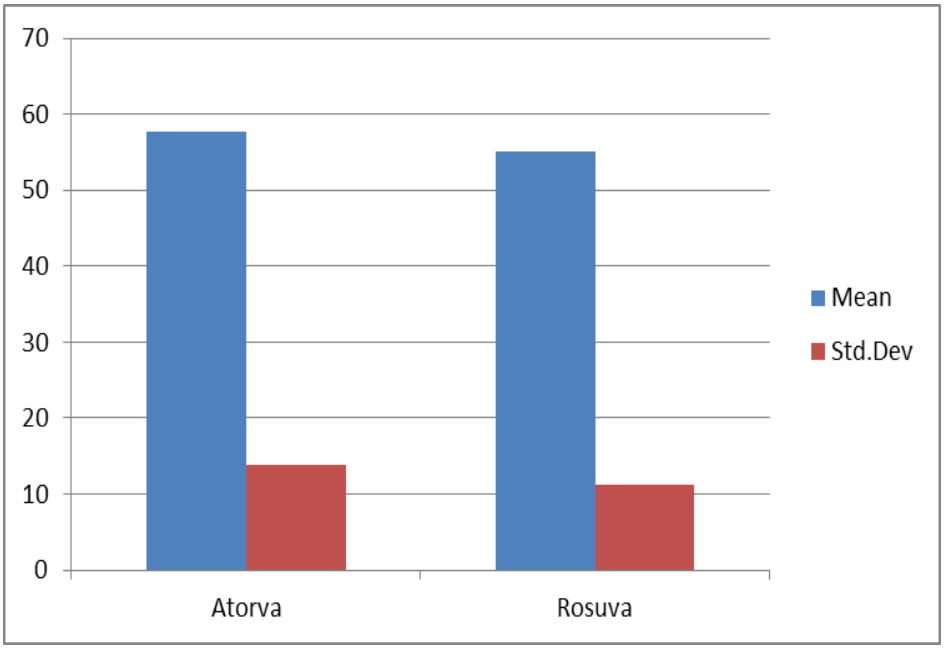

Fig No.5: Mean age and standard deviation age of both drugs

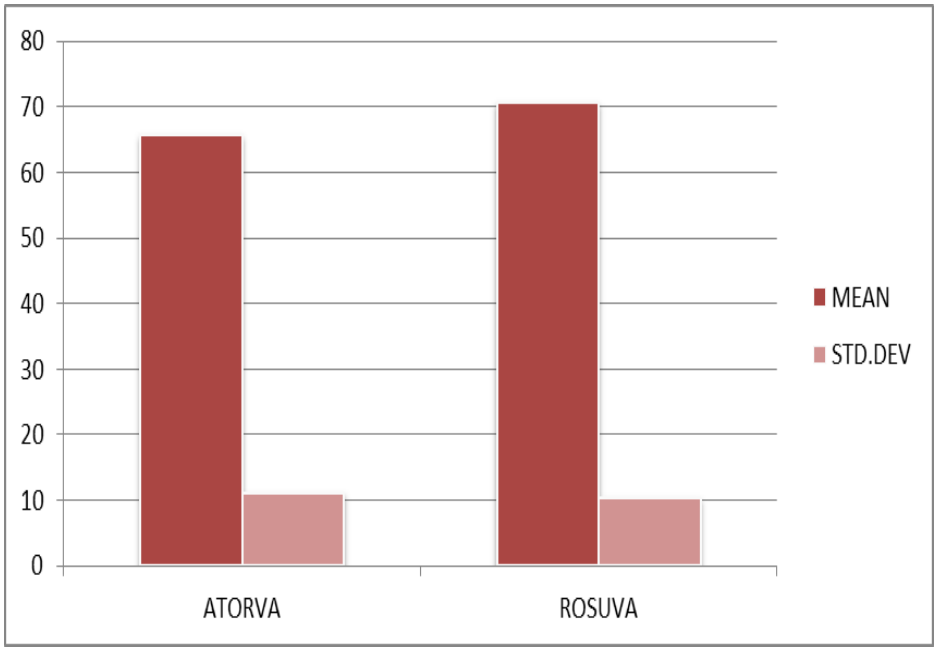

Fig No.6: Mean weight and standard deviation weight of both drugs-

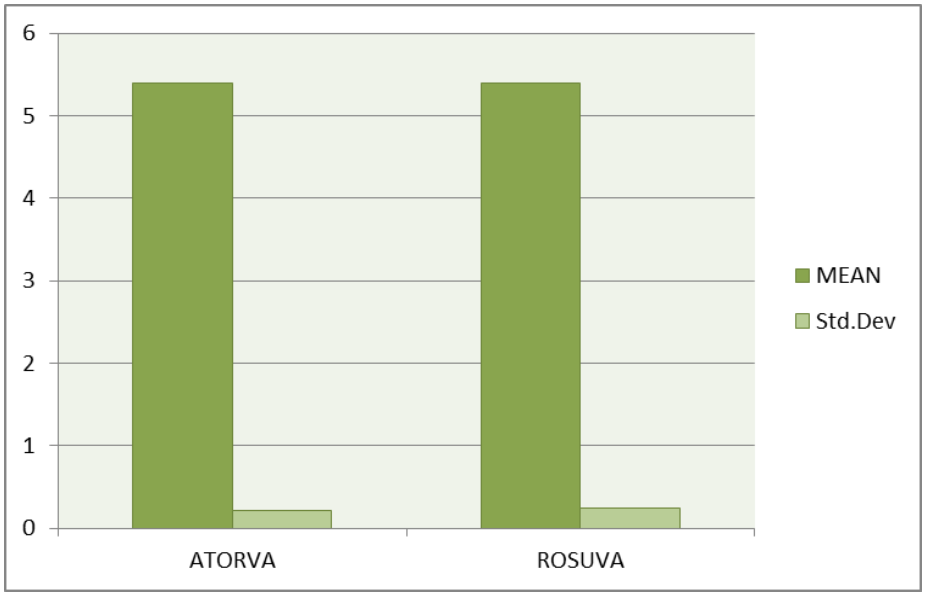

Fig No.7: Mean height and standard deviation height of both drugs-

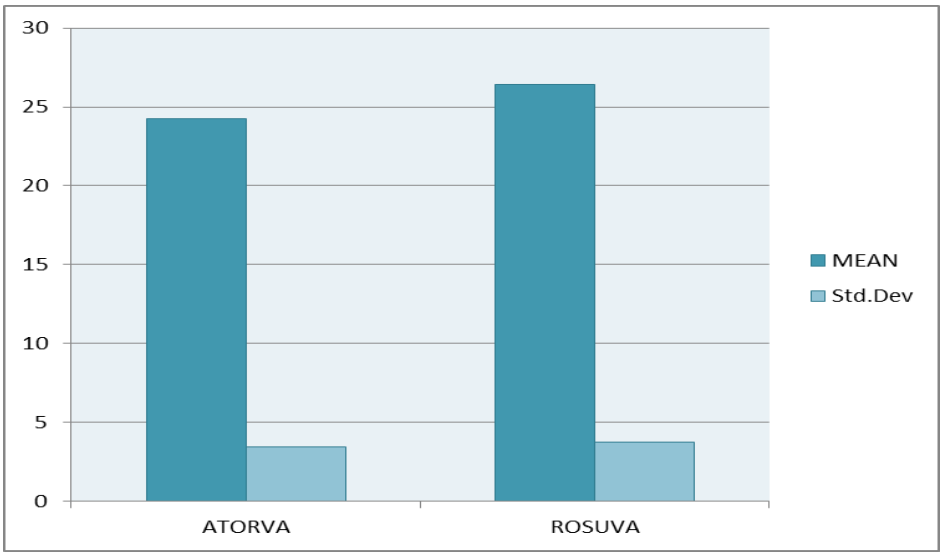

Fig No.8: Mean BMI and standard deviation BMI of both drugs

3- Different types of adverse drug reaction shown in Atorvastatin and Rosuvastatin

Most frequent adverse drug reaction associated with Atorvastatin was headache, weakness and constipation. Adverse drug reaction shown by Rosuvastain was headache, insomnia, myalgia, bloating and constipation. The details of the adverse drug reaction are given in Table (6, 7) and Fig (9, 10).

Table No.6: Different types of adverse drug reaction (Atorvastatin)

ADR	MILD	MODEARTE	SEVERE
HEADACHE	4	4	0
INSOMNIA	0	0	0
WEAKNESS	4	4	0
MYALGIA	0	0	0
DROWSINESS	0	0	0
DIZINESS	0	0	0
NAUSEA	0	0	0
PAIN	0	0	0
BLOATING	0	0	0
DIARRHOEA	0	0	0
CONSTIPATION	7	5	1
RASH	0	0	0

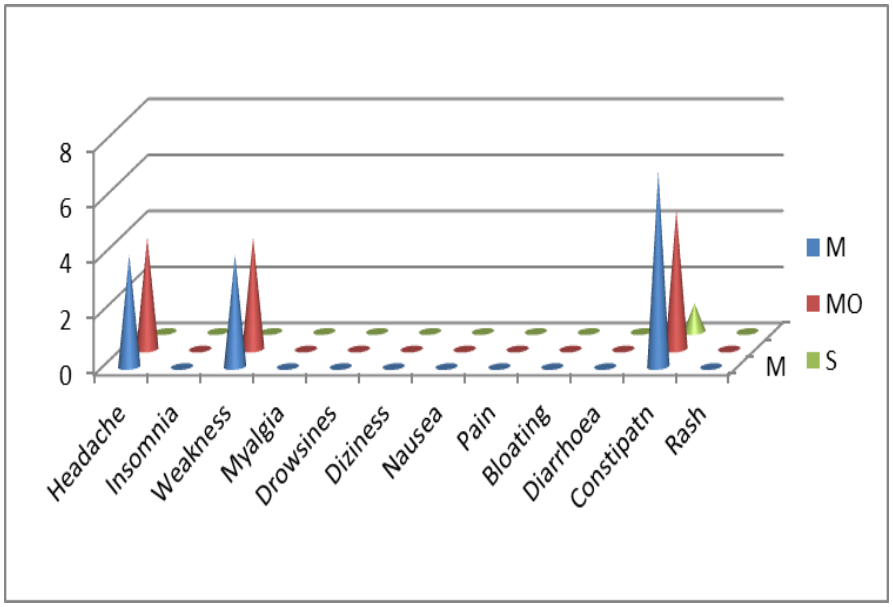

Fig No.9: Different types of adverse drug reaction in atorvastatin

Table No.7: Different types of adverse drug reaction in Rosuvastatin

ADR	MILD	MODEARTE	SEVERE
HEADACHE	0	1	0
INSOMNIA	0	1	1
WEAKNESS	0	3	0
MYALGIA	2	0	0
DROWSINESS	0	0	0
DIZINESS	0	0	0
NAUSEA	0	0	0
PAIN	0	0	0
BLOATING	0	8	0
DIARRHOEA	0	0	0
CONSTIPATION	0	11	1
RASH	0	0	0

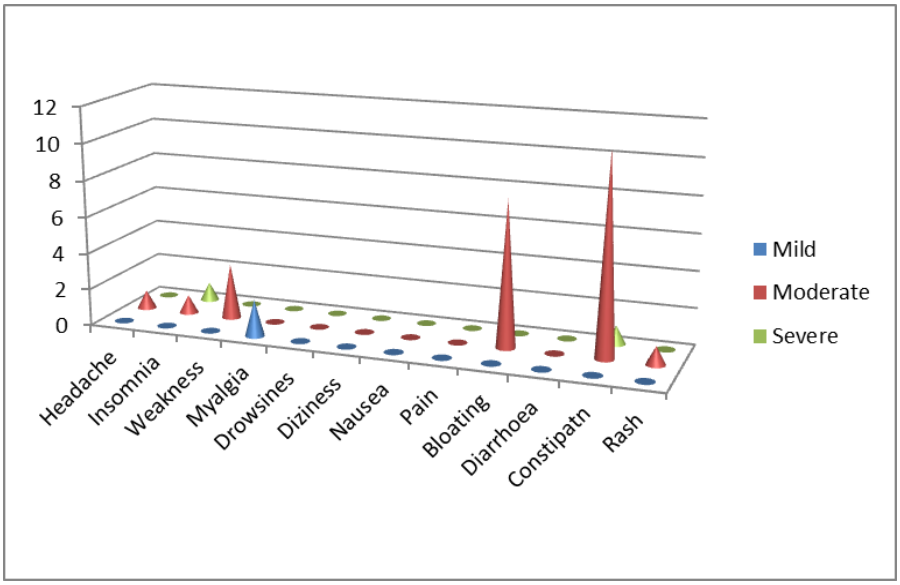

Fig No.10: Different types of adverse drug reaction in rosuvastatin

4- Comparison of total adverse drug reaction in atorvastatin and rosuvastatin

Analysis was done on the basis of mild, moderate and severe. Drugs, Atorvastatin and Rosuvastatin were compared, and adverse drug reaction was noted as mild, moderate and severe. The details of percentage of adverse drug reaction are given in Table 8 and Fig No.11.

Table No.8: Adverse drug reaction % of both drugs

DRUG	%MILD	%MODERATE	%SEVERE
ATORVASTATIN	51.72	44.8	3.45
ROSUVASTATIN	6.89	86.2	6.89

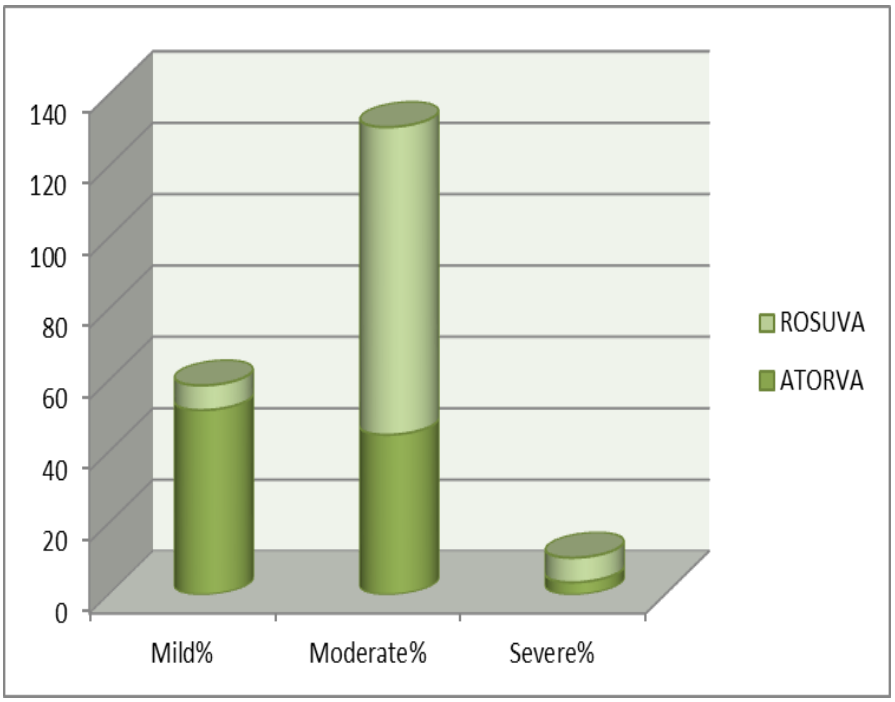

Fig No.11: Percentage of adverse drug reaction of both drugs

5- Mean and standard deviation for quality of life parameters for both drugs

Quality of life parameters were grouped in 8 parts for both drugs; they are physical functioning; role limitations due to physical functioning; role limitations due to emotional problem; energy/fatigue; emotional well-being; social functioning; pain; general health. The details of the distribution are given in table (9, 10) and Fig (12, 13).

Table No.9: Mean and standard deviation for quality of life parameters for Atorvastatin

QOL	MEAN	Std. Dev.
PF 1	77.5	18.5
RLPH 1	85	24.2
RLEP 1	95.5	19.02
EF 1	59.8	9.23
EWB 1	92.2	5.8
SF 1	85.4	10.4
PAIN 1	96.16	7.9
GH 1	73.8	9.7

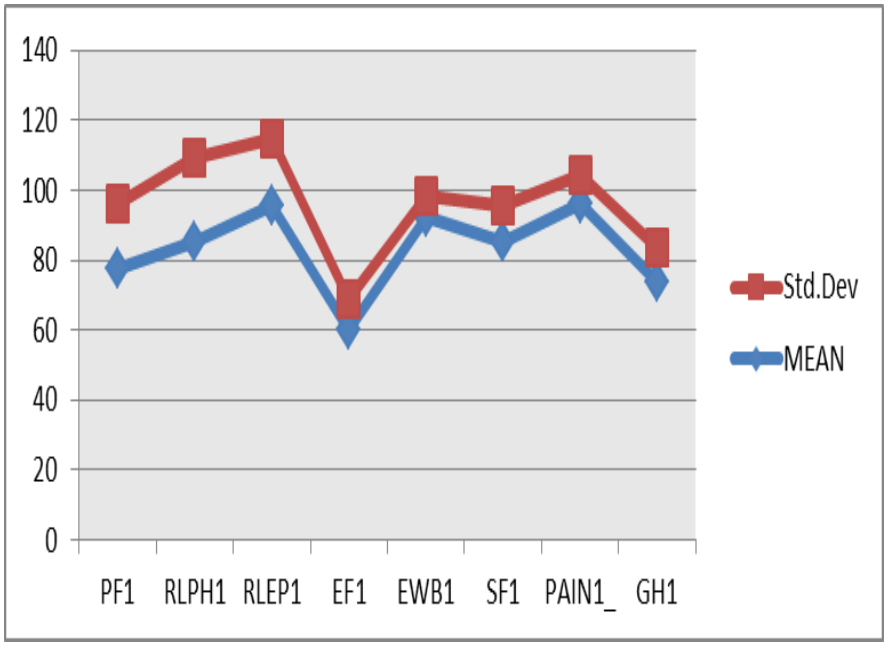

Fig.No.12: Mean and standard deviation for quality of life parameters for Atorvastatin

Table No.10: Mean and standard deviation for quality of life parameters for Rosuvastatin-

QOL	MEAN	Std. Dev.
PF 1	85.16	14.35
RLPH 1	84.16	22.24
RLEP 1	88.88	23.03
EF 1	64.13	10.05
EWB 1	92.46	12.44
SF 1	84.91	13.20
PAIN 1	96.08	9.16
GH 1	84.5	11.32

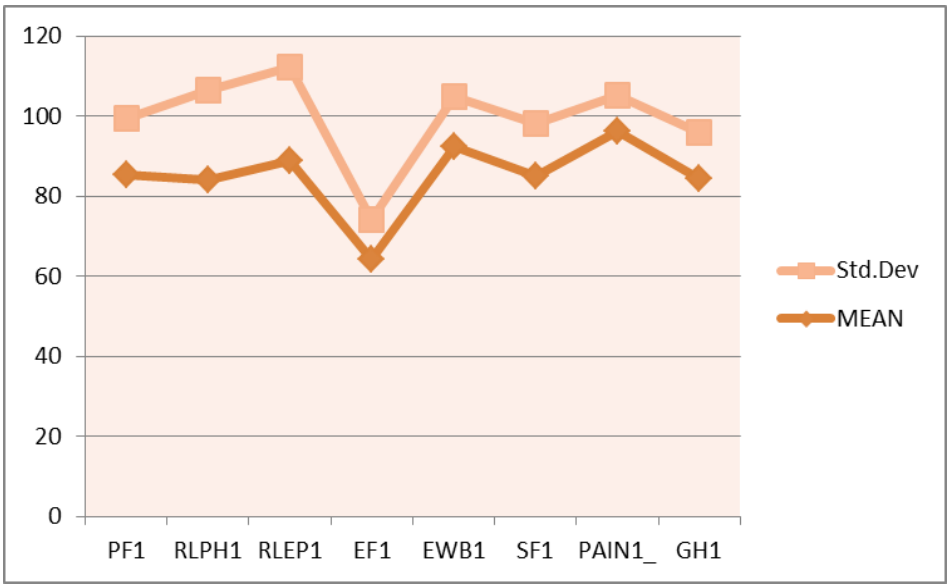

Fig.No.13: Mean and standard deviation for quality of life parameters for Rosuvastatin

6- Statistical evaluation of quality of life of both drugs

Statistical evaluation was done by finding out mean and standard deviation using excel spreadsheet .By using Mann Whitney –U test and Wilcoxon –W test and "t" value was obtained. The details of the statistical evaluation are given in Table no.11.

Table No.11: Statistical evaluation of quality of life of both drugs

Test Statistics[a]								
	PF1	RLPH1	RLEP1	EF1	EWB1	SF1	PAIN1_	GH1
Mann-Whitney U	334.500	437.500	390.000	320.000	328.000	432.500	436.500	218.500
Wilcoxon W	799.500	902.500	855.000	785.000	793.000	897.500	901.500	683.500
Z	-1.730	-.216	-1.502	-1.955	-1.854	-.277	-.277	-3.455
Asymp. Sig. (2-tailed)	**.084**	**.829**	**.133**	**.051**	**.064**	**.781**	**.782**	**.001**
a. Grouping Variable: Group								

Descriptive Statistics						
Group		**N**	**Minimum**	**Maximum**	**Mean**	**Std. Deviation**
1	AGE	30	28.00	88.00	57.6667	13.83981
	WEIGHT	30	52.00	100.00	65.6467	11.08459
	HEIGHT	30	4.90	5.90	5.4470	.20909
	BMI	30	19.10	32.50	24.2367	3.44539
	PF1	30	20.00	100.00	77.5000	18.55792
	RLPH1	30	.00	100.00	85.0000	24.21171
	RLEP1	30	.00	100.00	95.5667	19.02754
	EF1	30	45.00	85.00	59.8333	9.23667
	EWB1	30	76.00	100.00	92.2667	5.81872
	SF1	30	62.50	100.00	85.4167	10.42385
	PAIN1_	30	67.50	100.00	96.1667	7.97986
	GH1	30	60.00	95.00	73.8333	9.79825
	Valid N (listwise)	30				
2	AGE	30	35.00	86.00	55.0667	11.15698
	WEIGHT	30	54.90	100.00	70.5917	10.25459
	HEIGHT	30	4.90	5.90	5.4433	.25146
	BMI	30	21.40	36.70	26.4367	3.74050
	PF1	30	45.00	100.00	85.1667	14.35290
	RLPH1	30	50.00	100.00	84.1667	22.24795
	RLEP1	30	33.33	100.00	88.8863	23.30075
	EF1	30	45.00	89.00	64.1333	10.00598
	EWB1	30	44.00	100.00	92.4667	12.44778
	SF1	30	35.00	100.00	84.9167	13.20402
	PAIN1_	30	62.50	100.00	96.0833	9.16053
	GH1	30	65.00	100.00	84.5000	11.32209
	Valid N (listwise)	30				

DISCUSSION

The aim of using Atorvastatin and Rosuvastatin for Dyslipidemia is to increase the quality of life and to minimize the adverse drug reactions.

Statins, mainly reduce the risk of cardiovascular morbidity and mortality in patients with or at risk for coronary heart diseases. This study focuses on adverse drug reactions of Atorvastatin and Rosuvastain as well quality of life.

Study conducted in Warangal district of Andhra Pradesh with 1496 adults and older individual dyslipidemia was found in 52.7% males and 42.9% females[91] Our study is also consistent with their study; however their study had large number of subjects.

The prevalence of Dyslipidemia was high in males (70%) than in females (30%).

In earlier reference it was observed that the incidence of Dyslipidemia was predominant in age group 40–59

years.[90] In our study, the incidence of Dyslipidemia was prominent in the age group of 41- 60 years.

Earlier data also reported the symptoms of myalgia were common complaints by patients who are on statin therapy.[92] This study also shows mild myalgia when Rosuvastain was given.

In earlier study, the incidence of adverse drug reaction (both minor and severe adverse drug reactions) for Rosuvastatin (55%) and Atorvastatin (46%).[93] However our study is not consistent with them in sense that we report less severe adverse drug reaction in group I (3.45%) and minor adverse drug reaction (51.72%) whereas for group II severe adverse drug reaction was (6.89%) and minor drug reaction (46.5%).

The adverse event's severity can be categorized into mild, moderate and severe. The symptoms of mylgia occur in 0.04-0.2% of the patients who are on statins.[93] In our study mylagia symptoms occur in 0.06% of patients.

In present study, it was noticed that adverse drug reactions in group I was headache, weakness and constipation. Whereas, for group II noticed adverse drug reaction was headache, insomnia, weakness, myalgia, constipation.

CONCLUSION

The study was done to evaluate severity assessment of adverse drug reaction and quality of life of dyslipidemia patient using statin drug Atorvastatin and Rosuvastatin.

Quality-of-life measures are not aimed at the correct target, unless an opportunity to express patient's opinions and reactions is provided. Quality of life is a personal perception; which shows the way an individual feel about their health and the nonmedical aspects of their lives. Assessing the patients' experience of dyslipidemia and its treatment is a central component of health care. Quality-of-life measures capture personal and social context of patients. There is increasing interest in developing individualized tools that reflect perception; that quality of life is unique to individuals and cannot be adequately assessed standardized measures. Statins are been widely used for the treatment of dyslipidemia and show better result in quality of life.

As per our observation, Atorvastatin and Rosuvastatin show better result in quality of life and adverse drug reaction.

By detecting adverse drug reaction occur by these drugs like myalgia, headache, nausea and vomiting, abdominal pain, also clarify the safety assessment of statin drug by risk benefit ratio and there valuable option in lipid lowering therapy.

Using statin, in treatment of hyperlipidemia is an effort to reduce the prevalence of hypercholesterolemia and heart disease. The safety and tolerability of statins supports their use as first line treatment for dyslipidemia.

The study was also aimed to check the effect of Atorvastatin on adverse drug reaction as well as quality of life We conclude that Atorvastatin show less adverse drug reaction and minimum improvement in quality of life.

The effect of Rosuvastatin on adverse drug reaction and quality of life was maximum; it shows more adverse drug reaction and maximum improvement in quality of life. Myalgia was noticed in Rosuvastatin.

Comparing group I and group II it was clearly understood that group I (Atorvastatin) shows less adverse drug reaction as compare to group II .And quality of life was better in group II (Rosuvastatin).

For rapid treatment of disease and for patient care Rosuvastain was given. It was also seen that Atorvastatin given in mild or borderline cases, whereas Rosuvastain were given in severe cases.

In our study we followed the W.H.O guidelines and SF-36 was followed for the scores of quality of life and it was observed that social functioning was improved more in Atorvastatin as compare to Rosuvastatin.

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