ORIGINAL ARTICLE

Frequency of Statin-Induced Myopathy in Patients with Dyslipidemia Presenting in a Tertiary Care Hospital of Lahore

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ABSTRACT

Background: Frequency of dyslipidemia is on continuous rise in the developing countries including Pakistan. Many studies have shown that a raised LDL-cholesterol level, non-HDL cholesterol levels and decreased HDL-cholesterol levels are related with anraised risk of cardiovascular diseases and also certain muscle related symptoms.
Aim: To find the frequency of statin-induced myopathy in dyslipidemic patients presenting in a tertiary care hospital.
Methods It was a cross sectional study conducted among dyslipidemic patients presented at department of medicine and endocrinology, Unit-I Fatima Memorial hospital, Lahore. Non-probability consecutive sampling technique was used to select 230 dyslipidemic patients who met the inclusion criteria. Information was recorded on predesigned questionnaire regarding statin induced myopathy and socio-demographic variables.
Results: In this study, the mean age statin induced myopathy respondents was 49.9±8.6 years while it was 49.9±9.4 years among not having statin induced myopathy.Statin induced myopathy was seen in 55 (23.9%) respondents while in 175 (76.1%) there was no statin induced myopathy. Gender among peripheral neuropathy showed that males were 42 and females were 13 in number; and among non-statin induced myopathy group there were 121 males and 54 females. Most of the middle income respondents were suffering from statin induced myopathy as compared to other income groups.
Conclusion: This study reports an increased prevalence of statin induced myopathy among dyslipidemic patients. Male respondents were more in number than females but both had shown insignificant relationship with statin induced myopathy. The age>45 years of the respondents showed significant statistical difference with gender.
Keywords: Statin Induced Myopathy, Dyslipidemia, Lahore.

INTRODUCTION

An abnormal amount of lipids in the blood is called as Dyslipidemia. Itcan lead to cholesterol deposition in the arteries and can cause atherosclerosis, which decreases the size of the lumen ofthe artery and, on a long term, it can also affect the blood supply through the affected vessel. Dyslipidemia is a result of modern life style of today which involves sedentary habits and unhealthy eating habits. It may presents as an elevation of the total cholesteroland/or the increase in triglyceride values and a decline in the High Density Lipoprotein (HDL) cholesterolconcentration. A major risk factor for Coronary Heart Disease (CHD) is dyslipidemia, there is 1-2% increase in the incidence of CHD for every 1% increase in cholesterol level[1].

The prevalence of dyslipidemia is 30.3% as per the World Health organization (WHO), in the region of South East-Asia, 37% in Western Pacific, 48% in America, and 54% in Europe.[2] In general population various types of dyslipidemias were identified in diabetes mellitus. Raised total cholesterol, low-density lipoprotein cholesterol, and triglyceride and decreased high-density lipoprotein cholesterol (HDL-C) are all included within spectrum of dyslipidemia. Globally the prevalence of hyper-cholesterolemia among adults is 37% for males and 40% for females.[3] Frequency of dyslipidemia is on

continuous rise in the developing countries including Pakistan.[4] This trend is mostly attributed to unhealthy dietary patterns, obesity, tobacco use, alcohol abuse, reduced physical activity, aging of population and many other co-factors.[5] These risk factors of behavioral nature were considered as the major factors causing coronary heart disease and cerebrovascular disease in 80% of the cases[6]. People with type 2 diabetes showed double the risk of developing coronary artery disease due to increase in multiple risk factors and dyslipidemia is one of them.[7]Many studies of epidemiological nature have demonstrated that a raised LDL cholesterol and non-HDL cholesterol level and low HDL cholesterol levels are related with a raised risk of cardiovascular disease in diabetics[8].

Rationale of our study was to evaluate the frequency of statin-induced myopathy among dyslipidemia patients. It has been known that there may be various risk factors of statin-induced myopathy and has significant impact on life of dyslipidemic patients. But controversial evidence has been noticed from literature which showed the variables significance of association of statin-induced myopathy with various risk factors. Moreover, the above stated studies were obtained from various literatures which contain ambiguity in results. So we wanted to conduct this study to confirm the extent of problem in local population and implement the results of this study in future. Furthermore strategies could be made to detect positive cases early to decrease the long term morbidity.

The objective of the study was to find the frequency of statin-induced myopathy in dyslipidemic patients presenting in a tertiary care hospital.

OPERATIONAL DEFINITION

Dyslipidemia: Participants were considered to have Dyslipidemias if they had a decline in high-density lipoprotein (HDL-C) cholesterol concentration (i.e., ≤ 40 mg/dl) in the blood or elevation of the low density lipoprotein (LDL-C) cholesterol > 100 mg/dl and total cholesterol of more than 200 mg/dl.[16]

Statin induced Myopathy: Patients were considered to have Myositis if they had proximal muscle weakness (power of 3 or less) with raised CK up to 10 times the normal value. [17]

PATIENTS AND METHODS

Cross sectional descriptive study completed in Department of Medicine Fatima Memorial Hospital, Lahore. With a duration of Six months, 1st January 2018 to 30th June, 2018Sample size was 230 dyslipidemic patients using statin was calculated with 95% confidence level, 5% margin of error and taking expected percentage of myopathy i.e. 18%[18]. Sample was calculated with convenient Sampling

Inclusion Criteria: Patients having age from 30-60 years of either gender, patients with duration of more than 1 year of dyslipidemia (as per operational definition)

Exclusion Criteria: Patient already diagnosed with myopathy & patients with chronic musculoskeletal disease, hypothyroidism, Parkinson's disease, Vitamin B12 deficiency, Rheumatoid arthritis, cerebrovascular disease, , chronic kidney disease (S. Creatinine>1.3mg/dl) or liver failure (AST, ALT>40Iμ/L) and any type of cancer.

Data collection procedure: 230 dyslipidemic patients meeting the inclusion criteria coming to outpatient department of internal medicine at Fatima Memorial hospital, Lahore were included in the study. Patients were included in the study after taking the informed consent. Demographic information (name, age, address, education and socioeconomic level) were also noted. Responses were assessed and presence or absence of myopathy was noted. Blood samples were obtained by using 3cc syringe. All samples were sent for assessment of CK levels. Reports were assessed and if CK levels were more than 10 times the normal value or patient had proximal muscle weakness than statin induced myopathy were labeled as per operational definition.

Data analysis: SPSS version 25.0 was used for data entry and analysis. Quantitative variables were shown as mean and standard deviation. The qualitative variables were represented as percentage and frequency like gender, socioeconomic level and signs and symptoms (burning, tingling and numbness). Chi square test was calculated to measure association of socio-demographic variables with myopathy. P value ≤ 0.05 was considered as significant. Post stratification chi square test was calculated with p value ≤ 0.05 taken as significant.

RESULTS

Among statin induced myopathy respondents, mean age was 49.9±8.6 years while it was 49.9±9.4 years among not having statin induced myopathy; the mean LDL levels among statin induced myopathy respondents was 121.1±22.6 mg/dl whereas it was 123.8±20.3 mg/dl; the mean HDL levels among statin induced myopathy respondents was 36.6±5.1 mg/dl whereas it was 36.9±5.1 mg/dl; the mean cholesterol levels among statin induced myopathy respondents was 207.8±16.4 mg/dl whereas it was 209.9±15.5 mg/dl and the mean CK levels among statin induced myopathy respondents was 213.4±9.6 IU/liter whereas it was

106.4±45.4 IU/liter (Table 1). Gender among statin induced myopathy showed that males were 42 and females were 13 in number; and among non-statin induced myopathy group there were 121 males and 54 females (Table 1).

Education among statin induced myopathy group showed that 09 were illiterate, 30 were having middle education and 16 had matric while in non- statin induced myopathy group, there were 37 illiterate, 75 had passed middle, and63 had done matric (Table 1).

Socio-economic status among statin induced myopathy group showed that 04 were having low income, 49 were having middle status and 02 had high socio-economic status while in non-statin induced myopathy group, there were 13 respondents with low income, 154 had middle status and08 had high socio-economic status (Table 1).

Statin induced myopathy was seen in 55 (23.9%) respondents while in 175 (76.1%) there was no statin induced myopathy. (Figure I).

Statin induced myopathy was found in 42 males, while 13 females had also statin induced myopathy whereas 121 males had no statin induced myopathy and among 54 females there was no statin induced myopathy. The difference was statistically insignificant (0.304) (Table 2).

There were 09 illiterate people having statin induced myopathy, 30 had studied up to middle and 16 had done matric while among non-statin induced myopathy group, there were 37 illiterate respondents, 75 had got middle standard education and remaining 63 had done matric. The difference was statistically insignificant (0.315) (Table 2).

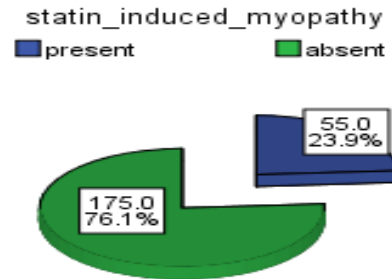Fig.1: Frequency distribution of Statin Induced Myopathy

statin_induced_myopathy
■ present ■ absent

55.0 23.9%

175.0 76.1%

Table 1: Comparison of Age, LDL, HDL, Cholesterol, CK Levels, Gender, Education Status & Socioeconomic status with Statin Induced Myopathy

Variables		Statin Induced Myopathy	
		Present	**Absent**
N		**55**	**175**
Age (years)	Mean	49.9	49.9
	SD	8.6	9.4
LDL (mg/dl)	Mean	121.1	123.8
	SD	22.6	20.3
HDL (mg/dl)	Mean	36.6	36.9
	SD	5.1	5.1
Cholesterol (mg/dl)	Mean	207.8	209.9
	SD	16.4	15.50
CK Levels (IU/L)	Mean	213.4	106.4
	SD	9.6	45.4
Gender	Male	42	121
	Female	13	54
Total		**55**	**175**
Education	Illiterate	09	37
	Middle	30	75
	Matric	16	63
Socio-economic Status	Low	04	13
	Middle	49	154
	High	02	08

Low income (<15000) was found in 04 respondents who were suffering from statin induced myopathy, middle income (15000-

50000) having statin induced myopathy were 49 and remaining 02 having statin induced myopathy had high income (>50000) while among non-statin induced myopathy respondents, 13 had Low income (<15000), 154 had middle income (15000-50000) and 08 had high income (>50000). The difference was statistically insignificant (0.955) (Table 2).

In respondent's ≤45 years, there were 09 males having statin induced myopathy and 39 were not having statin induced myopathy while there were 07 females having statin induced myopathy and 14 having no statin induced myopathy. While in respondent's >45 years, there were 33 males having statin induced myopathy and 82 were not having statin induced myopathy while there were 06 females having statin induced myopathy and 40 having no statin induced myopathy. Statistically significant difference was not found between the statin induced myopathy with gender in patients with age ≤ 45 years i.e., p-value=0.222 and with age >45 years showed significant p-value=0.036 respectively (Table 2).

In male respondent's, regarding ≤ 45 years age; there were 09 respondents having statin induced myopathy and 39 were not having statin induced myopathy whereas among >45 year there were 33 respondents having statin induced myopathy and 82 were having no statin induced myopathy. While in female respondent's, regarding ≤ 45 years age; there were 07 respondents having statin induced myopathy and 14 were not having statin induced myopathy whereas among >45 year there were 06 patients having statin induced myopathy and 40 were having no statin induced myopathy. Statistically significant difference was not found between the peripheral neuropathy with age in patients with respect to their gender. i.e., p-value=0.186 and p-value=0.053 respectively (Table 2).

In respondent's ≤ 45 years, there was 01 respondent having statin induced myopathy belonged to low socioeconomic status while 02 were not having statin induced myopathy were also having low socioeconomic class and 15 having statin induced myopathy belonged to middle income group and 50 were having no statin induced myopathy were in the same income group and there was 01 having no statin induced myopathy in this higher income group. While in respondent's > 45 years, there were 03 respondents having statin induced myopathy belonged to low socioeconomic status and 11 in this income group was not having the disease, 34 having statin induced myopathy belonged to middle income group and 104 were having no statin induced myopathy in the same income group and lastly there were 02 patients having statin induced myopathy in higher income group and 07 were having no statin induced myopathy in this higher income group. Statistically significant difference was not found between the statin induced myopathy with income in patients with age ≤ 45 years and with age >45 years. i.e., p-value=0.525 and p-value = 0.918 respectively (Table 2).

In male respondent's, there were 03 respondents having statin induced myopathy belonged to low socioeconomic status and 11 respondents were having no statin induced myopathy, 37 having statin induced myopathy belonged to middle income group and 103 patients were having no statin induced myopathy belonged to same income group and there were 02 patients having statin induced myopathy in higher income group and 07 were having no peripheral neuropathy in this higher income group. While in female respondent's, there was one respondent having statin induced myopathy belonged to low socioeconomic status and 02 respondents were having no statin induced myopathy, 12 females having statin induced myopathy belonged to middle income group and 51 were having no statin induced myopathy belonged to same income group and there was one patient having no statin induced myopathy in higher income group. Statistically significant difference was not found between the statin induced myopathy with income in male and female patients i.e., p-value=0.891 and p-value = 0.439 (Table 2).

Table-III: Frequency of Statins induced myopathy with regard to Age distribution, Gender, Education Status & Socioeconomic status

| | | Statin Induced Myopathy | | Total | P-value |
		Present	Absent		
Gender	Male	42	121	163	0.304
	Female	13	54	67	
Education	Illiterate	09	37	46	0.315
	Middle	30	75	105	
	Matric	16	63	79	
Socio-economic Status	Low	04	13	17	0.955
	Middle	49	154	203	
	High	02	08	10	
Age ≤ 45 years	Male	09	39	48	0.222
	Female	07	14	21	
Age >45 years	Male	33	82	115	0.036*
	Female	06	40	46	
Gender	Age in years				
Male	≤ 45	09	39	48	0.186
	>45	33	82	115	
Female	≤ 45	07	14	21	0.053
	>45	06	40	46	
Age (years)	Income (PKR)				
≤ 45	Low (<15000)	01	02	03	0.525
	Middle (15000-50000)	15	50	65	
	High (>50000)	00	01	01	
>45	Low (<15000)	03	11	14	0.918
	Middle (15000-50000)	34	104	138	
	High (>50000)	02	07	09	
Gender	Income (PKR)				
Male	Low (<15000)	03	11	14	0.891
	Middle (15000-50000)	37	103	140	
	High (>50000)	02	07	09	
Female	Low (<15000)	01	02	03	0.439
	Middle (15000-50000)	12	51	63	
	High (>50000)	00	01	01	

DISCUSSION

Statins are an extremely powerful and well established class of drugs. Numerous experimental and clinical data support their use for a wide range of indications and clinical situations. Most patients treated with statins tolerate statins without difficulty; even long term treatment has not been associated with deleterious impact to any particular organ system.[19]Given the increasing number of indications for statins and the growing number of users, more attention has been drawn to the side effects of statin therapy. Contrary to randomized clinical trials, where the occurrence of adverse reactions ranges between 1 and 5%, actual clinical experience, as reported in the literature, suggests that the number of undesirable effects stemming from statin use is much higher (15-20%).[20]Statins are highly effective in dyslipidemia as monotherapy and are the main pillar of management in patients with dyslipidemia[21].

In this study, we evaluated the frequency of the condition in dyslipidemic patients. We also determined the association of various patient related variables with statin induced myopathy.

In our study, the frequency of myopathy induced by statinsin patients who have already been diagnosed as having dyslipidemia was 23.9%. 28% of patients were reported to have muscular symptoms which is significantly more than what has been reported in previous studies (1-5%).[22,23] PRIMO study for example, reported that 11% of statin users had muscular symptoms.[24]EL-SALEM et al in his study, which was completed in Jordan,reported that 21% of the patients using statins had muscular symptoms[25].

In current study patients' mean age among statin induced myopathy respondents was 49.9±8.6 yearswhile it was 49.9±9.4 years among not having myopathy induced by statins; Gender among myopathy induced by statins showed that males were 42 and females were 13 in number; and among non-statin induced myopathy group there were 121 males and 54 were females.In their study, Lakhiar et al reported that 54 % were males and 46 % were females while the mean age was 45.19 years.[7]Another study reported that the age range was 39 - 90 years while the mean age was 58 ± 11.2 in statin induced myopathy subjects[28].

In our study, no significant impact of age or gender was found, on prevalence of statin induced myopathy. El-Salem et al in their study demonstrated with respect to gender, males were effected more when compared tofemales. However Sathasivam et al findings were different as they did not find any significant differences with respect to gender.[25, 29]

Lack of knowledge or financial resources could be the possible reasons which cause a delay in diagnosis. In our opinion, frequency of myopathy induced by statins can be variable. however our findings are helpful for the dyslipidemic patients and physicians as well for timely management of the morbidity.

CONCLUSION

This study reports an increased prevalence of statin induced myopathy in dyslipidemic patients. Male respondents were more in number than females but both had showninsignificant occurrence of statin induced myopathy. The age>45 years of the respondents showed significant statistical difference with gender and income showed insignificant association with age, gender and education.

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