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Non-achievement of low-density lipoprotein cholesterol goal and related factors among elderly outpatients in Viet Nam: A cross-sectional study

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ABSTRACT

Introduction: Dyslipidemia, particularly elevated serum low-density lipoprotein cholesterol (LDL-C), plays a crucial role in the development and progression of atherosclerosis. This study aimed to determine the rate of LDL-C non-achievement according to the European Society of Cardiology/European Atherosclerosis Society 2019 (ESC/EAS 2019) guidelines and related factors in the elderly. **Methods**: This was a cross-sectional study involving 555 individuals (age 69.30 \pm 6.54, male/female ratio 4.55/1) in an outpatient clinic in Ca Mau province from October 2020 to June 2021. Demographic information, medical history, clinical characteristics, and tested cholesterol, including LDL-C level, were collected to assess cardiovascular risk and determine factors related to LDL-C control status. Results: The non-achievement rate of the LDL-C goal in participants was 77.1%. In the adjusted model, factors associated with an increased risk of non-achievement of the LDL-C goal were non-adherence to treatment (odds ratio (OR) 7.75, 95% confidence interval (CI) 3.65-16.47, p < 0.001), being at very high risk (OR 15.48, 95% CI 6.34-37.76, p < 0.001), and at high risk (OR 4.03, 95% Cl 2.20-7.40, p < 0.001). Conversely, factors related to a decreased risk were exercise (OR 0.53, 95% CI 0.30-0.95, p = 0.032) and a history of myocardial infarction or unstable angina (OR 0.192, 95% CI 0.05-0.72, p = 0.014), or coronary revascularization (OR 0.20, 95% CI 0.08-0.48, p < 0.001). Conclusions: The rate of non-achievement in the LDL-C goal among participants was notable. Non-adherence to treatment and classification as high to very high risk were identified as factors associated with an increased risk of non-achievement of LDL-C, while regular exercise was linked to a decreased risk. This study emphasizes the necessity of an aggressive strategy for high and very high-risk groups with a comprehensive approach incorporating pharmacological and non-pharmacological individual treatment for achieving the LDL-C target.

Key words: Low-density lipoprotein cholesterol (LDL-C), dyslipidemia, ESC/EAS 2019 guidelines, elderly, SCORE Risk Charts

INTRODUCTION

Viet Nam is experiencing a rapid increase in its aging population, making it one of the fastest-aging countries in the world. In 2019, the percentage of individuals aged 60 and above in Viet Nam was 11.9%. Projections indicate that by 2038, this figure is expected to increase significantly to 20.2%¹. As individuals age, the prevalence of chronic conditions tends to increase. A systematic review and meta-analysis of 83 studies conducted between 2000 and 2020 revealed that in Vietnam, the estimated prevalence of hypertension is 6.0%, while the prevalence of type 2 diabetes stands at 25%. Additionally, the study found that among individuals aged 65-74, the prevalence of those having more than four out of nine major cardiovascular risk factors (hypertension, diabetes, dyslipidemia, obesity, smoking, excessive alcohol intake, unhealthy diet, physical inactivity, and stress) was 28.3% for women

and 36.2% for men². Notably, cerebrovascular disease and ischemic heart disease are the leading causes of mortality in Viet Nam³. Dyslipidemia, particularly elevated serum low-density lipoprotein cholesterol (LDL-C), plays a crucial role in the development and progression of atherosclerosis^{4,5}. According to the Framingham study, every 1% increase in LDL-C levels is associated with a 2% increase in the risk of developing coronary artery disease over 6 years⁶. Controlling LDL-C is a key measure of the overall risk of death and cardiovascular events. In 2019, the European Society of Cardiology and the European Society of Atherosclerosis (ESC/EAS 2019) published updated recommendations that offer a comprehensive approach to managing lipid levels, placing particular emphasis on achieving the target LDL-C based on cardiovascular risk stratification⁷. In South Asian countries, particularly Viet Nam, few studies have assessed

Cite this article : Ho D S, Le T V, Dinh H C, Nguyen T, Ngo D K, Nguyen C D. **Non-achievement of low-density lipoprotein cholesterol goal and related factors among elderly outpatients in Viet Nam: A cross-sectional study**. *Biomed. Res. Ther.* 2025; 12(1):7082-7089.

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- History
- Received: Jun 11, 2024
- Accepted: Nov 17, 2024
- Published Online: Jan 31, 2025

DOI : 10.15419/bmrat.v12i1.952

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the attainment of LDL-C goals and the associated factors. The objective of this study was to assess the rate of LDL-C non-attainment in elderly Vietnamese outpatients and identify the factors associated with this non-achievement.

METHODS

Study Design, Inclusion and Exclusion Criteria

The cross-sectional study was conducted in an outpatient clinic in Ca Mau province from October 2020 to June 2021. The inclusion criteria were as follows: elderly outpatients (\geq 60 years old) who voluntarily agreed to participate in the study and had been taking medication for dyslipidemia for at least 3 months. Exclusion criteria included: (1) cognitive impairment, severe dementia, or inability to communicate; (2) advanced cancer; (3) non-adherence to follow-up.

Procedure

From elderly outpatients who met the inclusion and exclusion criteria, we collected demographic and clinical information, including place of residence (urban or rural); smoking status (currently smoking or stopped < 1 year); alcohol use (> 1 alcohol unit/day, equivalent to 300 mL beer or 60 mL hard liquor); exercise frequency (> 30 minutes/day and \geq 5 days/week). Major cardiovascular risk factors were also recorded, including diabetes mellitus (DM)⁸; hypertension⁹; chronic kidney disease (CKD)¹⁰; atherosclerotic cardiovascular disease (AS-CVD), including a history of previous acute coronary syndrome (ACS) (myocardial infarction (MI) or unstable angina), coronary revascularization (percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG), and other arterial revascularization procedures), stroke or transient ischemic attack (TIA), and peripheral arterial disease. Cardiovascular risk stratification according to ESC/EAS 2019 included very-high risk, high risk, moderate risk, and low risk (Supplementary table). After that, fasting lipid profiles were measured by the clinic laboratory with standard processes and checked for accuracy by a biochemist. Participants were assessed to determine if they achieved the LDL-C goal based on risk stratification⁷.

Statistical Analysis

The data were analyzed using Statistical Product and Service Solutions (SPSS) software (version 22.0; IBM Corp., Armonk, NY, USA). The comparison of categorical variables employed the Chi-square test or Fisher's exact test for small sample sizes, while continuous variables were compared using a t-test. The multivariable logistic regression model included variables with p < 0.2 in the univariate logistic regression model. A two-sided p-value < 0.05 was predetermined as the threshold for statistical significance.

Ethics Declarations

The study protocol received approval from the Ethics Committee of the University of Medicine and Pharmacy at Ho Chi Minh City (reference number: 763/DHYD-HDDD), and each participant provided written informed consent.

RESULTS

Risk stratification of study patients according to the ESC/EAS 2019 guidelines categorized the patients as very-high risk (37.5%), high risk (45.0%), and moderate risk (17.5%) with a significant difference (p < 0.001) (Table 1). The overall achievement rate of the LDL-C goal in all participants was 22.9%. Females were more likely to achieve the LDL-C goal compared to males, with rates of 31.0% and 21.1% respectively (p = 0.036). Individuals who smoked or were noncompliant with treatment exhibited a lower percentage of LDL-C achievement (p < 0.001). The individuals in the achieved group showed a higher likelihood of having a history of MI, unstable angina, or coronary revascularization compared to those in the nonachieved group. There was also a descending trend in achieving the LDL-C goal in the order of moderate risk, high risk, and very-high risk, with 48.4%, 20.4%, and 13.9% respectively (p < 0.001) (Table 2).

The univariate logistic regression analysis revealed that males, individuals who smoked, and nonadherent individuals had a higher odds ratio for not achieving the LDL-C goal (**Table 3**). Although stroke and TIA did not show a significant association, individuals with a history of MI or unstable angina and those who underwent coronary revascularization had a lower odds ratio for non-achievement of the LDL-C goal. Regarding dyslipidemia treatment drugs, rosuvastatin was associated with a significantly lower odds ratio of 0.43 (95% CI: 0.22-0.82) for not achieving the LDL-C goal compared to atorvastatin (**Table 3**).

A multivariable logistic regression showed that patients not achieving target values were more frequently non-adherent to treatment and at very-high and high risk. By contrast, individuals who engaged in regular exercise and had a history of MI or unstable angina or coronary revascularization had a reduced risk of non-achievement of the LDL-C goal (**Table 4**).

Table 1: General characteristics of the participants

Characteristics	All (n = 555)	Male (n = 455)	Female (n = 100)	p-value
Age (years)	69.30 ± 6.54	69.22 ± 6.71	69.67 ± 5.77	0.536#
Age group				0.171*
60-69	328 (59.1)	275 (60.4)	53 (53.0)	
\geq 70	227 (40.9)	180 (39.6)	47 (47.0)	
Living Location				0.117*
Urban	446 (80.4)	360 (79.1)	86 (86.0)	
Rural	109 (19.6)	95 (20.9)	14 (14.0)	
BMI (kg/m ²)	24.49 ± 2.78	24.60 ± 2.77	24.00 ± 2.77	0.052#
BMI subgroups				0.057*
< 18.5	4 (0.7)	4 (0.9)	0 (0.0)	
18.5-22.9	156 (28.1)	122 (26.8)	34 (34.0)	
23.0-24.9	184 (33.2)	145 (31.9)	39 (39.0)	
\geq 25.0	211 (38.0)	184 (40.4)	27 (27.0)	
Exercise	447 (80.5)	367 (80.7)	80 (80.0)	0.880*
Smoking	156 (28.1)	154 (33.8)	2 (2.0)	< 0.001**
Alcohol use	250 (45.0)	245 (53.8)	5 (5.0)	< 0.001**
Non-adherence	159 (18.6)	139 (30.5)	20 (20.0)	0.035*
Diabetes mellitus				
Prevalence	205 (36.9)	168 (36.9)	37 (37.0)	0.998*
\geq 10 years	105(18.9)	85 (18.7)	20(20.0)	0.703*
Target organ damage	26 (4.7)	20 (4.4)	6 (6.0)	0.476*
Hypertension ASCVD	517 (93.2)	427 (93.8)	90 (90.0)	0.168*
MI or unstable angina	13 (2.3)	13 (2.9)	0 (0.0)	0.139**
Coronary revascularization	49 (8.8)	44 (9.7)	5 (5.0)	0.173**
Stroke and TIA	41 (7.4)	37 (8.1)	4 (4.0)	0.205**
Creatinine clerance ⁺	11 (7.1)	57 (0.1)	1(1.0)	< 0.001*
≥ 60	454 (81.8)	395 (86.8)	59 (59.0)	< 0.001
30-59	98 (17.7)	57 (12.5)	41 (41.0)	
< 30	3 (0.5)	3 (0.7)	0 (0.0)	
Lipid Level (mmol/L)	0 (0.0)			
Total cholesterol	4.98 ± 0.99	4.97 ± 1.01	5.00 ± 0.89	0.736#
LDL-C	2.55 ± 0.95	2.55 ± 0.97	2.54 ± 0.85	0.884#
HDL-C	1.31 ± 0.48	1.31 ± 0.48	1.34 ± 0.48	0.484#
Triglyceride	2.01 ± 0.90	2.05 ± 0.91	1.81 ± 0.81	0.015#
Cardiovascular risk				< 0.001*
Very-high risk	208 (37.5)	193 (42.4)	15 (15.0)	
High risk	250 (45.0)	203 (44.6)	47 (47.0)	
Moderate risk	97 (17.5)	59 (13.0)	38 (38.0)	

Continuous variables (age, BMI, blood lipids) were described by using mean (standard deviation). Other variables were described as frequencies (percentages). ⁺Using Cockcroft-Gault equation with unit as ml/min/1.73m². [^]based on ESC/EAS 2019 Guidelines for the management of dyslipidaemias. p-values were calculated using independent t-test (^{*}), chi-square test (^{*}), or Fisher's-exact test (^{**})

Abbreviations: ASCVD: Atherosclerotic cardiovascular disease, BMI: body mass index, HDL-C: High-density Lipoprotein Cholesterol, LDL-C: Low density lipoprotein Cholesterol, MI: myocardial infarction, TIA: transient is-chaemic attack

Characteristics	Achieved (n = 127)	Non-achieved (n = 428)	p-value
Sex			0.036*
Male	96 (75.6)	359 (83.9)	
Female	31 (24.4)	69 (16.1)	
Age group			0.472*
60-69	79 (62.2)	249 (58.2)	
\geq 70	48 (37.8)	179 (41.8)	
Living Location			0.800*
Urban	101 (79.5)	345 (80.6)	
Rural	26 (20.5)	83 (19.4)	
BMI	24.71 ± 2.79	24.42 ± 2.78	0.320#
Smoking	16 (12.6)	140 (32.7)	< 0.001*
Alcohol use	52 (40.9)	198 (46.3)	0.311*
Exercise	96 (75.6)	351 (82.0)	0.109*
Non-adherence	9 (7.1)	150 (35.0)	< 0.001*
Diabetes mellitus	50 (39.4)	155 (36.2)	0.531*
Hypertension	115 (90.6)	402 (93.9)	0.186*
ASCVD			
MI or unstable angina	6 (4.7)	7 (1.6)	0.043*
Coronary revascularization	17 (13.4)	32 (7.5)	0.039*
Stroke and TIA	8 (6.3)	33 (7.7)	0.593*
Cardiovascular risk^			< 0.001*
Very-high risk	29 (22.8)	179 (41.8)	
High risk	51 (40.2)	199 (46.5)	
Moderate risk	47 (37.0)	50 (11.7)	

Table 2: LDL-C achievement according to ESC/EAS 2019 for dyslipidemia management

BMI was described by using mean±standard deviation. Other variables were described as frequencies (percentages). based on ESC/EAS 2019 Guidelines for the management of dyslipidemias. p-values were calculated using independent t-test ([#]) and chi-square test (^{*}) Abbreviations: ASCVD: Atherosclerotic cardiovascular disease, BMI: body mass index, MI: myocardial infarction, TIA: transient ischaemic attack

DISCUSSION

In our investigation, patients categorized as very-high risk and high-risk groups exhibited a considerably lower likelihood of achieving their LDL-C target compared to those in the moderate risk group (17.5% versus 48.4%). In accordance with our findings, inadequate achievement of LDL-C goals among highrisk patients has been consistently reported in previous studies. First, the DA VINCI survey unveiled that only 18% of patients categorized as very high risk manage to reach their LDL-C target¹¹. A similar discovery was reported in a study among the Czech population, where only 19.4% of individuals classified as very high-risk atherosclerotic cardiovascular patients and 28.1% of those deemed high-risk, were able to achieve the LDL-C goal¹². The strict criteria of the ESC/EAS 2019 guidelines, compared to ESC/EAS 2016, may explain the relatively low rate of target achievement^{7,13}.

The absence of combined therapy or high-dose statin utilization for LDL-C management was notable in our study, contributing in part to the unsatisfactory achievement of LDL-C goals. Previous studies have documented a very low percentage of combined ther-

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Characteristics	р	OR	95% CI
	P	UK	73 70 CI
Age group 60-69	0.418	1.00	0.79-1.78
			0.79-1.78
≥ 70	0.418	1.18	1.0/ 0.50
Male	0.034	1.68	1.04-2.72
Urban Location (compared to rural)	0.788	1.07	0.65-1.75
Exercise	0.110	0.68	0.42-1.09
Smoking	< 0.001	3.37	1.92-5.91
Alcohol use	0.291	0.80	0.54-1.20
Non-adherence	< 0.001	7.07	3.49-14.36
Diabetes mellitus	0.518	0.87	0.58-1.31
Hypertension	0.190	0.62	0.30-1.27
ASCVD			
MI or unstable angina	0.053	0.33	0.11-1.02
Coronary revascularization	0.042	0.52	0.28-0.98
Stroke and TIA	0.594	1.24	0.46-2.76
Dyslipidemia treatment drug			
Atorvastatin		1.00	
Rosuvastatin	0.011	0.43	0.22-0.82
Fenofibrate	0.714	0.88	0.44-1.74
Cardiovascular risk^			
Moderate risk		1.00	
High risk	< 0.001	3.67	2.22-6.07
Very-high risk	< 0.001	5.80	3.32-10.15

Table 3: Univariate logistic regression of factors related to non-achievement of LDL-C

based on ESC/EAS 2019 guidelines for the management of dyslipidemias

Abbreviations: ASCVD: Atherosclerotic cardiovascular disease, MI: myocardial infarction, TIA: transient ischaemic attack

apy for LDL-C control in similar scenarios. For instance, a study conducted in a cardiac rehabilitation clinic in Iceland found that only 9% of patients were prescribed ezetimibe therapy, and only 13% received PCSK9 inhibitor¹⁴. Findings from the ESC-EORP EUROASPIRE V survey across 27 countries also revealed that only 8% of patients were prescribed statins in combination with ezetimibe, and only a negligible percentage of patients (0.4%) received treatment with PCSK9 inhibitors either alone or in combination with statins¹⁵. These medications were not prescribed in our study due to various factors, with the primary concern being the cost, as both medications are associated with high expenses. Additionally, most participants received treatment with low to medium doses of statins (rosuvastatin 5/10mg, atorvastatin 10/20 mg)

instead of the recommended high-intensity doses⁷. This discrepancy could potentially contribute to the causes of non-achievement of LDL-C targets.

Individuals who engaged in regular exercise or demonstrated adherence to their treatment regimen exhibited a higher success rate of achieving the LDL-C goal. This outcome aligns with a previous finding in Russia that patients who either forgot to take hypercholesterolemia treatment or deemed it acceptable to miss prescribed doses more than once per week experienced a significantly diminished likelihood of achieving their LDL-C goal ¹⁶. A study conducted in Korea by Kim et al. similarly revealed that patients who adhered to statin therapy tended to have lower LDL-C levels, consequently leading to higher rates of goal achievement ¹⁷. Moreover, research involving

Characteristics	р	OR	95% CI
Male	0.632	0.87	0.49-1.55
Exercise	0.032	0.53	0.30-0.95
Smoking	0.300	1.44	0.72-2.85
Non-adherence	< 0.001	7.75	3.65-16.47
Hypertension	0.659	0.82	0.34-1.99
ASCVD			
MI or unstable angina	0.014	0.19	0.05-0.72
Coronary revascularization	< 0.001	0.20	0.08-0.48
Dyslipidemia treatment drug			
Atorvastatin		1.00	
Rosuvastatin	0.076	0.52	0.25-1.07
Fenofibrate	0.381	0.70	0.32-1.54
Cardiovascular risk^			
Moderate risk		1.00	
High risk	< 0.001	4.03	2.20-7.40
Very-high risk	< 0.001	15.48	6.34-37.76

Table 4: Multivariable logistic regression of factors related to non-achievement of LDL-C

^based on ESC/EAS 2019 guidelines for the management of dyslipidemias

Abbreviations: ASCVD: Atherosclerotic cardiovascular disease, MI: myocar-

dial infarction, TIA: transient ischaemic attack

10,221 participants in Southwestern China indicated that the prevalence of dyslipidemia was negatively correlated with daily physical exercise ¹⁸. A systematic review concluded that exercise of both low and moderate intensity led to a significant reduction in total cholesterol, with notable effects on low-density lipoprotein levels ¹⁹.

Furthermore, our observations indicated that patients with a history of MI or unstable angina had better control of LDL-C. These results seemed contradictory when this group was at very high risk and had the lowest rate of achieving the LDL-C target. However, a study involving 654 patients with diabetes in France yielded similar results²⁰. The study reported a decreased risk of non-attainment of LDL-cholesterol target values in patients with a history of coronary artery disease (OR 0.64, CI 0.45–0.89), aligning with the findings in our study²⁰. This phenomenon could be attributed to the experience of a cardiovascular event in these patients, which may have heightened their awareness of the importance of managing risk factors, including LDL-C.

This study had some limitations that should be acknowledged. The investigation was exclusively conducted within a healthcare clinic of a province, potentially limiting the generalizability of the findings to the broader population. The findings and analyses should be interpreted with caution, as they reflect the profile of elderly outpatients from this location. An additional limitation stems from the cross-sectional nature of the study design, which is incapable of establishing causal relationships or determining the effectiveness of treatment over time. Furthermore, the study lacked comprehensive baseline levels of LDL-C, which would have provided important information for assessing the effectiveness of treatment. The absence of baseline information prevented the determination of the extent of LDL-C reduction achieved by the treatment.

CONCLUSION

The rate of non-achievement in LDL-C goals according to the ESC/EAS 2019 guidelines was notable among participants. Non-adherence to treatment and a high to very high-risk profile were associated with an increased risk of non-achievement of LDL-C goals, while regular exercise was associated with a decreased risk. Our study highlights the importance of cardiovascular risk stratification when setting and managing LDL-C targets, with an aggressive strategy for high and very-high risk groups. Furthermore, a comprehensive approach combining pharmacological and non-pharmacological individual treatment is essential to attain the LDL-C target.

ABBREVIATIONS

ACS - Acute Coronary Syndrome, ASCVD -Atherosclerotic Cardiovascular Disease, CABG -Coronary Artery Bypass Grafting, CI - Confidence Interval, CKD - Chronic Kidney Disease, DM -Diabetes Mellitus, ESC/EAS - European Society of Cardiology/European Atherosclerosis Society, LDL-C - Low-Density Lipoprotein Cholesterol, MI - Myocardial Infarction, OR - Odds Ratio, PCI - Percutaneous Coronary Intervention, PCSK9 -Proprotein Convertase Subtilisin/Kexin Type 9, SPSS - Statistical Product and Service Solutions, TIA -Transient Ischemic Attack

ACKNOWLEDGMENTS

The authors would like to thank the Health Protective Committee for High Ranking Cadre of Ca Mau Province, Viet Nam for their support.

AUTHOR'S CONTRIBUTIONS

DSH, TVL, and CDN contributed to the study conception and design. Material preparation, data collection, and analysis were performed by TVL, and DSH. The first draft of the manuscript was written by DSH, and HCD. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

FUNDING

None.

AVAILABILITY OF DATA AND MATERIALS

Data and materials used and/or analyzed during the current study are available from the corresponding author on reasonable request.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the local Ethics Committee of the University of Medicine and Pharmacy at Ho Chi Minh City (reference number: 763/ĐHYD-HĐĐĐ).

CONSENT FOR PUBLICATION

Not applicable.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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