Original Article

Frequency of Myalgia in Patients Using Statin Therapy in Patients with Obstructive Coronary Artery Diseases

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ABSTRACT

Objective: To determine the frequency of myalgia in patients using statin therapy for obstructive coronary artery diseases (CAD) presenting at Bannu Interventional Cardiac Center Bannu, Pakistan.

Study Design: Descriptive Study

Place and Duration of Study: This study was conducted at the Bannu Interventional Cardiac Center (BICC) Bannu, Pakistan, June 2020 to May, 2021.

Materials and Methods: Patients with Obstructive CAD, were recruited during the study period, following ethical approval and informed written consent, while stricltly following inclusion and exclusion Criteria. Demographic and clinical characteristics of the patients were recorded on predesign research proforma.

Results: A total of 267 using statin therapy for obstructive coronary artery diseases (CAD) were enrolled in this study. Mean age was 44.65 ± (8.87) (SD) years, ranging from 18-70 years. BMI was 27.21 ± (5.41) most of the patients were found overweight. Out of total n=267 Cases 165[62%] were male and 102 [38%] were female. Intensity of stain were categorized in to three categories, most of the 48[18%] patients were belonging to low intensity, 100[37.5%] were moderate intensity and most of them were belong to 119[44.6%] had high intensity. Frequency of myalgia was found to be 35[13%].

Conclusion: In our study the frequency of myalgia in patients using statin therapy for obstructive CAD was found to be only in 35[13%].

Key Words: Coronary artery diseases, Myalgia, Creatine kinase low-density lipoprotein cholesterol, non-high density lipoprotein, Statin

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INTRODUCTION

Statin therapy is generally well tolerated and very effective in the prevention and treatment of cardiovascular disease, regardless of cholesterol levels; however, it can be associated with various adverse events.

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Patients frequently discontinue statin therapy without medical advice because of perceived side effects especially statin-associated muscle symptoms. These symptoms most often consist of myalgia unaccompanied by significant creatine kinase (CK) elevations. Less often, myositis (elevated CK >10 times the upper limit of normal) or rhabdomyolysis (CK level >10,000 IU/L or accompanied by significant elevation in creatinine level) develops.

Despite Statins are generally safe and well tolerated, but not all patients are able to use a statin. Statin intolerance is most frequently attributed to muscle-related adverse symptoms.

However, statins are considered underutilized in patients for whom they are indicated and are frequently discontinued. Unfortunately, statin non-adherence correlates highly with risk for acute CV events, increasing the risk for recurrent MI and CHD.

Myalgia refers to patients with symptoms of muscle aches in the absence of an elevated CK, whereas myositis is the presence of symptoms with a CK elevation. Statins have long been associated with muscle-related toxicity, including myalgia myopathy

and myositis the last two of which involve significant CK elevations.

Muscle pain (myalgia) and weakness is experienced by up to 10% of patients taking statins. However, myalgia is commonly experienced by all people at some stage in their life, regardless of statin use.

Routine laboratory monitoring for statin-associated adverse effects is not recommended in asymptomatic patients. Statin discontinuation rates remain high, even among patients with CAD (over 50% after 1 year).[4, 6, 12]

A study conducted by Parker et al. reported myalgia in 9.4% of the patients using high intensity statin therapy

Since there is no information on the frequency of myalgia in patients using high intensity statin therapy for CAD under everyday conditions, the goal of the study were to develop a method to report myalgia in patients using high intensity statin.

MATERIALS AND METHODS

This descriptive Study was carried out at BICC, Bannu, Pakistan, from 1st June 2020 to 31st May, 2021, following ethicath approval from the ethical and research committee and informed written consent from the indvidual patient.

Sample size: Taking the frequency of Myalgia as 9.4% in patients using statin therapy[15], confidence interval at 95% and margin of error at 3.5% and putting this information in WHO sample size calculator version 2.0 the calculated sample size is 267.

Sample Technique: Non-probability consecutive sampling technique were used.

Objective: To determine the frequency of myalgia in patients using statin therapy for obstructive CAD presenting at BICC, Bannu.

Inclusion Criteria:

Patient of age between 18 to 70 years, either gender, on Statin therapy and diagnosed with obstructive CAD as per operational definition

Exclusion Criteria: Patients with prior history of Myalgia, CKD or baseline CK exceeded 10 times the ULN – (normal range; 22 to 198 U/L).

LFTs exceeded 3 times the ULN– (normal range; AST 8 to 48 U/L).

Operational Definitions: Obstructive CAD: It was defined as ≥70% stenosis in one or more of the major coronary arteries or ≥50% stenosis in left main (LM) coronary artery on coronary angiography at presentation.

Statin Therapy: Patient receiving any dosage of the Atorvastatin or Rosuvastatin for at least two months.

Intensity of Statin Therapy: Were classified as follow;

Low Intensity: simvastatin 10 mg/day, Pravastatin 10-20mg or pitavastatin 1 mg/day.

Moderate Intensity: Atorvastatin 10-20mg/day or Rosuvastatin: 5-10 mg/day

High Intensity: Atorvastatin 40-80mg/day or Rosuvastatin: 20-40mg/day[15]

Study Outcome: Myalgia:

were labelled "Yes" if patient met the study definition for "myalgia" if all of the following occurred[15]:

Reported new or increased muscle pain, cramps, or aching not associated with exercise

Symptoms persisted for at least 2 weeks

Symptoms resolved within 2 weeks of stopping the statin therapy.

Symptoms reoccurred within 4 weeks of restarting the statin therapy.

Effect Modifiers:

HTN and DM were labeled as "Yes" if patient has documented history of HTN or DM and on its medication for at least 6 months otherwisewere labeled as "No"

Smoking: were labeled as "Yes" if patient currently or has history of smoking 10 or more cigarettes per day for at least 5 years or 5 or more cigarettes per day for at least 10 years otherwise were labeled as "No"

Family history of CAD: were labeled as "Yes" if the patient has family history of CAD in first degree relatives, male less than 55 years of age or female less than 65 years of age, otherwise were labeled as "No".

Obesity: were labelled as "Yes" if the patient has BMI > 27.5 kg/m 2,

otherwise were labelled as "No". Kilograms BMI were calculated by using formula;

$$\text{BMI} = \frac{\textit{Weight in kilograms } kg}{\textit{Height in metters}^2}\,\frac{}{m^2}$$

Data Collection: All patients presenting with Obstructive CAD at BICC, Bannu and on Statin therapy were enrolled, following strict inclusion and exclusion criteria. A comprehensive history and physical examination were performed. Demographic and clinical characteristics of the patients were recorded at the time of presentation. Type and dosage of statin were recorded. Myalgia were recorded after two months of statin therapy for all the patients. All the collected data were recorded on predesigned proforma.

Data Analysis: Data were entered and analysis using SPSS version-16 (IBM Corp. Released 2016. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp). Shapiro-Wilk test were applied to check the hypothesis of normality for age (years), weight (kg), height (cm), and BMI (kg/m2) of the patients and were expressed using appropriate descriptive statistics such as mean ± SD, maximum and minimum. Frequency and percentages were calculated for categorical variables such as gender, age group, obesity, smoking status, DM, family history, hypertension, intensity of statin, and Myalgia. Effect modifiers like age groups, gender, obesity, smoking status, diabetic mellitus, and family history of CAD,

hypertension, and intensity of statin were controlled through stratification. Post stratification appropriate chi-square test or fisher exact test were applied. Two sided p-value of ~ 0.05 were taken as criteria of statistical significance. For the graphical presentation of data, bar graphs and pi-charts were used.

RESULTS

A total of 267 patients using statin therapy for obstructive CAD were enrolled in this study. Mean age was 44.65 ± (8.87) years, [18-70], average height and weight was found to be 165.91 ± (5.41) & 27.21 ± (5.41), BMI was 27.21 ± (5.41) most of the patients were found overweight. (Table-1)

Out of total n=267 Cases 165[62%] were male and 102[38%] were female. The maximum number of cases 116(43.4%) were between 51-70 years of age (Chart-1)

Intensity of statin therapy categories showed that, the lowest frequecy of 48 [18%] patients were belonging to low intensity, 100[37.5%] were moderate intensity and most of them were belong to 119[44.6%] had severe intensity. (Chart-2)

Almost half of the patients in our study were obese 138[51.7%]. Pertinent Family histor of CAD was present in 36[13%] as compared to 231 [87%] those having no family history (Table 02).

The most common presented risk factor was hypertension 136 [50.9%] followed by DM which was 128[48%] and smoking in 61 [22.58%] cases. (Table 02)

Frequency of myalgia in patients using statin therapy for obstructive CAD was found to be only in 35[13%]. (Chart-3)

Table No.1: Descriptive Statistics in patients using statin therapy for obstructive CAD (n=267)

Descriptive	Mean ± SD	Range [Max -Min]
Age in years	44.65 ± (8.87)	[70 - 18]
Weight kg	74.5 ± (0.09)	[110 - 55]
Height cm	165.91 ± (5.41)	[180 - 150]
BMI Kg/m2	27.21 ± (5.41)	[43.85 - 18.17]

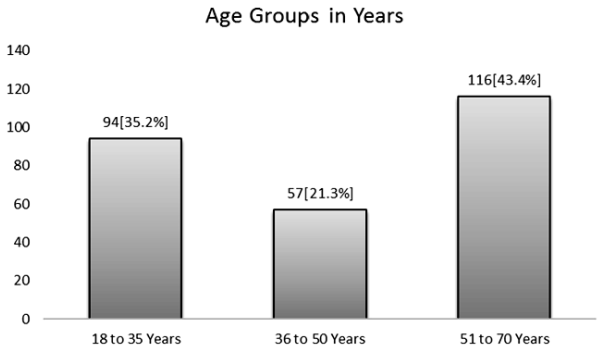

Figure No.1: Classification of age groups

Comparison of frequency of myalgia with intensity of statin were found statistically significant and observed that most of the myalgia patients had belong to high intensity and moderate intensity as compared to low intensity (P-value<0.001 *) (Table-3).

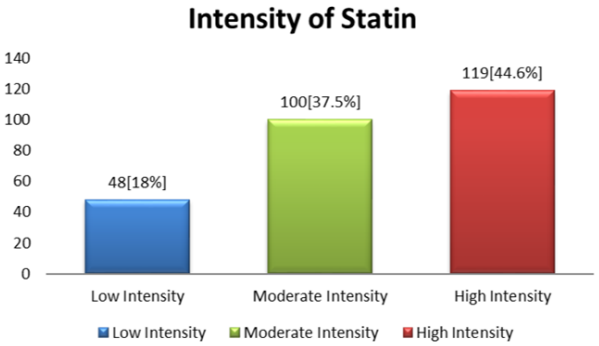

Figure No.2: Classification of intensity of stain

Table No.2: Frequencies of Risk Factor for Obstructive CAD

S.No	Risk Factor	Yes	No
1.	HTN	136 [50.9%]	131 [49.1%]
2.	DM	91[34.1%]	176[65.9%]
3.	Smking	61[22.8%]	206[77.2%]
4.	Obesity	138[51.7%]	129[48.3%]
5.	Family History	36[13%]	231 [87%]

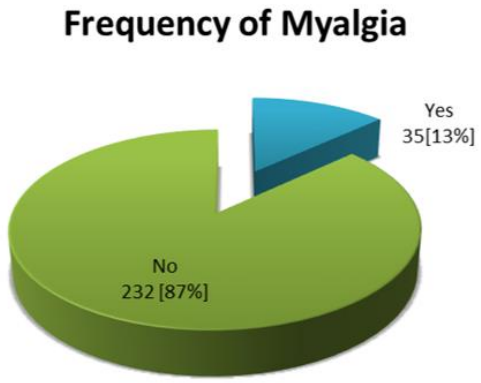

Figure No.3: Frequency of myalgia in patients using statin therapy for obstructive CAD

Table No.3: Comparison of frequency of myalgia in patients using statin therapy for obstructive CAD with intensity of statin (n=267)

Intensity of Statin	Myalgia			P-value
	Yes [n=35]	No [n=232]	Total [n=267]	
Low Intensity	1 [2.9%]	47 [20.3%]	48 [18%]	<0.001*
Moderate Intensity	8 [22.9%]	92 [39.7%]	100 [37.5%]	
High Intensity	26 [74.3%]	93 [40.1%]	119 [44.6%]	
Total	35 [100%]	232 [100%]	267 [100%]	

Comparisons of myalgia among demographics and confounding variables, indicate that, patients who had

documented history of diabetes mellitus and hypertension were found statistically associated with presence of myalgia (pvalue=0.007* & <0.001*), and those patient who do not obese, were found significant with myalgia (P-value=0.01 0*). (Table-4).

Table No.4: Comparison of myalgia in patients using statin therapy for obstructive CAD (n=267)

	Myalgia			
	Yes	No	Total	P-value
	[n=35]	[n=232]	[n=267]	
Gender				
Male	17 [6.4%]	148 [55.4%]	165 [61.8%]	0.084
Female	18 [6.7%]	84 [3 1.5%]	102 [38.2%]	
Total	35 [13.11%]	232 [86.89%]	267 [100%]	
Obesity				
Yes	3 [1.1%]	68 [25.5%]	71 [26.59%]	0.010*
No	32 [12%]	164 [61.4%]	196 [73.41%]	
Total	35 [13.11%]	232 [86.89%]	267 [100%]	
Family History of CAD				
Yes	3 [1.12%]	33 12.36%]	36 [13.48%]	0.361
No	32 [11.99%]	226 [84.6%]	231 [86.52%]	
Total	35 [13.11%]	232 [86.89%]	267 [100%]	
Diabetes Mellitus [DM]				
Yes	19 [7.12%]	72 [26.97%]	91 [34.08%]	0.007*
No	16 [5.99%]	160 [74.53%]	176 [64.92%]	
Total	35 [13.11%]	232 [86.89%]	267 [100%]	
Hypertension [HTN]				
Yes	29 [10.86%]	107 [40.07%]	136 [50.94%]	<0.001*
No	6 [2.25%]	125 [46.82%]	131 [49.06%]	
Total	35 [13.11%]	232 [86.89%]	267 [100%]	
Smoking Status				
Yes	10 [3.75%]	51 [19.10%]	61 [22.85%]	0.387
No	25 [9.36%]	181 [67.79%]	206 [77.15%]	
Total	35 [13.11%]	232 [86.89%]	267 [100%]	
Age Groups				
18 to 35 Years	16 [5.99%]	78 [29.21%]	94 [35.21%]	0.354
36 to 50 Years	7 [2.62%]	50 [18.73%]	57 [21.35%]	
51 to 70 Years	12 [4.49%]	104 [38.95%]	116 [43.45%]	
Total	35 [13.11%]	232 [86.89%]	267 [100%]	

DISCUSSION

The mean age of our patients was quite young 44.65 ± (8.87) years, in contrast to western nation where this is the disease of elderly population. Male were more predominant (62%) as compared to female in the present study. This is in consistent with other studies from the region. Khan S has reported even more male (Male:Female, 1:1.9) with Acute Myocardial infarction. Almost half of the patients with obstuctive CAD in our study were obese 138[51.7%]. Anne B et al reported that 84% of their patient were obese or overweight.

In our study the frequency of myalgia in patients using statin therapy for obstructive CAD was only 35[13%] which is most similar study conducted by Parker et al.[15] reported myalgia in 9.4% of the patients using high intensity statin therapy. Many studies reported the incidence rate of myalgia during statin therapy has varied from 1% to 25%. Hansen et al grouped patients with a number of statin-induced muscle disorders together. A study by El~Salem, K., et al. (201 1) has demonstrated a higher prevalence of myalgia muscle symptoms was reported (21%) among patients using statins, as compared with most other report in the literature has been reported same prevalence of myalgia respectively.

Most previous estimates of adverse muscle reactions of statins were derived from clinical trials originally designed to test their efficacy and case reports and case series. Another study done by Sadeeqa, S., et al. (201 8) prevalence of statin induced myopathy was 51%in local population. She also reported more prevalent myalgia in age range 40-50, with females 57% and males 47%. Statin's-associated muscle symptoms cover a broader range of clinical presentations, usually with normal or minimally elevated CK levels, with a prevalence of 7–29% in registries and observational studies (Stores et al., 201 5)[13].

According the associations this study indicates that, patients who had documented history of diabetes mellitus and hypertension were found statistically associated with presence of myalgia (p-value=0.007* & <0.001*), and those patient who do not obese, were found significant with myalgia (P-value=0.010*). These results should prompt additional studies examining muscular performance with long-term statin treatment in both healthy patients and those with confirmed statin-associated myalgia.

CONCLUSION

In our study the frequency of myalgia in patients using statin therapy for obstructive CAD was found to be only in 35[13%].

Author's Contribution:

Concept & Design of Study: Abdul Waris
Drafting: Samiullah Khan, Muhammad Niaz Khan

Data Analysis:	Muhammad kashif Iltaf, Raza Muhammad, Sadullah Shah
Revisiting Critically:	Abdul Waris, Samiullah Khan
Final Approval of version:	Abdul Waris

Conflict of Interest: The study has no conflict of interest to declare by any author.

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