RESEARCH ARTICLE

Statin practices for ASCVD Prevention: A Cross-Sectional Analysis of Guideline Adherence in a High-Risk Local Patient Population

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Abstract

Objective: To investigate the current practices of statin prescription and use for primary and secondary prevention of atherosclerotic cardiovascular disease.

Method: The cross-sectional study was conducted at the Combined Military Hospital, Lahore, Pakistan, from December 2022 to June 2023, and comprised individuals with indication for statin therapy as per international guidelines. Data was collected using a self-designed questionnaire. The subjects were divided into primary prevention group A, comprising individuals aged 40 having one or more risk factors, and secondary prevention group B, comprising patients of all ages with a history of cardiovascular events. Data was analysed using SPSS 23.

Results: Of the 397 subjects, 256(64.5%) were in group A and 141(35.5%) were in group B. Overall, 257(64.7%) subjects were males, 392(98.7%) were aged >40 years, and 275(69.3%) were taking statins, with a mean usage duration of 52±70 months. In group A, statin use prevalence was 148(57.8%) compared to 127(90.1%) in group B. Hypertension and diabetes mellitus was found in 293(73.8%) and 269(67.8%) participants, respectively. Individuals with a matriculation-level educational background had significantly higher odds of statin use compared to those below matriculation (p=0.044).

Conclusion: There was a high frequency of atherosclerotic cardiovascular disease risk factors, like diabetes mellitus, hypertension and smoking, and statin use was significantly higher in the secondary prevention group compared to the primary prevention group.

Keywords: Cardiovascular diseases, Hydroxymethylglutaryl-CoA reductase inhibitors, Prescriptions. (JPMA 75: 1747; 2025)

DOI: https://doi.org/10.47391/JPMA.20228

Introduction

Ischaemic heart disease (ISHD) and stroke disproportionately burden low- and middle-income countries (LIMICs), like Pakistan, leading to a significant global mortality burden. This burden is compounded by the high prevalence of atherosclerotic cardiovascular disease (ASCVD) risk factors within these populations. In Pakistan, the National Diabetes Survey of 2016-17 revealed a staggering 26.3% weighted prevalence of diabetes mellitus (DM), exceeding the global average of 10.5%.[1-3] Similarly, hypertension (HTN), a major ASCVD risk factor, affects nearly half the population (46.2%), with a concerning proportion being newly-diagnosed or self-diagnosed.[4] These figures surpass global age-adjusted prevalences for both genders.[4,5]

Fortunately, statins offer a proven and safe method for both primary and secondary prevention of ASCVD, demonstrably reducing ASCVD-related mortality.[1] Their efficacy lies in lowering blood cholesterol levels and mitigating the risk of adverse vascular events, such as acute coronary syndrome (ACS), non-fatal myocardial infarction (MI) and stroke.[6] Low-dose statins can achieve roughly one-third reduction in low-density lipoprotein cholesterol (LDL-C), while higher-potency regimens at increased dosages can reduce LDL-C by up to half, effectively decreasing the risk of atherosclerosis and its associated complications.[6]

The American College of Cardiology (ACC), the American Heart Association (AHA), and the United States Preventive Services Task Force (USPSTF) recommend statins as the initial therapy for reducing the risk of ASCVD, due to the strong evidence for improving clinical outcomes compared to other lipid-lowering agents.[7,8] The guidelines have defined four distinct groups of people who would benefit from statin therapy: those with established atherosclerotic ASCVD, those with LDL-C levels of 190mg/dL or higher, those aged 40-75 years with DM and LDL levels 70-189mg/dL, and those with a 10-year ASCVD risk of 7.5% or greater, otherwise. The guidelines also highlight the importance of a healthy lifestyle and the use of high-intensity statin therapy to reduce LDL-C levels by >50% in patients with clinical ASCVD. In patients with very high risk ASCVD, the guidelines recommended using a LDL-C threshold of 70mg/dL to consider adding non-statins to the statin therapy.[7,8]

While developed countries exhibit trends towards

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Submission completed: 11-06-2024 **1st Revision received:** 10-09-2024

Acceptance: 23-08-2025 **Last Revision received:** 22-08-2025

improved adherence to statin therapy guidelines, LMICs, like Pakistan, face numerous challenges hindering optimal utilisation. Despite the high prevalence of cardiovascular disease and associated risk factors, knowledge about primary and secondary prevention for reducing ASCVD risk was found to be inadequate, with patients often being undertreated as a direct result of non-adherence to international guidelines, as well as educational and awareness level of the physicians.[9] Additionally, statin availability and affordability pose a significant hurdle. A recent study found that the affordability of CVD medicines including simvastatin was lower in Pakistan compared to other countries like Egypt, India and China.[10] Moreover, the poverty rate in Pakistan at the national poverty line is 21.9%, further highlighting the non-compliance with treatment due to affordability issues.[11]

While the benefits of statin therapy remain unmatched, there is also significant proof of a number of side effects that come as an unpleasant consequence of statin usage. Statins have been associated with systemic effects, like myopathies, hepatotoxicity, type 2 DM (T2DM), polyneuropathies, behavioural changes and gastrointestinal (GI) disturbances, with myalgias and tendinopathies being the most common adverse effects that lead to the prescription of suboptimal dosage of statins.[12] However, studies have shown that each 1.0 mmol/L reduction in LDL cholesterol results in 11 fewer major cardiovascular events per 1,000 treated over 5 years, an advantage that far outweighs any known adverse effects of statin usage.[13]

The current study was planned to investigate the current practices of statin prescription and use for primary and secondary prevention of ASCVD.

Subjects and Methods

The quantitative, observational, cross-sectional study was conducted at the Combined Military Hospital (CMH), Lahore, Pakistan, from December 2022 to June 2023. After approval from the institutional ethics review committee, the sample size was calculated with 95% confidence level, 5% margin of error, and a population size of 13.9 million for Lahore,[14] using OpenEpi calculator.[15] The sample was raised using non-probability convenience sampling technique. Those included were patients visiting the outpatient department (OPD) who were already on a prescription of statin therapy for either primary or secondary prevention of cardiovascular disease. Patients who did not consent to being included and whose questionnaires were incomplete were excluded.

After taking informed consent from the subjects, data was collected using a self-designed questionnaire that was piloted on 20 participants. Revisions were made based on the feedback, and these participants were not included in the final cohort. Trained researchers administered the questionnaire through face-to-face interviews. The questionnaire consisted of a demographic section, and a clinical section. If the participant was using statins, then data was collected on the type and dosage of statin drug, frequency of liver function test (LFT) follow-up, statin-associated adverse effects, and dose adjustments.

On the basis of the collected data, the subjects were divided into primary prevention group A and secondary prevention group B as per the ACA/AHA guidelines [8]. Group A comprised individuals aged 40 and above with one or more risk factors, such as DM, HTN, dyslipidaemia and smoking, potentially accompanied by other comorbid conditions. Group B comprised patients of all ages with a history of cardiovascular event, including stroke, MI and ISHD, with or without additional comorbidities.

Data was analysed using SPSS 23. Data was expressed as frequencies and percentages. Logistic regression model was applied to evaluate the association between different categorical variables. $P<0.05$ was considered statistically significant.

Results

Of the 402 patients approached, 397(98.8%) were included; 256(64.5%) in group A and 141(35.5%) in group B. Overall, 257(64.7%) subjects were males, 392(98.7%) were aged >40 years, 299(75.3%) resided in developed urban areas, 181)45.3%) had completed education up to matriculation level, 293(73.8%) had HTN, 269(67.8%) had DM, and 275(69.3%) were taking statins, with a mean usage duration of 52±70 months.

In group A, statin use prevalence was 148(57.8%) compared to 127(90.1%) in group B (Table 1). Individuals with a matriculation-level educational background had significantly higher odds of statin use compared to those

Table-1: Prevention group characteristics.

	Primary prevention (Group 1) n (%)	**Secondary prevention (Group 2)** n (%)
Age (years)		
< 40	-	5 (3.5)
>40	256	136 (96.5)
Gender		
Male	158 (61.7)	99 (70.3)
Female	98 (38.3)	42 (29.7)
Statin Use		
Yes	148 (57.8)	127 (90.1)
No	108 (42.2)	14 (9.9)
Smoker		
Yes	57 (22.5)	27 (19.1)

below matriculation (p=0.044) (Table 2) The clinical profile of the two groups was compared in detail (Table 3).

Among the 13(4.4%) patients having all the three major risk factors (DM, HTN and dyslipidaemia), statin use was highest 11(84.6%)], and all 13(100%) kept a regular eye on their LFTs. There were 124(31.2%) patients with DM and HTN, and they showed moderate statin use 79(63.7%), with LFT monitoring being less regular 41(51.9%). Similar trends were noted in 54(13.6%) patients with DM alone, and 62(15.6%) having HTN alone, with statin use decreasing and LFT monitoring becoming less frequent as the number of risk factors diminished. There were 3(0.8%) patients with isolated dyslipidaemia, and all 3(100%) used statins (exclusively atorvastatin) and indulged in regular LFT monitoring. Regarding adverse effects in group A, 2(0.8%) reported myalgia, and 3(1.2%) experienced LFT abnormalities.

In group B, there were 7(5%) patients with both ISHD and stroke, while ISHD alone was found in 105(74.4%) and stroke alone in 15(10.6%)]. Among those with stroke alone, myalgias were noted in 2(13.3%). Besides, 6(4.3%) experienced adverse effects, with myalgias 4(3.8%) being more common than deranged LFTs 2(1.4%).

Table-2: Socio-demographic predictors of statin use.

Variables	Coef (B)	Odds Ratio	95% CI	p-value
Gender	-0.25	0.78	0.48-1.26	0.31
Education				
Matriculation	1.34	3.8	1.04-14	0.044
Graduate	0.44	1.55	0.42-5.78	0.51
Residence	-0.17	0.98	0.56-1.72	0.95

Coef (B): Beta coefficient, CI: Confidence interval; Reference category: Male for Gender, Below Matriculation for Education, and Rural for residence.

Table-3: Statin use practices.

		Group 1	Group 2
		n (%)	n (%)
Statin Users	**Total**	148	127
Drugs & Doses	**Atorvastatin** (Total)	112	87
	5mg	2 (1.8)	0 (0)
	10mg	81 (72.3)	28 (32.2)
	20mg	28 (25)	55 (63.2)
	40mg	1 (0.9)	4 (4.6)
	Rosuvastatin (Total)	36	36
	5mg	2 (5.6)	2 (5.5)
	10mg	25 (69.4)	14 (39)
	20mg	8 (22.2)	18 (50)
	40mg	1 (2.8)	2 (5.5)
	Simvastatin (Total)	0	4
	5mg	-	-
	10mg	-	2 (50)
	20mg	-	2 (50)
	40mg	-	-
LFT Follow-up	**Total**	72	32
	1 monthly	4 (5.5)	3 (9.4)
	3 monthly	6 (8.3)	5 (15.6)
	6 monthly	25 (34.7)	12 (37.5)
	Yearly	37 (51.4)	12 (37.5)
Adverse effects	Myalgias	2 (1.3)	4 (3.1)
	Deranged LFTs	3 (2)	2 (1.6)
	Deranged RFTs	-	-
Dose Adjustments	Total	14 (9.5)	20 (15.7)

LFT: Liver function test. RFT: Renal function test.

Discussion

The current study investigated the current trends of statin prescription and use for both primary and secondary prevention of ASCVD. Examining statin prescription patterns and adherence remains crucial in Pakistan, with limited research currently available.[16,17] Statin use was found in 57.8% group A individuals. A study using National Health and Nutrition Examination Survey (NHANES) data from 2013 to 2020 reported a primary prevention prevalence of 25.5%,[18] while Thompson et al. using NHANES data from 2011 to 2018 reported 34.3% prevalence among eligible individuals.[19] A single-centre study in Saudi Arabia reported a primary prevention statin use rate of 69.1%.[20]

In group 2 of the current study, 90.1% patients were taking statin medication. Thompson et al. found a statin use rate of 60.3% among American patients for whom statins were recommended, and 74.5% among those for whom they were considered.[19] A cohort study reported significant disparities in statin utilisation across income categories, with rates ranging from 3.3% in low-income countries to 66.5% in high-income countries.[21] However, it is important to acknowledge limitations in these studies as their sampling frames may not have been nationally representative, and data collection often predated the inclusion of statins in the World Health Organisation (WHO) Essential Medicine List in 2007.[21]

The current study found a 69.3% composite prevalence of statin use in the eligible population. Thompson et al. reported a composite prevalence of 47.4%, which they described as being "suboptimal" since less than half of the eligible population was on a statin regimen.[19] Another study reported that about 54.5% of the eligible patients in the United States were using statins.[22] The current study had a hospital-based sample, and that might be the cause of such discrepancies. A US cross-sectional study across 140 clinics noted similar variation, with statin use at 62.3% and 82.2% for primary and secondary prevention, respectively,[23] which aligned with the current findings.

Similar to Thompson-Paul et al.,[19] the current study showed a higher prevalence of statin use in secondary prevention

compared to primary prevention; 1.558 times higher. This trend parallels an almost identical New Zealand study revealing a 1.55 times higher adherence and lower discontinuation rate in secondary prevention.[24] This discrepancy could be attributed to heightened patient awareness and caution, particularly among those who have experienced a serious cardiovascular or cerebrovascular event. Additionally, the similarity in adverse effect profiles in both primary and secondary groups, coupled with greater health benefits in latter prevention, may serve as a foundation for the higher utilisation of statins in this population, a proposition supported by Sigglekow et al.[24]

In the primary prevention group, composed mainly of individuals with DM aged >40, 91.9% were receiving moderate-intensity statins and 6.8% were receiving high-intensity statins. However, the secondary prevention group showed a concerning deviation from the guidelines, with 79.5% receiving moderate-intensity statins, and only 18.9% receiving high-intensity therapy despite clear recommendations for it as the initial treatment.[25] This gap cannot solely be attributed to dose adjustments, which occurred in only 15.7% patients of the group. This underutilisation of high-intensity statins is not necessarily up to par with the current guidelines, and, so, potentially undermines optimal primary prevention efforts.

The current study found a low overall incidence of statin-related adverse effects leading to dose adjustment or discontinuation (myopathy=3/8%, deranged LFTs 1.4%). While these figures are low, they may be linked to the significant underutilization of statins by patients and under prescription by providers. In fact, a study found that the most common reason for statin discontinuation or decline was the fear of adverse events.[26] While this caution and fear is understandable, it is crucial to consider the potential benefits of high-intensity statin therapy for eligible patients. High-intensity regimens demonstrably lower LDL-C and reduce cardiovascular events.[6] Furthermore, statins exhibit potential pleiotropic effects, influencing inflammatory mediators. A randomised trial reported a significant decrease in C-reactive protein (CRP) and lower cardiovascular and all-cause mortality with statins in non-hyperlipidaemic patients.[27]

Lastly, the current study indicated that education level of matriculation was associated with higher odds of being on statin therapy. While a stronger association was not observed with graduate level of education, this does highlight that education tends to increase statin use in the population. A study in Denmark showed that higher education resulted in earlier statin prescription and that basic education resulted in a higher prevalence of statin prescription overall. The same study, however, noted that the education level was not associated with reaching goals for strain therapy.[28]

The current study has limitations. First, ASCVD risk assessment could not be calculated for most patients due to the absence of recent lipid and BP data. It was assumed that statin prescription must have been based on risk assessment by the attending physician. A previous research in Pakistan has shown inadequate lipid assessment practices hindering therapy optimisation.[9] Second, the study was conducted at a single urban centre with largely free healthcare access. Economic constraints and uneven access to health facilities are likely to affect statin prescription and adherence. Large-scale, nationwide studies are needed to accurately assess statin utilisation and effectiveness, and to validate the current findings.

Conclusion

Statin use was more frequent for secondary prevention than for primary prevention. Overall, patients with matriculation demonstrated higher odds of statin use compared to those below matriculation. Statin-related adverse effects had a low incidence.

Disclaimer: None.

Conflict of Interest: None.

Source of Funding: None.

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Author Contribution:

RK: Concept, design, material preparation, data collection, analysis, revision and final approval.
HM: Discussion and final approval.
MF: Results and final approval.
MTI: Methodology and final approval.
ZA: Introduction and final approval.