

Impact of Adherence, Patient Perception, and Knowledge to Statin Therapy – A Cross-Sectional Study

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Abstract

Background and Objective: Cardiovascular diseases and its risk factors, such as diabetes and hyperlipidemia, are common in Indian population. Statin utilization is high across the country and it is important to assess the adherence because it plays an important role in treatment outcome. Statin adherence is not studied well in India. This study aims at measuring the adherence, perception, and knowledge of individuals on statin therapy. **Study Design:** Cross-sectional observational study on 130 consented individuals visiting a tertiary care teaching hospital. Study was conducted for a duration of 9 months. **Methods and Materials:** After obtaining approval from the institutional ethics committee the study subjects were assessed for knowledge, perception, and adherence to statin therapy using a systematically developed interview questionnaire. **Results:** Good adherence was seen in 42.30% patients. Higher proportions of females were reported to have good adherence. Good adherence was observed in patients with a history of coronary heart disease and atorvastatin as monotherapy ($P = 0.0029$) and fixed dose combination ($P = 0.0012$), whereas lipid reduction was found directly related to type of adherence. Lack of knowledge, cost, re-fill issues, and adverse effects were some of the barriers identified. **Interpretation and Conclusion:** Knowledge and patient perception plays a very important role in determining the adherence to statin therapy. A history of coronary heart disease, choice of statin, and cost of therapy are the contributing factors to adherence. Patient counselling and improving the cost-effectiveness of statin therapy can be considered as interventional strategies to overcome adherence issues.

Keywords: Adherence, knowledge, lipid reduction, patient perception, statin

INTRODUCTION

The burden of atherosclerotic cardiovascular diseases is high in India Also, it is known as the diabetic capital of the world. In 2016, there was an estimated 62.5 million years of life lost prematurely due to cardiovascular diseases in India and ischemic disease and stroke accounted for approximately 15%--20% deaths in the country.^[1] One of the well-established modifiable risk factors for cardiovascular diseases is dyslipidemia.^[2,3] Statins are effective lipid-lowering drugs and prescribed widely for both primary prevention and secondary prevention of atherosclerotic cardiovascular diseases such as coronary heart diseases, stroke and peripheral artery diseases. Statin therapy is beneficial in preventing cardiovascular diseases and conditions like stroke. These facts justify the wide use of statins in India. Over past few decades they have proven to minimize the cardiovascular morbidity and mortality in patients with dyslipidemia. Clinical trials of primary prevention

have shown that statins reduce the incidence of coronary artery diseases by approximately 30%.^[2] The proven efficacy of statins is applicable in the real-world with good prescribing practices and patient adherence. Non-adherence to prescribed medication can result in adverse outcomes and higher costs of care. Discontinuation of statins can cause changes in platelet activity or inflammation, impair vascular homeostasis or lead to endothelial dysfunction. These effects are independent of changes in cholesterol levels and thereby increase the risk of cardiovascular events.^[3] A survey study reported in 2007 suggested that patients who were concerned about the adverse

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effects of statins or uncertain about the potential benefits were more likely to discontinue statin use.^[4] Adherence to statin therapy is not studied well in India. This study was undertaken to identify the adherence, perception to statin therapy and barriers associated with it.

METHODS AND MATERIALS

Methods

The study was performed in accordance with the Declaration of Helsinki and was approved by the Bharati Vidyapeeth Deemed University Medical College, Pune, Institutional Ethics Committee. Reference number for study approval is BVDU/MC/E3 (29 August 2016). This was a cross-sectional observational study conducted on a sample size of 130 individuals including both males and females, above the age of 21 years for a period of 1 year. After obtaining informed consent the patients were enrolled in the study from the outpatient clinic and inpatient ward of Department of General Medicine, Bharati Hospital and Research Center, Pune. Confidentiality of patients was maintained. The study participants were assessed for adherence and knowledge to statin therapy. This study was not restricted to a particular type or dose or brand of statin. All the patients prescribed for either atorvastatin (10 mg/20 mg/40 mg/80 mg) or rosuvastatin (5 mg/10 mg/20 mg/40 mg) single-dose or fixed-dose were included. Pregnant women and individuals less than 21 years were excluded from this study. The pattern of adherence and level of knowledge were assessed according to gender, indication, and type of statin (atorvastatin/rosuvastatin). Patients with any of the following risk factors---diabetes, hypertension, dyslipidemia, smoking, and without clinical atherosclerotic cardiovascular diseases (ASCVD) were categorized as primary prevention patients; whereas those with a clinical ASCVD (coronary heart disease, stroke, and peripheral vascular disorder) were categorized as secondary prevention patients.

Materials

A systematically developed and validated questionnaire was used for the assessment of statin adherence and knowledge. Adherence was measured as good, moderate, and poor. Inverse rating scale was used to score the patient's medication adherence, that is, patient scores a point with every non-adherent characteristic. There were six questions scored for 1 point each. People with score = 0 did not show to have any characteristic for medication non-adherence and were classified as those with good adherence. Those with score 1-3 were classified as moderate adherence and those with score 4-6 were classified as low adherence. This was logical classification of categories based on total score and number of categories. The questionnaire was developed using standard adherence scales such as the Morisky Medication Adherence Scale and Hill Bone Compliance scale.^[5] The questionnaire was pilot tested, revised, and validated by clinicians in the study team and Department of Clinical Pharmacy, Bharati Hospital and Research Center. An approval for its use was sought from the

institutional ethics committee. Every question was accounted for at one point. The patients were scored and categorized for types of adherence and knowledge [Refer questionnaire].

Statistical analysis

A convenience sampling technique was used for this study. A total of 130 individuals were enrolled according to the inclusion criteria mentioned in study protocol. The proportions of gender, age and adherence were calculated using analysis of variance, Students 't' test and Chi-square test, respectively. The proportions adherence patterns of alterations in the lipid levels in ASCVD patients were also calculated and were compared within each group by Chi-square test. The *P* values of <0.05 were considered to be statistically significant. The statistical analysis was done using MedCalc software (version 12.7.0.0).

RESULTS

Adherence to statin therapy was assessed in 130 patients. 42.31% had good adherence, 23.07% had moderate adherence, and 34.62% had poor adherence. Approximately, 68% were males and 32% were females. The number of males were significantly higher than females. Good adherence and poor adherence were significantly higher in females. The inter-gender comparison of type of adherence suggested significantly higher moderate adherence in males than females. Male vs female comparison was 60% vs. 40% with good adherence, 86.66% vs. 13.33% with moderate adherence, and 64.44% vs. 35.55% with low adherence. Adherence pattern within men had no significant difference whereas females with good adherence were significantly higher. The mean age was 63.29 (\pm 12.64) years. Age distribution and adherence pattern had no statistical significance. Type of adherence and average number of drugs prescribed per individual were independent of each other. 16.15% were prescribed statin for primary prevention, whereas 83.85% were prescribed for secondary prevention of ASCVD [Table 1].

Good adherence was significantly observed in Atorvastatin therapy [Table 2]. Lipid reduction was dependent on type of adherence. Individuals with moderate or poor adherence showed significantly higher lipoprotein levels. The spectrum of observed disorders showed a distribution as 38.54% coronary heart disease, 33.02% stroke, 8.25% kidney impairment, 2.75% peripheral artery disease, and 17.44% two or more atherosclerotic cardiovascular disorders. Figure one illustrates the adherence pattern observed in each disorder [Figure 1].

Poor knowledge about statin therapy and/or cholesterol was significantly observed in the study population [Figure 2]. A total of 72.73% of those with good knowledge had a history of ASCVD and 84.85% patients were well educated. Among individuals with moderate knowledge, 72.73% had a history of ASCVD, and 77.27% were well educated and 67.19% with poor knowledge had a history ASCVD and 86.17% patients had low education. Poor knowledge, high cost of statins, and refill issues were the leading causes for poor adherence. A total of 13% of those with poor adherence discontinued the

Table 1: Demographic details of patients based on their adherence to statins

Parameter	Category	Good (n=55)	Moderate (n=30)	Poor (n=45)
Gender	Male (%)	37.20	30.24	32.56
	Female (%)	52.27	9.09	38.63
Mean age (±SD)	Male%	65.90 (±13.08)	62.84 (±12.22)	62.72 (±13.69)
	Female%	60.5 (±12.39)	69 (±11.74)	62.06 (±11.39)
Age categories (%)	P	0.0330	0.0512	0.8042
	21-40	2 (3.63)	1 (3.33)	3 (6.66)
	41-60	24 (43.63)	10 (33.33)	16 (35.55)
	61-80	23 (41.81)	17 (56.66)	25 (55.55)
	>80	6 (10.90)	2 (6.66)	1 (2.22)
Average number of drugs prescribed		4.981	4.7	4.711
Atorvastatin (n=72)		45.83	22.23	31.94
Rosuvastatin (n=25)		28	32	40
FDC -Atorvastatin (n=25)		56	12	32
FDC -Rosuvastatin (n=8)		12.5	37.5	50

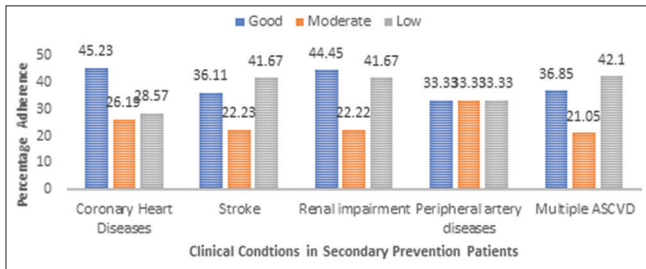


Figure 1: Adherence pattern in various clinical conditions

therapy due to adverse effects, such as joint pain and sleep disturbances. Individuals with poor knowledge were not aware of their disease condition and/or statin use or indication. Three individuals were apparently counselled in the past for statin therapy but could not remember the information provided during counselling sessions [Figure 3].

Perception of patients: Statins were assumed to have a blood thinning effect along with a cardio-protective effect. When asked about the indication of statin, 11.32% of the patients knew its indication and 4.3% were aware of the dose and brand of their statin therapy. Cholesterol was defined by the individuals with various terminologies such as a ‘type of body fat’ or a ‘clot forming substance.’ Misconceptions, such as, ‘statin use is restricted to obese individuals, for weight reduction,’ and ‘statin help to reduce blood pressure’ were observed. ‘Drug holiday’ helps in improving the effectiveness of statins and home remedies, such as use of ginger, garlic, and lemon juice is better than statin therapy for cholesterol reduction was reported by some individuals.

DISCUSSION

A higher number of individuals were observed to have good adherence. Evidence suggests that good adherence to statin therapy is observed in large studies but small-scale studies, such as cohort studies, have reported poor adherence suggesting a need to conduct multi-centric and systematically

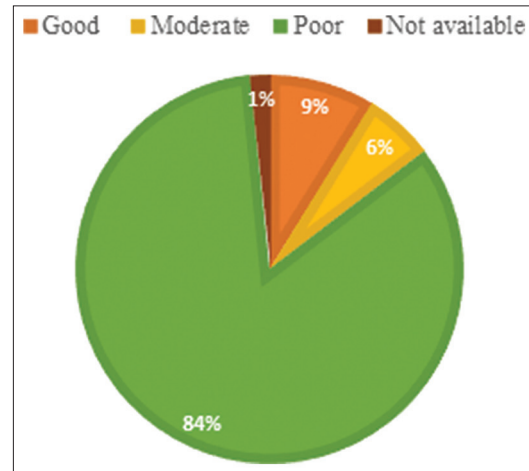


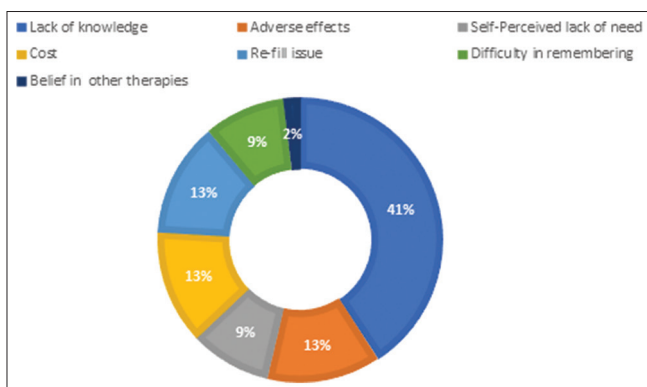
Figure 2: Pattern of knowledge about statin therapy and cholesterol in the total study population (N = 130)

planned studies on various cohorts to determine the pattern of adherence.^[6] Demographic characteristics are independently associated with adherence. In this study, females were observed to have significant-good and low adherence. As 43.42% of female patients fall under the age between 41 and 60 years, therefore, shows high adherence than the remaining population. The study observed poor adherence of females directly associated with the effect of socioeconomic factors associated with women’s health. Women’s role as caregivers for family members lowers medication adherence.^[7] Also, the female population validates the role of lack of knowledge to adherence pattern in female patients. It is difficult to establish conclusions about the relationship between gender and adherence because we have evidence suggesting better adherence in males as well as in females.^[8-11] Therefore, it is challenging to determine the association of such a small cohort and thus a larger cohort needs to be analyzed to establish this association.

Lack of knowledge plays an important role in adherence to therapy. Evidence suggests that inadequate knowledge about cholesterol or statin therapy is prevalent among statin

Table 2: Outcomes of the patients based on the adherence to statins

Parameter	Category	Good (n=55)	Moderate (n=30)	Poor (n=45)
Secondary outcome (%)		16 (29.09)	10 (33.33)	20 (44.45)
Lipid profile available (%)		32 (58.18)	16 (53.34)	26 (57.78)
Lipid reduction (%)		6 (18.75)	3 (18.75)	2 (7.69)
Lipid increment (%)		4 (12.5)	2 (12.50)	8 (30.76)
TC >200 mg/dL (%)		2 (6.25)	1 (18.75)	6 (23.07)
TG >193 mg/dL (%)		5 (15.625)	5 (31.25)	5 (19.23)
HDL <40 mg/dL (%)		13 (40.62)	8 (50)	15 (57.69)
VLDL >34 mg/dL (%)		6 (18.75)	14 (87.5)	9 (34.61)
LDL >130 mg/dL (%)		2 (6.25)	7 (43.75)	14 (53.84)

**Figure 3: Factors associated with poor adherence**

users.^[12-14] Similar findings were observed in this study. Alwhaibi *et al.*^[6] have discussed barriers, such as missing the dose due to difficulty in remembering and refill issues. A study conducted by Similarly, Wouters *et al.*^[14] have discussed the barriers such lack of knowledge, lack of need to continue, cost issues, missing dose, and polypharmacy. These findings can be correlated to this study.

Poor knowledge is the main barrier to adherence. Approximately, 73% of the study population with good knowledge had a history of ASCVD. This suggests that patients with a history of major coronary events have adequate knowledge which contributes to better adherence. This can be correlated to the study conducted by Merryson Roy Mathew in India.^[13] A study conducted by Olson *et al.*^[15] suggested that the likelihood of non-adherence is two times higher in those without history of coronary event. The perception of patients plays an important role in determining the adherence to any drug therapy. The concept 'drug holiday' and beliefs in other therapies are well-documented factors that lead to non-adherence.^[9] Similar findings were observed in this study.

Higher adherence to statin therapy in cardiovascular disorders is corroborative to the knowledge and perception of disease and statin therapy. The cardio-protective effect of statin is well understood in those with coronary heart diseases. Hence, good adherence to statin therapy can be observed. This is further explained by the low adherence observed in all conditions other than coronary heart diseases. This study was conducted

in a clinical setting which is easily accessible to people with lower socioeconomic background. Hence, the majority of the patient population belonged to this class of the society, the understanding of diseases and therapy in such poorly educated and low-income strata of society is very primitive and often misleading. This plays a very important role in self-evaluation of the requirement of drug therapy which has an indirect effect on the adherence. We can reasonably assume that poor adherence in those other than coronary heart diseases can be due to lack of understanding the diseases, disease pathology, complications, and role of statins in managing their condition. The study conducted by Wouters *et al.*^[15] reported similar findings, wherein the patients doubted the necessity or lacked the knowledge about efficacy of statins. Another important socioeconomic factor leading to non-adherence is affordability of statin therapy. Chronic use of costly drugs can lead to non-adherence. This can be supported by this study's finding of a significantly higher adherence to atorvastatin than rosuvastatin. Similar findings were observed in a study in Singapore by Aung *et al.*^[3] in which the patients with higher income and cardiovascular diseases were found to have better adherence. The study conducted by Alwhaibi *et al.*^[6] also reported a better adherence in those with cardiovascular disorders.

The formulation of statin used may has an effect on adherence. We lack evidence to support this assumption. Clinicians prefer fixed-dose combination for several reasons; one of the important being ensuring adherence to prescribed medications, lesser number of pills per day, availability, and reduced cost. This strategy often works well. This can be supported by the finding of a significant good adherence observed in 56% of individuals prescribed fixed-dose combination of atorvastatin. The low adherence to rosuvastatin can be attributed to the higher cost. We need more studies to establish the association between type or formulation of statin and adherence.

Good adherence to statins ensures effective 3 hydroxy-3-methylglutaryl (3HMG) CoA reductase inhibition and decreases the cholesterol synthesis. The relation between reduction in secondary outcome with good adherence was observed in this study. Especially, benefits of good adherence on lowering reduction low density lipo-proteins and cardiovascular event were significant. We have strong evidence supporting this

finding.^[16-19] It highlights the importance of adherence to reducing the cholesterol and cardiovascular diseases. This study has several limitations: (1) Short duration and small sample size. (2) Majority of the population belonged to a lower socio-economic background. Thus, we cannot ascertain these findings for people with different socio-economic backgrounds. (3) This was an observational study involving an interview questionnaire. Hence, we can assume measurement bias and recall bias while determining the adherence. This study can be conducted on a larger cohort to identify the association of statin adherence with multiple factors, such as gender, different socio-economic background, type, and of statin formulation. This study determines the potential research questions and scope for interventions to improve the adherence to a life-saving drug which has helped in reducing the morbidity and mortality of cardiovascular diseases.

CONCLUSION

The knowledge, type of disease, and choice of statin plays an important role in statin therapy. Socioeconomic status can be considered as determinant for adherence to statin therapy in future studies. Good adherence can improve the treatment outcome and reduce the risk of cardiovascular diseases. Patient-counselling at various levels of healthcare is required. Physicians, pharmacists, nurses, and manufacturers of statins can contribute toward improving the adherence. The prescribers should consider the cost of statin and can consider fixed dose formulations. Pharmacists can record the prescriptions and assess the adherence during re-fill or follow-up over a phone-call, text, or email. Pharmaceutical companies can contribute in improvising the affordability and providing multilingual patient information leaflets. Larger studies are required in a representative sample of the population to determine the overall statin adherence and barriers.

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Conflicts of interest

There are no conflicts of interest.

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