CHARACTERISTICS OF LDL-C ELEVATION AND THE TREATMENT OUTCOMES OF ROSUVASTATIN IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION AT TRA VINH GENERAL HOSPITAL 2021-2022

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ABSTRACT

Background*: Myocardial infarction (MI), sometimes referred to as a heart attack, is a leading cause of mortality on a global scale. This medical ailment is sometimes referred to as a myocardial infarction. To mitigate the issue, it is essential to promptly conduct diagnostic examinations and start therapy for lipid abnormalities.* ***Objectives****: The aim of this study is to provide a comprehensive description of the variables associated with elevated low-density lipoprotein cholesterol (LDL-c) levels and to evaluate the treatment results of rosuvastatin in patients diagnosed with acute myocardial infarction at Tra Vinh General Hospital throughout the period of 2021-2022.* ***Materials and methods:*** *The objective of each of these experiments was to ascertain the attributes associated with high low-density lipoprotein cholesterol (LDL-c). Both of these trials were designed to be carried out on individuals who had a previous record of increased levels of low-density lipoprotein cholesterol (LDL-c). Enumerated here are the many procedures and components: A total of 199 individuals were included in a cross-sectional research, all of whom presented with both early-onset acute myocardial infarction and dyslipidemia. The aforementioned people originated from four separate familial lineages characterized by a historical prevalence of the aforementioned ailment. The research described in this study was conducted inside the Department of Cardiology-Geriatrics, with no intervention being necessary.* ***Results****: The findings indicate that 52.5% of those who had LDL-c level assessments demonstrated ideal levels, while 24.2% exhibited levels that were somewhat near to the normal range. Additionally, 3.0% of the participants displayed LDL-c levels that significantly above the normal range. Following the conclusion of the therapeutic intervention, the LDL-c concentrations of the participants exhibited a notable reduction, with an average value of 1.10±0.61mmol/L. Furthermore, a significant proportion of the participants, namely 63.8%, achieved the predetermined control objective.* ***Conclusions****: The administration of the rosuvastatin regimen has been shown to be a highly successful approach in attaining the necessary elevation of LDL-c levels, hence playing a crucial role in the management and prevention of many medical conditions among patients and their families.*

Keywords: *myocardial infarction (MI), rosuvastatin, patient family pedigrees*.

I. INTRODUCTION

Today, myocardial infarction (MI) remains one of the major causes of death and disability worldwide. In 2020, it is estimated that about every 40 seconds, an American will have an acute MI and the disease is becoming more common [1]. Causes of acute MI that appear early include lifestyle, smoking, and atherosclerosis, which are one of important causes. The main cause in about 85% of cases of familial hypercholesterolemia is a mutation in the gene encoding the low-density lipoprotein receptor, which causes elevated levels of

total cholesterol and LDL-cholesterol in the blood, causing atherosclerosis. [2], [3]. Patients with acute MI and untreated LDL-cholesterol levels ≥155mg/dL (≥4.0mmol/L) are a group of subjects likely to have familial hypercholesterolemia [4]. Therefore, screening, early diagnosis, and prompt treatment of dyslipidemia, specifically an elevated LDL-c index in the patient's family pedigree, are necessary to prevent or reduce the severity of vascular disease. rim. Therefore, we conducted the research with the following two objectives: 1). Describe the characteristics of LDL-c elevation in patients with acute myocardial infarction at Tra Vinh General Hospital 2021-2022; 2). Describe the evaluate the treatment outcomes of rosuvastatin in patients with acute myocardial infarction at Tra Vinh General Hospital 2021-2022.

II. MATERIALS AND METHODS

2.1. Research subjects: Patients with early-onset acute MI (male <55 years old, female <65 years old) with dyslipidemia have been diagnosed and are being treated at the Department of Cardiology and Geriatrics at Tra Vinh General Hospital from 2021-2022. All members of the patient's three generations.

Standards for selection and elimination:

The patient was diagnosed with an acute MI with early onset including non-ST-segment elevation MI and ST-segment elevation according to the criteria of the Ministry of Health 2019 (Appendix 1) [5]. There is a possibility of familial hypercholesterolemia when untreated LDL-c levels are ≥155 mg/dL (≥4.0 mmol/L) [4].

The patient was excluded with medical comorbidities such as severe chronic renal failure, cirrhosis, active hepatitis, secondary hyperlipidemia, and taking strong inhibitors of CYP3A4; members did not agree to participate in the study.

2.2. Research methods

2.2.1. Study design: a cross-sectional descriptive study, intervention (no control group).

2.2.2. Sample size

We apply the formula for calculating the sample size to estimate a proportion:

$$n = \frac{Z^2_{(1-\alpha/2)} \times p \times (1 - p)}{d}$$

In which: n: is the smallest sample size; Z=95%; Z1-α/2 = 1.96.

p: is the rate of LDLR mutation in the family pedigree of FH patients. According to research by Hoang Thi Yen on three genealogies, this rate is 65.3% [6].

With the above data, we calculated n=87, in fact, our study was performed on 4 genealogies of patients with early-onset acute MI with 99 subjects.

2.2.3. Study contents

General characteristics of research subjects: age, gender, ethnicity, address, occupation, body mass index, and cardiovascular risk factors.

Characteristics of LDL-c elevation in patients with acute myocardial infarction at Tra Vinh General Hospital 2021-2022: level of elevation of LDL-c: optimal: <2.59 mmol/L (<100 mg/dL); near-normal: 2.59-3.35 mmol/L (100-129 mg/dL); elevated limit: 3.36-4.14 mmol/L (130-159 mg/dL); elevated: 4.15-4.88 mmol/L (160-189 mg/dL); very high: ≥4.89 mmol/L (≥190 mg/dL).

Treatment outcomes of rosuvastatin in patients with acute myocardial infarction at Tra Vinh General Hospital 2021-2022

Patients with elevated LDL-c are treated according to the European Society of Cardiology and European Atherosclerosis 2019 protocol: control LDL-c with diet, exercise, and a rosuvastatin 10mg tablet per day with 12 weeks of treatment. Test LDL-c and AST, ALT every month. If LDL-c is on target, maintain a dose of rosuvastatin, if LDL-c is not on target, increase the rosuvastatin dose from 10 mg to 20 mg. It is called the goal after treatment when: <2.5 mmol/L (adult); <1.4 mmol/L (adults with coronary artery disease or diabetes with chronic complications); <3.5 mmol/L (>10 years old); <4 mmol/L (8-10 years old); LDL-c concentration decreased by more than 50% from baseline and there was a change in the mean value of LDL-c before and after treatment.

Characteristics of the side effects of the drug: functional symptoms: headache, muscle pain, rash, digestive disorders (abdominal pain, nausea, constipation or diarrhea, etc...); increased AST and ALT more than 4 times higher than normal values; some factors related to: age, sex, LDLR gene mutation.

2.2.4. Statistical analysis: the data were analyzed using SPSS 20.0 software.

III. RESULTS

3.1. General characteristics of research subjects

Table 1. General characteristics of research subjects

General characteristics		Frequency (n)	Rate (%)
Age	≥60	14	14.1
	50-59	9	9.1
	40-49	25	25.3
	30-39	20	20.2
	20-29	5	5.1
	<20	26	26.3
	Average: 37.30±18.46. Limit: 7-72		
Gender	Male	56	56.6
	Female	43	43.4
Address	City	19	19.2
	Countryside	80	80.8
Ethnicity	Kinh	98	99.0
	Others	1	1.0
Occupation	Manual labor	58	58.6
	Intellectual labor	2	2.0
	Student	30	30.3
	Old/retired	9	9.1

The group <20 years old accounted for the highest rate (26.3%), and the average was 37.30±18.46 years old. Males account for a higher proportion (56.6%). Most of the members live in rural areas (80.8%), Kinh members (99.0%), and 58.6% do manual labor.

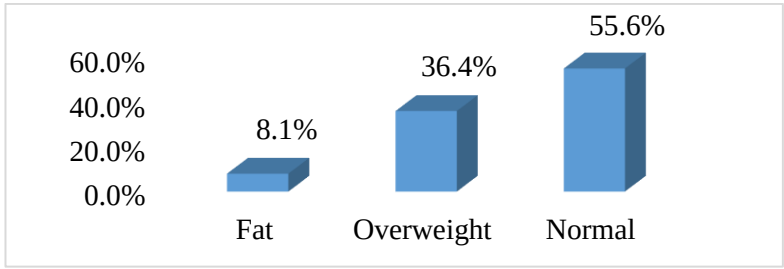

Figure 1. Classification of body mass index

Family members of AMI patients with early onset MI had the lowest obesity rate of 8.1%, 36.4% were overweight and 55.6% were not overweight.

Table 2. Other cardiovascular risk factors

Some other risk factors	Frequency (n)	Rate (%)
Smoking	11	11.1
No physical training	62	62.6
Hypertension	10	10.1
Diabetes	7	7.1
History of MI	8	8.1

The patient's family members were 62.6% physically inactive, 11.1% smoked, 10.1% had hypertension, 7.1% had diabetes, and 8.1% had a history of MI.

3.2. Characteristics of LDL-c elevation in patients with acute myocardial infarction at Tra Vinh General Hospital 2021-2022

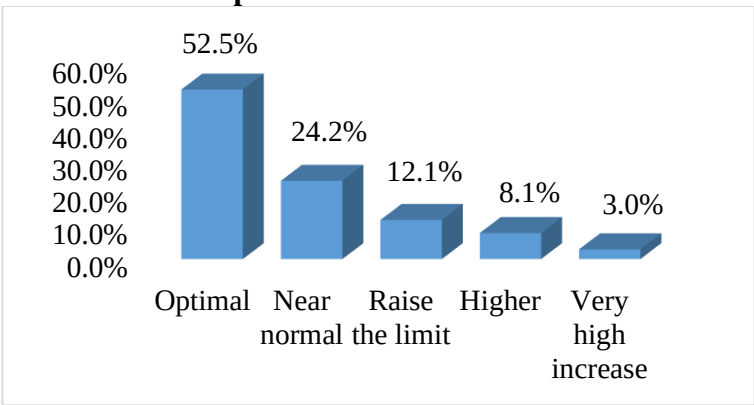

Figure 2. Levels of elevation of LDL-c

52.5% of the family pedigree of patients with early-onset acute MI had optimal levels of LDL-c, 24.2% were near normal, and very high elevations, accounted for 3.0%.

Table 3. The prevalence of LDL-c disorders by risk groups

Rate of disorder LDL-c	Frequency (n)	Rate (%)
8-10 years (LDL-c ≥3,5mmol/L)	0	0.0
11-17 years (LDL-c ≥4mmol/L)	0	0.0
Adults (LDL-c ≥2,6mmol/L)	33	33.3
High cardiovascular risk (LDL-c ≥1,8mmol/L)	10	21.7
Very high cardiovascular risk (LDL-c ≥1,4mmol/L)	4	8.5
Total	47	100

Members of the family pedigree of patients in the high cardiovascular risk group accounted for 21.7%, 8.5% in the very high cardiovascular risk group, and 33.3% in adults. No increase in LDL-c was observed in the 8-10 and 11-17-year-old age groups.

3.3. Treatment outcomes of rosuvastatin in patients with acute myocardial infarction at Tra Vinh General Hospital 2021-2022

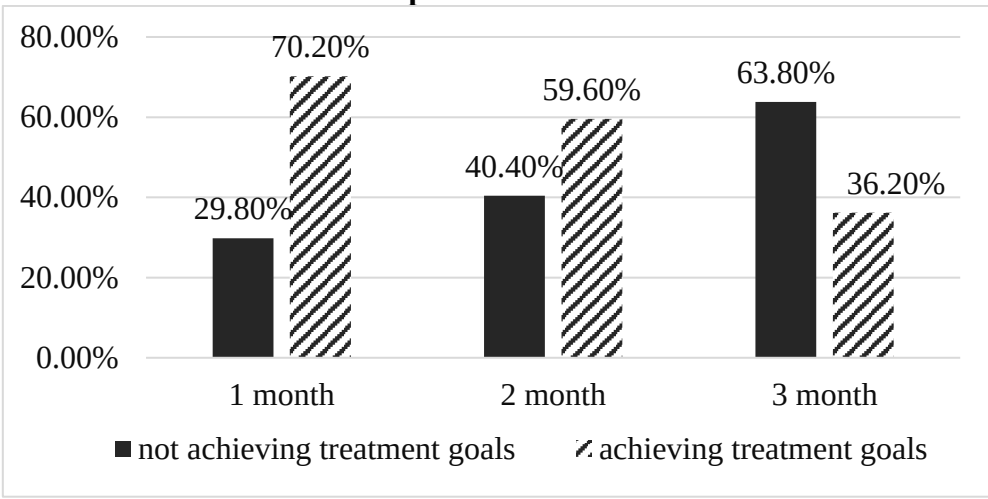

Figure 3. Rate of LDL-C reaching the target after treatment

The rate of LDL-c reaching the target after treatment increased gradually over time and after 3 months, 63.8% of the members achieved the goal of LDL-c control.

Table 4**.** Relationship between LDL-c reaching treatment goals with age group and gender

Age and Gender	LDL-c achieves goal after treatment				Total		OR (CI 95%)	p; χ^2
	Yes		No					
	(n)	(%)	(n)	(%)	(n)	(%)		
≥50 years	10	66.7	5	33.3	15	100	1,20 (0.33-4.36)	0.782; 0.077
<50 years	20	62.5	12	37.5	32	100		
Male	18	75.0	6	25.0	24	100	2,75 (0.80-9.44)	0.104; 2.651
Female	12	52.2	11	47.8	23	100		

The age group ≥50 achieved the LDL-c goal after treatment, which was lower than the age group <50. Men achieve the goal after treatment faster than women. However, these two differences were not statistically significant with p>0.05.

Table 5. Average LDL-c concentration before and after treatment

LDL-c concentration (mmol/L)	Before treatment	After treatment	p
	3.56±1.27	2.45±1.12	0.0000

The difference in LDL-c concentration before and after treatment was statistically significant with p<0.05.

Table 6. The value of LDL-c concentration changes after treatment

The value of LDL-c concentration changed after treatment (mmol/L)	Average	Smallest	Largest
	1.10±0.61	0.32	3.72

The mean value of LDL-c change after treatment is 1,08±0,61mmol/L.

Table 7. Side effects of medications

Side effects of medications	Frequency (n=47)	Rate (%)
Increase AST	2	4.3
Increase ALT	3	6.4
Muscle pain	0	0.0
Digestive disorders	0	0.0

There was a 4.3% increase in AST, a 6.4% increase in ALT, and no other side effects were noted.

IV. DISCUSSION

4.1. General characteristics of research subjects

Family pedigree members in the age group <20 years old accounted for the highest percentage and the lowest rate was in the group 20-29 years old, where the mean age was 37.30±18.46. Men account for a higher percentage than women. The results are consistent with Friedlander Y's study with women with an average age of 37.7±5.3 years [7]. Wang CL et al studied 24,361,345 subjects with an average age of 41.7±15.6 [8]. This result is lower than that of Beheshti S et al. [9], and Ekberg S et al. [10]. The difference in age and gender is due to the difference in subjects and research objectives. Most of the members of the family pedigree live in rural areas, with a proportion of 80.8%, 99.0% of Kinh ethnicity, more than 50% manual labor, and only 2.0% intellectual labor. The natural distribution of the research sample on ethnicity, residence, and occupation depends on the research location. Our research results are consistent with the geographical, economic, and social characteristics of Tra Vinh province. We recorded that members of the family pedigree of patients with early-onset acute MI had the lowest obesity rate of 8.1% and 55.6% had a normal mass index, and the smoking rate among members was 11.1%. Beheshti S et al recorded that the smoking prevalence in the family pedigree of patients with AMI with early onset was 58.0% [9]. We recorded members with a rate of hypertension of 10.1%, lower than the study of Beheshti S et al. with 60% [9]. Nielsen M et al., in a cohort study of family members of AMI patients, recorded 2.7% diabetes and 9.8% hypertension [11].

4.2. Characteristics of LDL-c elevation in patients with acute myocardial infarction at Tra Vinh General Hospital 2021-2022

We recorded an increased level of LDL-c: more than 50% of the patient's family pedigree was at the optimal level of 52.5% and very high, accounting for 3.0%, in terms of the risk group, of increased LDL-c in the group. Very high cardiovascular risk accounted for 8.5%, and the high cardiovascular risk group accounted for 21.7%. No increase in LDL-c was observed in the 8-10 and 11-17-year-old age groups. Levels and classifications of elevated LDL-c index are different in each group of subjects; in our study, we studied family pedigree members of early-onset acute MI with three levels of relatives. Therefore, members of the family pedigree of patients with high levels of LDL-c disorder account for a low percentage.

4.3. Treatment outcomes of rosuvastatin in patients with acute myocardial infarction at Tra Vinh General Hospital 2021-2022

Currently, many clinical trials have shown that LDL-c lowering treatment with statins has reduced the risk of cardiovascular disease by 25-45% [12]. After 3 months of

treatment, the rate of LDL-c reaching the goal after treatment was 63.8% of the members, the age group ≥50 reaching the goal after treatment was lower than that in the age group <50 and men had a lower rate than women. We have not found a correlation with $p<0.05$ between the rate of LDL-c achievement and age and sex groups. LDL-c concentration in the family pedigree decreased compared to before treatment and this difference was statistically significant. The value of LDL-c concentration after treatment is 1.10±0.61 mmol/L. Braamskamp MJAM et al. reported that at 24 months, LDL-c decreased by 43%, 45%, and 35% from baseline in patients 6-9 years old, 10-13 years old, and 14-17 years old, respectively (p) <0.001 for all groups) [13]. We recorded a few side effects of the drug with a 4.3% increase in SGOT, a 6.4% increase in SGAT, and no other side effects. Braamskamp MJAM et al reported intermittent myalgia in 11 (6%) patients, 9 (5%) of whom reported serious adverse events [13].

V. CONCLUSION

The magnitude of the elevation of LDL-c levels is of concern and has implications for providing treatment and prevention for patients and their families. The high proportion of family members of patients with early-onset AMI with elevated LDL-c reaching the LDL-c goal with rosuvastatin is quite high, indicating that the rosuvastatin regimen is effective.

REFERENCES

1. Viraniss, Alonso A., et al. Heart disease and stroke statistics-2020 Update: A report from the American Heart Association, Chapter 19: Coronary heart disease, acute coronary syndrome, and angina pectoris. *Circulation*. 2020. 141, 347-368.
2. Alonso R., Perez de Isla L., et al. Familial hypercholesterolaemia diagnosis and management. *Eur Cardiol*. 2018. 13(1), 14-20.
3. Mytilinaiou M., Kyrou I., et al. Familial hypercholesterolemia: new horizons for diagnosis and effective management. *Front Pharmacol*. 2018. 9(707), 1-29.
4. Mach F., Baigent C., et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk, *Atherosclerosis*. 2019. 290, 40-205.
5. Ministry of Health. Decision on promulgation of professional document: Guidelines for diagnosis and management of acute coronary syndromes. Decision No. 2187/QĐ-BYT dated June 3, 2019.
6. Hoang Thi Yen. Research on LDLR gene mutations in people with familial hypercholesterolemia. Doctor of Medicine Thesis. Hanoi Medical University. 2020.
7. Friedlander Y., Friedlander P., et al. Family history as a risk factor for early onset myocardial infarction in young women. *Atherosclerosis*. 2002. 156, 201-207.
8. Wang C.L., Kuo C.F., et al. Familial aggregation of myocardial infarction and coaggregation of myocardial infarction and autoimmune disease: a nationwide population-based cross-sectional study in Taiwan. *BMJ Open*. 2019. 9, 1-9.
9. Beheshti S., Beheshti C.M., et al. How to identify familial premature myocardial infarction: comparing approaches to identify familial hypercholesterolemia. *J Clin Endocrinol Metab*. 2019. 104(7), 2657-2667.
10. Ekberg S., Ploner A., et al. Familial effects on survival after myocardial infarction: a registry-based sib-pair study. *Eur J Epidemiol*. 2012. 27, 911-914.
11. Nielsen M., Andersson C., et al. Familial clustering of myocardial infarction in first-degree relatives: a nationwide study. *European Heart Journal*. 2013. 34, 1198-1203.

12. Expert Dyslipidemia Panel of the International Atherosclerosis Society Panel members. An International Atherosclerosis Society position paper: global recommendations for the management of dyslipidemia-full report. *J Clin Lipidol*. 2014. 8(1), 29-60.
13. Braamskamp M.J.A.M., Langslet G., et al. Efficacy and safety of rosuvastatin therapy in children and adolescents with familial hypercholesterolemia: Results from the Charon study. *J Clin Lipidol*. 2015. 9(6), 741-750.