








## Research Paper

# Underlying Factors Associated With Failure to Achieve Therapeutic Lipid Goals by Intensive Statin Therapy in Post-myocardial Infarction Patients



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## ABSTRACT

**Background and Aim:** Treatment of hyperlipidemia, as a significant risk factor of cardiovascular disease with a leading role in atherosclerosis and adverse cardiovascular effects, is now a medical dilemma worldwide. Despite the comprehensive knowledge about the impact of this factor on the cardiovascular system, the achievement of therapeutic goals of medical therapy remains an unattained desire. This study aims to evaluate the underlying causes apart from the medication itself.

**Materials and Methods:** This cross-sectional study was conducted for 6 months from March 2016. During which, 50 patients were thoroughly evaluated and followed up. The inclusion criteria were patients with acute myocardial infarction who were newly diagnosed when the first total dose of statin (atorvastatin 80 mg) was started. The exclusion criteria were a history of taking fat-reducing drugs before the study. Predetermined data extraction forms, including medical and laboratory variables and the multidimensional scale of perceived social support questionnaire (MSPSS), were completed for all patients at the first visit and after 6 months. The obtained data were analyzed using SPSS software.

**Results:** Among 50 studied patients, 28 were men (56%), and 22 were women (44%) ( $P>0.05$ ), with Mean $\pm$ SD age of  $60\pm 10.19$  years. Only 20 patients (40%) could achieve the therapeutic goal of low-density lipoprotein cholesterol ( $>70$  mg/dL). Irregular drug consumption was the only factor that significantly differed between patients who achieved the goals and those who could not ( $P=0.034$ ). Subgroup analysis among patients with regular and irregular drug consumption demonstrates that low educational levels and poor socioeconomic support significantly differed between these patients ( $P>0.05$ ).

**Conclusion:** Some conditions independently influence the efficacy of a medical treatment to improve hyperlipidemia, including educational and socioeconomic determinants. These factors are independent of the medication. Therefore, patient's lifestyle and their condition have to be considered in planning medical therapy.

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## 1. Introduction

**E**levated blood cholesterol and triglyceride levels are among the most common problems that can be inherited, primary, and secondary [1]. Hyperlipidemia is a significant risk factor for cardiovascular disease and is strongly associated with atherosclerosis and subsequent vessel stenosis [2, 3]. Studies show that people with normal fasting triglyceride levels of 150 mg/dL or more are at higher risk for heart disease or stroke [4, 5]. Therefore, proper reduction without its side effects significantly impacts the community and individual health and the prevention of cardiovascular disease [6]. Primary and secondary prevention by modification of lipid profile, particularly of low-density lipoprotein cholesterol (LDL-c), is considered a unique approach to risk reduction and cardiovascular disease outcomes improvement [7]. Despite these apparent benefits, today, the success rate of therapeutic goals of LDL-c reduction has become a dilemma [8]. Several factors are influential in this regard, including the efficacy of medical therapy using hydroxymethylglutaryl (HMG)-CoA reductase inhibitors (statins) [9], lifestyle-related issues such as physical activity [6], behavioral and socioeconomic parameters [10, 11], and genetic factors [12]. Nevertheless, low administration of lipid-lowering agents is known as the leading cause of this failure [8]. This study investigates effective parameters in achieving the therapeutic target of serum lipid levels. In other words, we mean determining the most crucial reason for treatment failure.

## 2. Materials and Methods

The present study is a prospective cohort of post-myocardial infarction patients for whom a similar lipid-lowering therapy is initiated. The samples were recruited via a convenience sampling method. The research site was the heart clinic of Shahid Beheshti Hospital in Qom City, Iran. The research proposal was approved by the Ethics Committee of Qom University of Medical Sciences (IR.MUQ.REC.1395.83). Patients with newly diagnosed acute myocardial infarction for whom the full-dose statin (atorvastatin 80 mg) was initiated for the first time were eligible candidates for this study and followed up for at least 6 months from March 2016. Predetermined data extracting forms were completed for all patients during each scheduled visit to the Cardiology Clinic. The patient's demographic information, in addition to laboratory and physical examination findings, was recorded. Laboratory variables, including lipid profile and fasting plasma glucose, were assessed at the first visit, just

before the treatment began, and after 6 months. LDL-c level of >70 mg/dL after 6 months is marked as a failure to achieve therapeutic goals [10]. Patients were also asked for their past medical history, concomitant disease, family history, and lifestyle status during the 6-month follow-up visit. Patients were excluded if they took any lipid-lowering agent prior to the study.

Data on patients' social support were obtained using a multidimensional scale of perceived social support (MSPSS) questionnaire at the 6-month follow-up visit. It is designed to estimate patients' support with 12 items by which the higher scores indicate more perceived support [13]. The questionnaire is well validated and translated into Persian [14]. The obtained data were analyzed in SPSS software version 24.0 for windows (SPSS INC., Chicago, IL). The continuous variables were expressed as Mean $\pm$ SD and were analyzed using t-test or analysis of variance (ANOVA) for normal distribution or the Mann-Whitney U-test.

## 3. Results

A total number of 54 patients were enrolled in this prospective cohort study. Of whom, 50 were completely followed up for at least 6 months. They comprised 28 men (56%) and 22 women (44%) ( $P>0.05$ ), with Mean $\pm$ SD age of 60 $\pm$ 10.19 years. Statistical analyses of data during a 6-month follow-up show that 30 patients out of 50 (60%) failed to achieve the therapeutic goal of LDL-c, 40 patients (80%) for HDL-c, 42 (84%) for triglyceride (TG), and 47 (94%) for total cholesterol.

Among patients who could not achieve the treatment goal of LDL-c, 6 patients (20%) had irregular drug intake, significantly different from those who attained the goal ( $P=0.034$ ). Between-group analyses of patients with or without regular drug consumption show that the level of social support is significantly lower in patients with irregular drug intake (mean score of 3.71 vs 5.91,  $P<0.05$ ), and most complaints of these patients were forgetting of drug use and high costs of medications (6 and 4 patients out of 6, respectively). Interestingly, all patients with irregular drug use were illiterate and of older ages (mean age score of 71.3 vs 58.52 years,  $P<0.05$ ).

Other clinical variables, including blood pressure, angiographic findings, cardiac function by estimated ejection fraction, level of physical activity, and body mass index (BMI), were similar between patients who achieved treatment goals and those who could not ( $P>0.05$ ). The patients' characteristics and clinical findings are summarized in Tables 1 and 2.

**Table 1.** Study patients' characteristics

Variables		Achieved Therapeutic Goal (n=20)	Not achieved Therapeutic Goal (n=30)	Sig. / P
Age (y) Mean±SD		56.31±8.12	62.56±13.43	<0.05
Gender	Male	11	17	>0.05
	Female	9	13	>0.05
BMI (kg/m <sup>2</sup> )		29.4	29.9	>0.05
HTN (mm Hg)		13	19	>0.05
Diabetes		6	10	>0.05
Smoker		4	7	>0.05
Irregular drug use		0	6	<0.05
Illiterate		9	23	<0.05
MSPSS Mean±SD		6.73±1.12	4.93±1.06	<0.05
EF Mean±SD		46.05±13.6	45.46±11.8	>0.05

BMI: body mass index; HTN: hypertension; MSPSS: the multidimensional scale of perceived social support; EF: ejection fraction.

## 4. Discussion

Hyperlipidemia, particularly elevated levels of LDL-c, is essential in patients with acute myocardial infarction [15]. There are multiple strategies to successfully reduce serum lipid levels. Most of them consist of lifestyle modifications and medical therapy [16]. Nevertheless, in many cases, the desired outcome is not achieved despite the proper approach [7, 15, 17-19].

As poor medication adherence is considered the leading cause of failure to achieve therapeutic targets [17], we only enrolled patients who received a similar lipid-lowering agent (atorvastatin) with an equal dosage (total dose of 80 mg). We intended to eliminate the probable role of this factor and consequently assess other influencing factors. Noteworthy is that, despite the intensive therapy with full-dose statin prescription, we still witnessed a high percentage of failure to achieve goals (60%). This finding suggests the stunning role of other factors besides the treatment of disease.

Another influencing factor mentioned in the literature is medication adherence [15]. This factor has been discussed from various perspectives, including the patients' social support or educational and socioeconomic statuses. Our findings demonstrate that patients who were not taking their medications regularly could not achieve the therapeutic goals of LDL-c. In other words, there was no patient with irregular drug consumption that was successfully treated with statins. This finding can be explained by poor social support, especially in older

patients who have mostly lower educational levels and make an excuse of forgetting on-time drug use.

In a study on patients with acute myocardial infarction, Martin et al. [7, 20] showed that after 6 months of follow-up, one in three patients failed to attain the LDL-c goal of <100 mg/dL. The authors proposed that the most critical factors associated with failure to achieve the LDL-c goal are the absence of a medication prescription at discharge and lack of adherence to statin therapy among patients. In our study, all patients received statin at discharge, albeit 6 out of 50 (12%) discontinued drug consumption with the excuse of forgetfulness and high costs of medications.

In another study conducted by Lee et al. [15], factors associated with LDL-c target achievement were assessed, and the authors indicated that good adherence to medication is the strongest independent factor associated with the achievement of target levels. The authors also identified cardiovascular risk factors, including diabetes, hypertension, smoking, and lower levels of high-density lipoprotein cholesterol as influencing factors related to LDL-c target failure. In our series, nonetheless, we had no significant correlation between these cardiovascular risk factors and failure to achieve LDL-c therapeutic targets.

As can be seen, by eliminating the influence of inappropriate medical therapy, therapeutic goal achievement of LDL-c may still be failed even under vigorous treatment. This finding suggests that treating hyperlipidemia is not merely drug related but a multifactor-

**Table 2.** Patients' test results

Variables	Stages	Mean±SD		Sig. / P
		Achieved Therapeutic Goal	Not Achieved Therapeutic Goal	
Total cholesterol	Pre-treatment	168.7±39.8	163.13±42.4	P<0.05
	Post-treatment	135.61±43.5	145.39±47.7	
Triglyceride	Pre-treatment	156.3±96.7	158.53±73.9	P<0.05
	Post-treatment	133.92±71.4	155.58±64.6	
LDL-c	Pre-treatment	102.37±33.9	99.92±29.8	P<0.05
	Post-treatment	54.26±21	76.77±24.3	
HDL-c	Pre-treatment	37.41±8.1	35.16±11.6	P<0.05
	Post-treatment	47.72±10.4	42.88±12.3	

LDL-c: low-density lipoprotein cholesterol; HDL-c: high-density lipoprotein cholesterol.

rial condition that various perspectives can influence it. However, our results primarily follow medication itself, so it is expected that the therapeutic goals of LDL-c are attained by regular medication consumption at an appropriate dosage. A greater study population is required to more precisely examine the underlying variables of successful treatment.

### Study strengths and limitations

It may be considered the strength of the present study that patients have been matched for the therapeutic approach so that all patients received full-dose atorvastatin (80 mg) with no adjunctive therapy and a history of taking lipid-lowering agents. This condition allows evaluating the independent role of other underlying factors. Another strength of our study is the prospective design of patient follow-up and data collection, which inherently has higher generalizability due to less potential biases. Our study also has some limitations, mainly because of the restricted study population, which probably interferes with generalizing the findings. Designing and conducting studies with a larger population is strongly suggested. Surely it would also be better if various treatment groups were compared in patients with different demographic and socioeconomic statuses.

## 5. Conclusion

Treating hyperlipidemia is an imperative measure for patients with cardiovascular disease. However, it might become a dilemma due to therapeutic predicaments regarding failure to achieve target goals. Apart from issues related to the medication itself, some

conditions independently influence the outcomes, including educational and socioeconomic determinants, which are often directly related to medication use. In conclusion, based on our findings, it is expected that patients with hyperlipidemia achieve therapeutic goals and a reasonable course of treatment if they receive medication regularly with an appropriate dosage.

## Ethical Considerations

### Compliance with ethical guidelines

The Ethics Committee of Qom University of Medical Sciences approved this study (Code: IR.MUQ.REC.1395.83) approved the study.

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### Authors' contributions

All authors equally contributed to preparing this article.

### Conflict of interest

The authors declared no conflict of interests.

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