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Original Article

The relationship between acute cardiac attack and LDL-C serum levels in cardiac and CCU inpatients in Hajar hospital: Replying to a paradox

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Abstract
Background and aims: Acute myocardial infarction (MI) is one of the most prevalent heart diseases across the world, including in Iran. The purpose of the present study was to investigate the relationship between acute MI and serum low-density lipoprotein (LDL) levels in patients with acute MI.
Methods: In this descriptive-inferential study, 1274 MI patients hospitalized in Shahrekord Hajar Hospital were selected using the census method. The required information was drawn from the patient's medical records according to inclusion criteria. Statistical analyses were performed using analysis of variance (ANOVA) and chi-square test to examine the relationship between the LDL level and awareness in patients.
Results: In this study, the average age of patients with acute heart attack was 13.79 ± 63.18 years. Of the 1274 studied patients, 78% (999 people) were men and the rest were women. In both male and female genders, most patients had LDL levels between 70 and 129 mg/dL. Regarding statin use, 757, 287, and 162 people had a history of statin use, hypertension (HTN), and cardiovascular disease, respectively. In addition, 150 and 152 people had diabetes and a history of smoking, respectively. In this study, a significant relationship was found between the history of statin use ($P<0.0001$) and the frequency of MI ($P=0.049$) in LDL groups.
Conclusion: The results of this research revealed a significant relationship between LDL groups and the number of times acute heart attack occurs as a long-term complication in people who have had one.
Keywords: Angiography, Acute myocardial infarction, Low-density lipoprotein

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Introduction

Acute myocardial infarction (MI) is a major cause of mortality worldwide. Atherosclerosis is the most common cause of myocardial ischemia. The risk factors of MI include increased plasma low-density lipoprotein (LDL) levels, decreased plasma high-density lipoprotein levels, smoking, diabetes, and hypertension (HTN). Older age, male gender, and family history are the risk factors that cannot be ameliorated, while factors such as obesity, sedentary lifestyle, HTN, diabetic hyperlipidemia, and smoking are controllable. Among the above-mentioned factors, hyperlipidemia has been recognized as a major mortality and morbidity factor in people with cardiac atherosclerosis conditions (1). Hyperlipidemia is a common disorder whose prevalence varies across populations. However, it has a comparably higher prevalence (80%-88%) in individuals with coronary artery diseases (2). Hyperlipidemia develops because of a primary disorder of lipid metabolism or a secondary disorder due to a precondition (3). Such preconditions may include type I diabetes, excessive alcohol consumption, cholestatic liver conditions, nephrotic syndrome, chronic renal failure, hypothyroidism, smoking, obesity, and drugs (4).

The role of different lipids in the development of atherosclerosis has been well established previously. Oxidized LDL causes disorders in coronary endothelium, the release of inflammatory mediators, and the formation of lipids on the walls of veins (5). A drastic decrease in blood lipid also plays a role in preventing the progression and enlargement of atherosclerosis plaques. Particularly, maintaining LDL-cholesterol (LDL-C) levels < 70 mg/dL plays the most important role in preventing plaque formation progression (6).

Several studies have confirmed the effective role of statins in reducing mortality due to cardiac-coronary events (7-11), which can also be used to prevent primary and secondary atherosclerosis (12-14). These types of drugs play a significant role in reducing LDL-C by

decreasing the internal synthesis of cholesterol (15). In a study, Hulten et al investigated the relationship between the preventive effects of LDL reducers and the CT angiography results. After a 3.5-year follow-up of 2839 patients, they concluded that 1-week treatment with statin and aspirin had a direct association with the severity of involvement of coronary veins in CT angiography (16).

In another study conducted by Tonelli et al on the relationship between acute MI risk level and LDL-C, 7762 patients with acute MI were assigned to different glomerular filtration rate (GFR) groups to investigate the relationship between LDL and acute MI risk in chronic kidney disease patients. The researchers found that as GFR decreased to below the normal level, the correlation between LDL and coronary diseases decreased so that patients with lower LDL had a lower risk of having acute MI (17). In contrast, Shin et al have recently concentrated on the relationship between a severe reduction in LDL and coronary atherosclerosis progression. In a three-year study on 467 patients using CT angiography, they concluded that coronary atherosclerosis progression was slower in patients with LDL-C < 70 mg/dL than in patients with higher LDL-C levels (18).

In addition, Reddy et al studied the relationship between serum LDL-C levels and intra-hospital mortality due to acute MI. They observed a lipid paradox, in which lower levels of LDL-C were associated with higher rates of intra-hospital mortality (19).

Similarly, Kyung et al investigated the relationship between LDL levels and awareness of acute MI. To this end, they enrolled 9,751 acute MI patients who had undergone percutaneous coronary intervention (PCI). They recorded patient data such as age, gender, vital symptoms at admission, and incidents at admission, including death, hypotension, and cardiogenic shock, as well as the need for cardiopulmonary resuscitation (CPR), arrhythmia, and the need for a pacemaker. Patients were assigned to five groups in terms of LDL levels (< 70, 70-99, 100-129, 130-159, and > 160 mg/dL). They conducted one-month and 12-month follow-up examinations after MI to monitor the occurrence of major cardiovascular incidents such as mortality, repeated MI, and the need for coronary bypass graft. They found that patients with higher LDL levels (except for LDL levels > 160 mg/dL) had higher awareness (20).

The relationship between lipid profiles and cardiovascular conditions can be affected by factors such as genetics, race, diet, and lifestyle. Therefore, this study aimed to evaluate the relationship in Chaharmahal and Bakhtiari province, southwest Iran, to provide a foundation for future studies and the development of domestic clinical guidelines for the treatment of dyslipidemia. Based on available evidence, cardiologists have realized that patients hospitalized due to acute MI or coronary syndromes do not necessarily have high lipid levels. In addition, recent studies have shown that patients with low LDL at MI had a higher rate of mortality and a worse prognosis in the long term.

Objectives

The current study addressed the question of whether a higher LDL level is associated with a better prognosis in terms of the frequency of hospitalization due to coronary syndromes, recurrent MI, and intra-hospital mortality. The findings of our study will shed light on the role of LDL levels and the effectiveness of treatment with atorvastatin.

Patients and Methods

This cross-sectional, descriptive-inferential, retrospective study aimed to examine the relationship between LDL levels in ST-elevation MI patients and their awareness in terms of the frequency of hospitalization due to cardiovascular incidents, intra-hospital mortality, and other conditions predetermined in the inclusion checklist.

The patients' names and record numbers were listed after obtaining approval from the institutional ethics Committee and ensuring the confidentiality of patients' data. Sampling was performed using a census, including all the patients referred through the study period (N = 1390). On the other hand, patients with diabetes and incomplete records were excluded from the study. The final number of enrolled samples was 1274.

A checklist was designed to record the information, including demographics (age and gender), risk factors (smoking), statin intake history, angiography result, intra-hospital mortality, the need for CPR, and MI frequency.

Based on the baseline LDL level, patients were assigned to four groups, including LDL levels < 70, 70-129, 130-159, and > 160 mg/dL. Patients who took statin and those who did not, constitute the other two groups. This design helped to investigate the relationship between baseline LDL levels and long-term awareness of patients who had experienced MI.

Data were analyzed using SPSS v22. Continuous variables were summarized using the median and mean ± standard deviation (SD). Qualitative variables were provided using percentages and frequencies. The normality of data distribution was evaluated before conducting the chi-square and Fisher's exact tests. The significance level was considered to be < 0.05.

Results

The mean age of our participants was 63.18 ± 13.79 (range: 24-95 years). Among 1274 patients, 78% (999/1274) were males. The LDL level range of hospitalized patients with acute MI was 23-273 (mean: 110 ± 34.9) mg/dL during the study period. Based on LDL levels at MI, patients were assigned to four groups (Table 1). According to our findings, 11% (143/1274), 64% (818/1274), 16% (205/1274), and 9% (108/1274) of patients were categorized into LDL groups 1 (LDL ≤ 70), 2 (71 ≤ LDL ≤ 129), 3 (130 ≤ LDL ≤ 159), and 4 (LDL ≥ 160), respectively. The majority of patients with an acute heart attack (in both males and females) were in LDL group 2 (71 ≤ LDL ≤ 129;

Table 1. Basic characteristics of the patients in four LDL groups

Variables	LDL Groups				*P* value
	≤70 (mg/dL)	70-129 (mg/dL)	130-159 (mg/dL)	≥160 (mg/dL)	
Gender					0.003
Male	113	657	159	70	
Female	30	161	46	38	
Urbanity					0.034
Urban	102	652	155	81	
Rural	40	166	50	27	
HTN	42	176	44	25	0.215
Diabetes	129	717	182	96	0.824
CHD family history	18	113	20	11	0.372
Smoking history	15	103	23	9	0.563
Statin intake history	104	497	109	47	0.000
ECG					0.792
Anterior	73	431	114	61	
Posterior	38	165	43	20	
Other types	32	221	48	27	
Electrocardio shock need	10	37	6	5	0.360
Cardiogenic shock	1	7	2	0	0.797
CPR need	5	34	3	3	0.297
Mortality	3	20	4	5	0.502
Valve failure	1	15	4	2	0.797
MI frequency					0.049
1	134	770	182	98	
2	9	47	21	10	
3	0	1	2	0	

Note. LDL: Low-density lipoprotein; *HTN: Hypertension; *CHD: Coronary heart disease; *ECG: Electrocardiogram; *CPR: Cardiopulmonary resuscitation; *MI: Myocardial infarction.

Table 1). Among our patients, 23% (287/1274) reported having a history of HTN, thus 12% (152/1274) reported a history of smoking.

Regarding the relationship between the history of HTN and smoking with the LDL level, the statistical test represented no significant relationship between HTN ($P=0.215$) and smoking ($P=0.563$) with the 4 LDL groups.

Approximately 13% (162/1274) of our patients reported having a family history of cardiovascular diseases; no statistically significant relationship was found between the LDL level and family history of cardiovascular diseases ($P=0.372$). Nearly 60% (757/1274) of patients reported statin intake, and the highest number was found in LDL group 2 ($71 \leq LDL \leq 129$). As the LDL level increased, the likelihood of statin intake demonstrated a decrease. In addition, a statistically significant relationship was observed between statin intake and LDL level ($P<0.0001$).

The majority of participants suffered from primary infarction and had LDL levels $71 \leq$ and ≤ 129. Further, 53% (679/1274), 21% (266/1274), and 26% (328/1274) of patients with acute MI had anterior electrocardiogram (ECG), inferior ECG, and other types of ECG, respectively, and there was a statistically significant relationship between ECG and LDL level ($P=0.792$). Moreover, 99% (1258/1274), 1% (14/1274), and 0.5% (n: 6) of patients had a sinusoidal rhythm at MI, atrial fibrillation rhythm, and ventricular tachycardia rhythm, respectively, and only four patients showed ventricular fibrillation rhythm. The findings demonstrated that 2% (58/1274) of patients needed electroshock at the time of acute MI and 1% (10/1274) had extremely low blood pressure and suffered from cardiogenic shock. Nearly 4% (45/1274) of patients needed CPR, and the mortality rate from MI was 3% (32/1274).

Our findings also revealed that acute MI patients at Hajar hospital were hospitalized 1-18 (mean: 1.5) times during the study period. The mean hospitalization frequency due to cardiovascular incidents was 1.55 ± 1.402. Approximately 7% (87/1274) and 1% (3/1274) of patients were hospitalized two and three times, respectively, and the remaining patients experienced acute MI once (1184/1274). A statistically significant relationship was found between aggregate LDL and the number of MIs ($P=0.049$). The mean number of acute MIs and the mean number of clogged arteries in angiography were 1.07 ± 0.26 and 1.21 ± 0.43 (range: 1-3), respectively.

Most patients who needed cardiac and pulmonary rehabilitation at acute MI, suffered from electroshock, heart valve failure, and arrhythmia, or those who died had LDL levels of $71 \leq$ and ≤ 129. The chi-square test results (Table 1) also showed that there was no statistically significant association between the LDL level and the need for CPR ($P=0.297$), electroshock ($P=0.360$), the occurrence of cardiogenic shock ($P=0.797$), heart valve failure ($P=0.797$), death ($P=0.502$), and arrhythmia ($P=0.670$).

Out of 1274 patients in this study, 150 cases (11.8%) reported diabetes. Among 1124 patients who did not report diabetes, 663 cases (59%) had a history of statin intake. The results represented a statistically significant association between statin intake and LDL groups ($P<0.0001$).

Based on the results of the examination of the level of LDL with HTN in non-diabetic people, 184 of the non-diabetic acute heart attack patients had HTN, and the Chi-square statistical test demonstrated a significant relationship between the level of LDL and the HTN in these patients ($P=0.028$).

The results revealed a non-statistically significant relationship between the LDL-G level and MI in patients with a non-diabetic acute heart attack ($P=0.073$, Table 2).

The number of participants in the study who had a history of statin intake was 757. The majority of acute MI patients 67% (497/757) who took had an LDL level of 70-129.

The results of this research showed that in people with a history of just statin use, HTN ($P=0.011$) and ECG

Table 2. Distribution of non-diabetic patients by statin intake and HTN in 4 LDL groups

Variables		LDL Groups				*P* value
		<70 (mg/dL)	70-129 (mg/dL)	130-159 (mg/dL)	>160 (mg/dL)	
		Number (%)				
Statin	Takes	95 (8.5)	431 (38.4)	97 (8.6)	40 (3.6)	<0.0001
	Does not take	34 (3)	286 (25.4)	85 (7.6)	56 (5)	
	Total	129 (11.5)	717 (63.8)	182 (16.2)	96 (8.5)	
History of HTN	Positive	33 (2.9)	109 (9.7)	28 (2.5)	14 (1.2)	0.028
	Negative	96 (8.5)	608 (54.1)	154 (13.7)	82 (7.3)	
	Total	129 (11.4)	717 (63.8)	182 (16.2)	96 (8.5)	

Note. HTN: Hypertension; LDL: Low-density lipoprotein.

($P=0.002$) have a significant relationship with LDL groups. Other variables, including gender ($P=0.569$), place of residence ($P=0.817$), family history of cardiovascular diseases ($P=0.453$), smoking history ($P=0.423$), need for electrocardio shock ($P=0.172$), cardiogenetic shock ($P=0.933$), the need for CPR ($P=0.130$), death ($P=0.147$), valvular disorder ($P=0.191$), and angiography ($P=0.387$) indicated no statistically significant relationship with LDL groups (Table 3).

Table 3. Distribution of patients with a history of statin use in four LDL groups

Variables	LDL Groups				*P* value
	≤70 (mg/dL)	70-129 (mg/dL)	130-159 (mg/dL)	≥160 (mg/dL)	
Gender					0.569
Male	79	390	81	29	
Female	25	107	28	18	
Urbanity					0.817
Urban	81	400	90	39	
Rural	23	97	19	8	
HTN	21	112	34	19	0.011
CHD family history	15	96	16	10	0.453
Smoking history	12	90	18	7	0.423
Statin intake history	95	431	97	40	0.002
ECG					0.002
Anterior	68	380	73	31	
Posterior	29	97	21	11	
Other types	7	20	15	5	
Electrocardio shock need	1	28	6	1	0.172
Cardiogenic shock	1	4	1	0	0.933
CPR need	2	28	2	1	0.130
Mortality	3	20	4	5	0.147
Valve failure	1	21	5	0	0.191
MI frequency					0.073
1	120	676	161	90	
2	9	40	19	6	
3	0	1	2	0	

Note. LDL: Low-density lipoprotein; HTN: Hypertension; CHD: Coronary heart disease; CPR: Cardiopulmonary resuscitation; MI: Myocardial infarction.

Discussion

Cardiovascular conditions, particularly coronary conditions and acute MI, are among the major causes of mortality worldwide. Such conditions impose stupendous expenses on patients and health systems and substantially reduce the quality of life of the patients. Disorders in LDL, high-density lipoprotein, and triglyceride levels are the main factors predisposing to atherosclerosis. Several studies have shown that high levels of LDL play a substantial role in the development of congestive heart diseases and MI (21).

Intra-hospital incidents included all intra-hospital mortalities due to acute MI, the need for CPR, the need for electroshock, cardiogenic shock, arrhythmia, mitral valve failure, and the number of clogged arteries. The results of our study demonstrated that a higher LDL level (except for LDL<70) was associated with awareness of these conditions.

In a study investigating the relationship between LDL and clinical outcomes after PCI in patients with acute MI, Cho et al assigned 9,571 patients who underwent PCI to five LDL groups (lower than 70, 70-99, 100-129, 130-159, and higher than 160). Then, the clinical outcomes were reviewed at admission and 1- and 12-month follow-ups after PCI. Patients with higher LDL levels had more acceptable hemodynamic and clinical outcomes. In addition, the clinical outcomes improved (except for LDL>160) with increasing LDL levels. In the mentioned study, the conditions were examined during hospitalization and 1- and 12-month follow-ups. Intra-hospital conditions included PCI success, mortality, cardiogenic shock, hypotension at admission, arrhythmia, the need for a balloon or pacemaker, and major incidents such as death, the need for coronary artery bypass graft, and multiple clogged arteries. The 1- and 12-month conditions included cardiovascular mortality, MI, recurrent PCI, and coronary artery bypass graft. The researchers reported that as the LDL level increased, PCI success and intra-hospital mortality represented a reduction. Further, the 12-month mortality rate was higher in patients with LDL levels<70 than in those with LDL levels>70. Therefore, a high LDL-C level (except for LDL≥160) was associated with improved awareness. LDL can be considered an

independent factor for patient awareness. High levels of LDL may indicate better nutrition and health that increase stress tolerance. Moreover, patients with higher LDL levels were more likely to regularly refer to health centers and take hypocholesterolemic medications (20).

In our study, the LDL level was measured in patients with acute MI in the early hours of admission. Patients were assigned to four groups based on their LDL levels (LDL < 70, 70 < LDL < 129, 129 < LDL < 160, and LDL > 160) and underwent PCI. The majority (64%) of patients with acute MI had an LDL level of 71-129. The distribution of patients in other LDL groups was 16%, 11%, and 9% in groups 3, 1, and 4, respectively. In the study of Cho et al, the majority of patients fell into the 100 < LDL < 129 groups (89). Kwame et al assigned 232 MI patients to two groups based on their LDL: LDL < 100 and LDL > 160 mg/dL. Patients with LDL > 160 were treated with a statin. In the one-year follow-up examinations, both groups showed similar awareness (22). In the study of Vanesa et al, the majority of participants had an LDL level of > 77 mg/dL (19).

Some of the consequences of acute MI include intra-hospital mortality, recurrent ischemia, recurrent acute MI, and congestive heart failure. In our study, 53% of the participants suffered from primary infarction, 26% had unknown infarction, and 21% had inferior infarction.

Beker et al predicted these consequences using variables such as primary ischemia, class Killip > 1, age over 70 years, and combined hypotension and tachycardia at admission (23).

Arrhythmia, especially atrial fibrillation, plays a significant role in patient awareness. In this study, 98% of the patients had sinusoidal rhythm, 14% represented atrial fibrillation, 0.5% had ventricular tachycardia, and 0.5% demonstrated ventricular tachycardia rhythms. In a study on 3220 patients, Jebra et al categorized patients into four groups with respect to atrial fibrillation and followed up on their mortality after six years. The highest number of mortality associated with atrial fibrillation occurred within 30 days following acute MI (24).

Our results revealed a statistically significant relationship between the LDL-G level and MI, especially in patients in LDL group 2 (129 < LDL < 159; $P = 0.023$), in whom MI was more likely. Additionally, based on the results, there was a statistically significant relationship between the LDL-G level and angiography results in patients with statin treatment, especially in LDL group 2 (129 < LDL < 159; $P = 0.031$), in whom MI was more likely.

In our study, the Chi-square test results showed no statistically significant association between ECG, gender, hospitalization frequency, LDL group membership, the need for electroshock, cardiac shock, arrhythmia, and family history of smoking, urbanity, and heart attack involving the entire cardiac wall ($P < 0.05$).

Moreover, there was also no statistically significant relationship between cardiac shock and ECG type, arrhythmia, and valve disorder.

Conclusion

Overall, there is a significant relationship between LDL groups and the number of times acute heart attack occurs as a long-term complication in people who have had one.

Limitations of the Study

Despite the efforts of the researchers, some of the examined files were not complete, and the required information was not recorded in the checklist used in the study of the files. As a result, some of our samples were lost. Thus, it is suggested that medical records be recorded more carefully so that in future studies, the results can fully cover all the issues considered in this regard.

Authors' contribution

ARKH, ML and FH were the principal investigators of the study. ARKH, ML and FH contributed to the study conception and design. AK revisited the manuscript and critically evaluated intellectual contents. All authors contributed to preparing the final version of the manuscript, revising the manuscript and critically evaluating the intellectual content. All authors have read and approved the final version of the manuscript and confirmed the accuracy or integrity of all steps of the study.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical Approval

The research followed the tents of the Declaration of Helsinki. The institutional ethical committee at Shahrekord University of Medical Sciences approved all study protocols (IR.SKUMS.REC.1396.238). Accordingly, written informed consent taken from all participants before any intervention.

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