SHORT REPORT

Prescription of statins after acute coronary syndrome; a single-centre observational study

Muhammad Muzaffar Mahmood,[1] Muhammad Jabran Nawaz[2]

Abstract

There is limited information about the current use of high-intensity statins (HIS) after acute coronary syndrome (ACS) in Pakistani patients. We studied the prescription of HIS in patients admitted with ACS to Ittefaq Hospital, Lahore, Pakistan, from February 2019 to December 2019. Among the 411 patients, 221 (53.8%) patients underwent Percutaneous Coronary Intervention (PCI), 62 (15.1%) were referred for Coronary Artery Bypass Graft (CABG), and 128 (31.1%) were treated medically. Overall 408 (99.3%) patients were prescribed statins and 198 (48.2%) received HIS, with 45 (10.9%) patients receiving maximally allowed dose (Atorvastatin 80mg or Rosuvastatin 40mg). Patients treated with PCI were more likely to be prescribed HIS (73.3% vs 26.7%, p <0.001), while older patients (>75 years of age), those treated medically, and patients with severely reduced LV systolic function were significantly less likely to receive HIS (p <0.001). Our study, therefore, identifies a gap in implementation of guidelines for HIS use, particularly among the medically treated ACS patients.

Keywords: Statins, High-Intensity Statins, Acute Coronary Syndrome.

DOI: 10.47391/JPMA.4328

Submission completion date: 27-07-2021
Acceptance date: 03-09-2022

Introduction

High-intensity statins reduce LDL-C by more than 50% from the baseline and are recommended after acute coronary syndrome (ACS) based on evidence from multiple randomised controlled trials (RCTs).[1,2]

Earlier studies showed that Asians, in particular East Asians, have a higher plasma exposure to Rosuvastatin[3] with better reduction in lipids at lower doses compared to whites. This led to a recommendation for using lower doses of statins among Asians. However, prospective as well as registry data indicate that unlike East Asians, south Asians achieve similar reduction in LDL-C from statins compared to Western population.[4]

Studies highlight that one of the most important predictors of long-term use of high-intensity statins is prescribing the drugs before discharge from the hospital.[5] There is limited information about the use of high-intensity statins in contemporary management of patients with ACS in Pakistan. The prescription of statins, in particular high-intensity statins, to patients with ACS at our centre was studied, with the aim to identify any factors associated with more frequent use of high-intensity statins.

Methods

The study included patients admitted with ACS to coronary care unit at Ittefaq Hospital (Trust), Lahore, from February 2019 to December 2019. Only patients surviving till discharge from the hospital were included in the study, while patients whose complete dataset was not available were excluded.

Prescription of statins was recorded by review of drug prescription charts. High-intensity statin was defined as Rosuvastatin 20mg and 40mg and Atorvastatin 40mg and 80mg in accordance with the European Society of Cardiology (ESC) and American College of Cardiology (ACC) guidelines. Other statins and dose strengths were recorded as non-high-intensity statins. Patients who were not prescribed statins were included in the non-high-intensity statins cohort. ACS included unstable angina pectoris (UAP), non-ST elevation acute coronary syndrome (NSTE-ACS), and ST-elevation acute coronary syndrome (STE-ACS). UAP, NSTE-ACS and STE-ACS were diagnosed using the conventional criteria of suggestive clinical presentation and/or the universal definition of myocardial infarction. The left ventricular ejection fraction was measured by biplane method and/or visual estimation using Vivid 7 echocardiography machine (GE healthcare, Horten, Norway).

Only patients who underwent percutaneous coronary intervention (PCI) or were referred for coronary artery bypass grafting (CABG) during the index hospital admission were included in the PCI and CABG cohort.

[1]Department of Cardiology, [2]Department of Medicine, Ittefaq Hospital, Lahore, Pakistan. **Correspondence:** Muhammad Muzaffar Mahmood. Email: muzafar.mahmood@gmail.com
ORCID ID: 000-0002-5162-5276

Patients who were initially treated without revascularisation either after or without undergoing coronary angiography were included in the medically treated cohort.

Sample size was calculated to be 385 using a 95% confidence level and 5% margin of error with expected rate of patients prescribed HIS as 50.0% (conservative approach) using an online calculator[6]. Statistical analysis was performed on SPSS 20. Data for age was presented by using Mean ±SD, while data for type of disease, comorbid conditions, gender, type, and dosage of statin were described by using frequency and percentages. Chi-square test was applied to check the association of various factors with the intensity of statin dosage, and binary logistic regression was used to account for potential confounders. P-value ≤0.05 was considered significant.

Results

Overall 411 patients were included in the study (age range 27-96 years, mean 60±12.7 years. Among them, 266 (64.7%) were males. Diabetes (n=235, 57%) and hypertension (n=341, 83%) were frequent. Of all the patients, 221 (53.8%) underwent PCI, 62 (15.1%) were referred for CABG and 128 (31.1%) were treated medically. Chronic kidney disease (CKD) stage III or higher was present in 60 (14.5%) patients (Table 1). The mean serum cholesterol concentration was 197±31 mg/dl, LDL-C concentration was 137±22 mg/dl, HDL-C concentration was 36±6 and triglyceride concentration was 170±38 mg/dl. Patients who were treated medically were older (mean age 65.8 ±12.8 years) compared to patients who underwent PCI (57.3 ±12.2 years) or CABG (57.7 ±10 years) (Table 1). Almost all patients (n=408, 99.3%) were prescribed statins and 198 (48.2%) patients were prescribed high-intensity statins.The prescription of high-intensity statins was similar between both genders (p= 0.269). Patients above 75 years of age received high-intensity statins less frequently (p <0.0001, adjusted odds ratio (aOR) 0.17, 95% confidence interval (CI) 0.04-0.71). Patients treated with PCI were more likely to receive high-intensity statins (p <0.001, aOR 4.93, CI 2.49-9.85), while those treated medically were significantly less likely to receive high-intensity statins (p <0.001, aOR 0.16, CI 0.07-0.38). Patients with severely impaired LV systolic function received high-intensity statins less frequently (p <0.001, aOR 0.42, CI 0.18-0.98). The association of various factors with the use of high-intensity statins is presented in Table 2.

Table-1: Demographic and clinical characteristics of the study population.

		Treatment			
	Total N	**CABG N (%)**	**PCI N (%)**	**Med N (%)**	***P*-value**
Mean ±SD	60 ±12.7	57.7 ±10	57.3 ±12.2	65.8 ±12.8	
Age (Years)					
<40	26	3 (11.5)	21 (80.8)	2 (7.7)	<0.001
41-65	245	46 (18.8)	137 (55.9)	62 (25.3)	
66-75	93	11 (11.8)	50 (53.8)	32 (34.4)	
>75	47	2 (4.3)	13 (27.7)	32 (68.1)	
Gender					
Male	266	47 (17.7)	158 (59.4)	61 (22.9)	<0.001
Female	145	15 (10.3)	63 (43.4)	67 (46.2)	
Diagnosis					
UAP	39	8 (20.5)	24 (61.5)	7 (17.9)	
NSTEMI	220	33 (15)	86 (39.1)	101 (45.9)	<0.001
STEMI	152	21 (13.8)	111 (73)	20 (13.2)	
CKD					
Normal-Stage II	351	61 (17.4)	175(49.9)	115 (32.8)	<0.001
Stage III or above	60	1 (1.7)	46 (76.7)	13 (21.7)	
Smoker					
Yes	157	15 (9.6)	118 (75.2)	24 (15.3)	<0.001
No	254	47 (18.5)	103 (40.6)	104 (40.9)	
DM					
Yes	235	39 (16.6)	127 (54)	69 (29.4)	0.497
No	176	23 (13.1)	94 (53.4)	59 (33.5)	
HTN					
Yes	341	56 (16.4)	165 (48.4)	120 (35.2)	<0.001
No	70	6 (8.6)	56 (80.0)	8 (11.4)	
Dyslipidaemia					
Yes	228	37 (16.2)	140 (61.4)	51 (22.4)	<0.001
No	183	25 (13.7)	81 (44.3)	77 (42.1)	
LVEF					
Normal	195	30 (15.4)	109 (55.9)	56 (28.7)	
Mild	85	19 (22.4)	51 (60.0)	15 (17.6)	
Moderate	69	7 (10.1)	39 (56.5)	23 (33.3)	<0.001
Severe	62	6 (9.7)	22 (35.5)	34 (54.8)	

CABG; Coronary artery Bypass Graft, CKD; Chronic Kidney Disease, DM; Diabetes Mellitus, HTN; Hypertension, LVEF; Left Ventricular Ejection Fraction, NSTEMI; Non ST-elevation Myocardial Infarction, PCI; Percutaneous Coronary Intervention, STEMI; ST-elevation Myocardial Infarction, UAP; Unstable Angina Pectoris

Table-2: Association of demographic and clinical factors with the prescription of high-intensity statins (HIS)

Variable	**HIS n (%)**	**Non HIS n (%)**	**P-value**	**Adj. OR (95% CI)**
Gender				
Male	134 (50.4)	132 (49.6)		1.51 (0.83 - 2.74)
Female	64 (44.1)	81 (55.9)	0.269	Ref
Age (years)				
≤ 40	20 (76.9)	6 (23.1)		Ref
41 - 65	128 (52.2)	117 (47.8)		0.52 (0.17 - 1.56)

Contd. on Next Page

Contd. from previous page

Variable	HIS n (%)	Non HIS n (%)	P-value	Adj. OR (95% CI)
65 - 75	42 (45.2)	51 (54.8)		0.45 (0.14 - 1.48)
> 75	8 (17.0)	39 (83.0)	< 0.001	0.17 (0.04 - 0.71)
Diagnosis				
NSTEMI	85 (38.6)	135 (61.4)		Ref
STEMI	95 (62.5)	57 (37.5)		1.18 (0.66 - 2.1)
UAP	18 (46.2)	21 (53.8)	< 0.001	0.57 (0.25 - 1.32)
Treatment modalities				
CABG	25 (40.3)	37 (59.7)		Ref
Medically	11 (8.6)	117 (91.4)		0.16 (0.07 - 0.38)
PCI	162 (73.3)	59 (26.7)	< 0.001	4.93 (2.47 - 9.85)
CKD Stage				
0 - II	166 (47.3)	185 (52.7)		Ref
III & Above	32 (53.3)	28 (46.7)	0.468	1.33 (0.64 - 2.79)
Smoker				
Smoker	91 (58.0)	66 (42.0)		Ref
Non-smoker	107 (42.1)	147 (57.9)	0.003	1.08 (0.61 - 1.92)
LVEF (%)				
Normal	95 (48.7)	100 (51.3)		Ref
Mild	52 (61.2)	33 (38.8)		1.30 (0.66 - 2.57)
Moderate	36 (52.2)	33 (47.8)		1.24 (0.59 - 2.58)
Severe	15 (24.2)	47 (75.8)	< 0.001	0.42 (0.18 - 0.98)
DM				
Yes	120 (51.1)	115 (48.9)		Ref
No	78 (44.3)	98 (55.7)	0.210	0.69 (0.41 - 1.16)
HTN				
Yes	154 (45.2)	187 (54.8)		Ref
No	44 (62.9)	26 (37.1)	0.010	1.16 (0.6 - 2.25)
Dyslipidaemia				
Yes	114 (50)	114 (50)		Ref
No	84 (45.9)	99 (54.1)	0.467	1.71 (0.99 - 2.96)

CABG; Coronary artery Bypass Graft, CKD; Chronic Kidney Disease, DM; Diabetes Mellitus, HTN; Hypertension, LVEF; Left Ventricular Ejection Fraction, NSTEMI; Non ST-elevation Myocardial Infarction, PCI; Percutaneous Coronary Intervention, STEMI; ST-elevation Myocardial Infarction, UAP; Unstable Angina Pectoris

Discussion

The key findings of the current study are: 1) statins were universally prescribed to the patients with ACS; 2) only half of the patients received high-intensity statins; 3) maximally allowed doses of high-intensity statins were prescribed in one in 10 patients; and 4) presentation with NSTE-ACS, severely impaired LV systolic function, and in particular initial medical treatment of ACS were associated with less frequent high-intensity statins use.

The findings of International registry data indicate that the use of high-intensity statins has increased over the last few years with 72% of the patients with ACS being discharged on high-intensity statins in a US registry.[7] Our overall use of high-intensity statins, at 48.2%, was comparatively low. However, even among the international reports, revascularisation was associated with higher use of high-intensity statins with 61% to 84% patients receiving high-intensity statins.[8] The use of high-intensity statins in the current study was similarly high in patients who underwent revascularisation (73.3% for PCI, 40.3% for CABG).

The finding of lower use of high-intensity statins among medically treated patients has important implications, especially as more patients are treated medically among the Asian population.[9] To a lesser degree, the finding of underuse of statins in medically treated patients has previously been reported internationally. In a registry study of 19,867 New Zealand patients with ACS who had undergone coronary angiography, medically treated patients received high-intensity statins less often (69.6%) as compared to those treated with PCI (82.8%) or CABG (84.2%)5 Only 10.9% of the patients the current study received maximally allowed doses of statins (Atorvastatin 80mg or Rosuvastatin 40mg). This is considerably less as compared to 36% in New Zealand.[5]

Some of the plausible explanations for reduced prescription of high-intensity statins are: cost of the drugs,[10] co-morbid conditions in particularly older and sicker patients,[1] less frequent coronary angiogram in medically treated patients,[11] and intolerance of higher doses.[1]

Our study has some limitations. First, the observational single-centre design of the study may limit generalisability of the findings to wider patient population. Second, as the study was retrospective, we are unable to provide information on some of the important aspects such as body mass index and previous intolerance of high-intensity statins. Third, we do not have information on patient compliance with high-intensity statins after discharge from the hospital, which should be researched in further studies to further help identify the factors responsible for lower use of high-intensity statins.

Conclusion

Almost all patients were prescribed statins after ACS, although only half of the patients received high-intensity statins. Older age, presentation with NSTE-ACS, severely impaired LV function, and in particular initial medical treatment of ACS were associated with reduced high-intensity statin use.

Disclaimer: None to declare.

Conflict of Interest: None to declare.

Funding Disclosure: None to declare.

References

1. Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, Blumenthal RS, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2019; 73:3168-209. doi:10.1016/j.jacc.2018.11.002.
2. Christopher PC, Eugene B, Carolyn HM, Daniel JR, Jean LR, Rene B, et al. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. N Engl J Med . 2004; 350:1495-504. doi:10.1056/NEJMoa040583
3. Krauss RM, Mangravite LM, Smith JD, Medina MW, Wang D, Guo X, et al. Variation in the 3-hydroxyl-3-methylglutaryl coenzyme A reductase gene is associated with racial differences in low-density lipoprotein cholesterol response to simvastatin treatment. Circulation. 2008; 117:1537-44. doi:10.1161/CIRCULATIONAHA.107.708388
4. Gupta M, Martineau P, Tran T, Després JP, Gaw A, De Teresa E, et al. Low-density lipoprotein cholesterol and high-sensitivity c-reactive protein lowering with atorvastatin in patients of south Asian compared with European origin: Insights from the Achieve Cholesterol Targets Fast with Atorvastatin Stratified Titration. J Clin Pharmacol. 2012; 52:850-8. doi:10.1177/0091270011407196.
5. Kerr AJ, Mitnala S, Lee M, White HD. Utilisation and maintenance of high-intensity statins following acute coronary syndrome and coronary angiography: Opportunities to improve care (ANZACS-QI 26). N Z Med J. 2020; 133:21-40.
6. Dhand NK, Khatkar MS. Statulator: An online statistical calculator. Sample Size Calculator for Estimating a Single Proportion. [Online] [Cited 2022 October 29]. Available from: URL: http://statulator.com/SampleSize/ss1P.html.
7. Rosenson RS, Farkouh ME, Mefford M, Bittner V, Brown TM, Taylor B, et al. Trends in Use of High-Intensity Statin Therapy After Myocardial Infarction, 2011 to 2014. J Am Coll Cardiol. 2017; 69:2696-706. doi:10.1016/j.jacc.2017.03.585
8. Guedeney P, Baber U, Claessen B, Aquino M, Camaj A, Sorrentino S, et al. Temporal trends, determinants, and impact of high-intensity statin prescriptions after percutaneous coronary intervention: Results from a large single-centreprospective registry. Am Heart J. 2019; 207:10-8. doi:10.1016/j.ahj.2018.09.001
9. Huo Y, Thompson P, Buddhari W, Ge J, Harding S, Ramanathan L, et al. Challenges and solutions in medically managed ACS in the Asia-Pacific region: Expert recommendations from the Asia-Pacific ACS Medical Management Working Group. Int J Cardiol. 2015; 183:63-75. doi:10.1016/j.ijcard.2014.11.195
10. Rosenson RS, Kent ST, Brown TM, Farkouh ME, Levitan EB, Yun H,et al. Underutilisation of high-intensity statin therapy after hospitalisation for coronary heart disease. J Am Coll Cardiol. 2015; 65:270-7. doi:10.1016/j.jacc.2014.09.088
11. Karády J, Taron J, Kammerlander AA, Hoffmann U. Outcomes of anatomical vs functional testing for coronary artery disease: Lessons from the major trials. Herz. 2020; 45:421-30. doi:10.1007/s00059-020-04950-y