RESEARCH PAPER

Comparative Evaluation of Statin Monotherapy, Statin Plus Ezetimibe, and Statin Plus Ezetimibe Plus Bempedoic Acid for LDL-C Reduction in Patients with Acute Coronary Syndrome: A Prospective Study

Dr. Akshay Pujari[1], Dr. Suresh Patted[2], Dr. Sanjay Porwal[3], Dr. Sameer Ambar[4], Dr. Prasad MR[5], Dr. Vijay B Metgudmath[6], Dr. Vishwanath Hesarur[7], Dr. Suhasini Atharga[8]

[1]Senior Resident and Post Graduate, Department of Cardiology, Jawaharlal Nehru Medical College and Kles Dr. Prabhakar Kore Hospital and Medical Research Center, Belagavi.
Email: rpakshay07@gmail.com
[2] Professor and Consultant Department of Cardiology, Jawaharlal Nehru Medical College and Kles Dr. Prabhakar Kore Hospital and Medical Research Center, Belagavi.
[3]Professor and Head of Department of Cardiology, Jawaharlal Nehru Medical College and Kles Dr. Prabhakar Kore Hospital and Medical Research Center, Belagavi.
[4]Professor and Consultant Department of Cardiology, Jawaharlal Nehru Medical College and Kles Dr. Prabhakar Kore Hospital and Medical Research Center, Belagavi.
[5]Associate Professor and Consultant Department of Cardiology, Jawaharlal Nehru Medical College and Kles Dr. Prabhakar Kore Hospital and Medical Research Center, Belagavi.
[6]Associate Professor and Consultant Department of Cardiology, Jawaharlal Nehru Medical College and Kles Dr. Prabhakar Kore Hospital and Medical Research Center, Belagavi.
[7]Assistant Professor and Consultant Department of Cardiology, Jawaharlal Nehru Medical College and Kles Dr. Prabhakar Kore Hospital and Medical Research Center, Belagavi.
[8]Assistant Professor and Consultant Department of Cardiology, Jawaharlal Nehru Medical College and Kles Dr. Prabhakar Kore Hospital and Medical Research Center, Belagavi.

Received: 28-6-2026; Revised: 12-7-2026; Accepted: 02-08-2026; Available Online: 05-08-2026

ABSTRACT

Background: Acute coronary syndrome (ACS) is associated with a high risk of recurrent cardiovascular events, and intensive reduction of low-density lipoprotein cholesterol (LDL-C) is a key component of secondary prevention. Although statins remain the cornerstone of lipid-lowering therapy, many patients fail to achieve recommended LDL-C targets with statin monotherapy alone. Addition of ezetimibe and bempedoic acid may provide greater LDL-C reduction through complementary mechanisms.

Aim and Objectives: To compare the efficacy of statin monotherapy, statin plus ezetimibe, and statin plus ezetimibe plus bempedoic acid in reducing LDL-C levels among patients with ACS. The study assessed percentage LDL-C reduction at 1 month and 3 months, achievement of LDL-C <55 mg/dL, and comparative efficacy of dual and triple therapy over statin monotherapy.

Methods: This single-center prospective study included 300 patients with ACS, divided equally into three groups of 100 patients each: statin monotherapy, statin plus ezetimibe, and statin plus ezetimibe plus bempedoic acid. LDL-C levels were assessed at baseline, 1 month, and 3 months. Statistical analysis was performed using SPSS version 27.0, with $p<0.05$ considered statistically significant.

Results: At 1 month, mean percentage LDL-C reduction was 43.4% with statin monotherapy, 50.1% with statin plus ezetimibe, and 69.1% with triple therapy. At 3 months, the corresponding reductions were 52.0%, 60.6%, and 75.7%, respectively. Target LDL-C <55 mg/dL at 1 month was achieved by 36.0%, 53.0%, and 72.0% of patients, respectively. At 3 months, target attainment was 64.2%, 80.7%, and 90.9%, respectively. Mean LDL-C levels differed significantly among the three groups at 1 month ($F=13.51$, $p<0.001$) and 3 months ($F=23.43$, $p<0.001$). Triple therapy demonstrated significantly lower LDL-C levels compared with the other treatment groups.

Conclusion: Progressive intensification of lipid-lowering therapy resulted in greater LDL-C reduction and higher target attainment in patients with ACS. Triple therapy with statin, ezetimibe, and bempedoic acid showed the greatest efficacy at both 1 month and 3 months, followed by dual therapy and statin monotherapy.

Keywords: Acute coronary syndrome; LDL-C; Statin; Ezetimibe; Bempedoic acid; Lipid-lowering therapy; Dyslipidemia; Secondary prevention; Combination therapy; Cardiovascular risk

How to cite this article: Pujari A, Patted S, Porwal S, Ambar S, Prasad MR, Metgudmath VB, Hesarur V, Atharga S., Comparative Evaluation of Statin Monotherapy, Statin Plus Ezetimibe, and Statin Plus Ezetimibe Plus Bempedoic Acid for LDL-C Reduction in Patients with Acute Coronary Syndrome: A Prospective Study. Int J Drug Deliv Technol. 2026;16(82s): 1417; DOI: 10.25258/ijddt.16.82s.140

INTRODUCTION

Acute coronary syndrome (ACS), encompassing ST-elevation myocardial infarction, non-ST-elevation

myocardial infarction, and unstable angina, represents one of the most important clinical manifestations of atherosclerotic cardiovascular disease (1). Despite major advances in coronary revascularization, antithrombotic therapy, and secondary prevention, patients surviving an ACS remain at substantial risk of recurrent cardiovascular events (2). Dyslipidemia, particularly elevated low-density lipoprotein cholesterol (LDL-C), is a major modifiable contributor to the development and progression of coronary atherosclerosis. Consequently, intensive LDL-C reduction has become a fundamental component of secondary prevention following ACS (3).

The relationship between LDL-C and atherosclerotic cardiovascular disease is continuous, with greater absolute reductions in LDL-C being associated with greater reductions in cardiovascular risk. Current recommendations therefore emphasize early initiation of intensive lipid-lowering therapy following ACS (4). In patients undergoing secondary prevention after ACS, the European Society of Cardiology recommends an LDL-C target of less than 55 mg/dL together with a reduction of at least 50% from baseline. Lipid levels are generally reassessed within 4–6 weeks to evaluate treatment response and determine whether additional lipid-lowering therapy is required (5).

High-intensity statins remain the cornerstone of lipid-lowering treatment because of their established ability to reduce LDL-C and subsequent cardiovascular morbidity and mortality. However, statin monotherapy may not provide sufficient LDL-C reduction to achieve recommended targets in a considerable proportion of high-risk patients (6). This has led to increasing use of combination lipid-lowering strategies. Ezetimibe inhibits intestinal cholesterol absorption through inhibition of the Niemann-Pick C1-like 1 transporter and provides additional LDL-C reduction when combined with statin therapy (7). In patients who fail to achieve LDL-C targets with maximally tolerated statin therapy, the addition of ezetimibe is recommended as an important treatment intensification strategy (8).

Bempedoic acid represents another therapeutic option for further LDL-C reduction. It is an oral inhibitor of adenosine triphosphate citrate lyase, an enzyme involved in hepatic cholesterol synthesis upstream of hydroxymethylglutaryl-coenzyme A reductase (9). By reducing hepatic cholesterol synthesis, bempedoic acid increases LDL-receptor expression and enhances circulating LDL-C clearance. Clinical studies have demonstrated LDL-C reductions of approximately 17–28% with bempedoic acid (10). The CLEAR Outcomes trial further demonstrated that bempedoic acid produced a significant reduction in LDL-C and was associated with a lower incidence of major adverse cardiovascular events in statin-intolerant patients with, or at high risk for, cardiovascular disease (11).

Although statins, ezetimibe, and bempedoic acid act through complementary mechanisms, direct comparative evidence evaluating progressive intensification from statin monotherapy to dual statin–ezetimibe therapy and triple statin–ezetimibe–bempedoic acid therapy in patients presenting with ACS remains relatively limited (10). Determining the magnitude and speed of LDL-C reduction with these strategies is clinically important because early achievement of recommended lipid targets may improve secondary prevention (12).

Therefore, the present prospective study was undertaken to compare statin monotherapy, statin plus ezetimibe, and statin plus ezetimibe plus bempedoic acid for LDL-C reduction in patients with acute coronary syndrome, with particular emphasis on percentage LDL-C reduction and attainment of an LDL-C target of <55 mg/dL at one month and three months.

AIM AND OBJECTIVES

Aim

To compare the efficacy of statin monotherapy, statin plus ezetimibe, and statin plus ezetimibe plus bempedoic acid in reducing LDL-C levels among patients with acute coronary syndrome.

Objectives

Primary Objective

- To compare the percentage reduction in LDL-C levels from baseline to 1 month and 3 months among patients receiving statin monotherapy, statin plus ezetimibe, and statin plus ezetimibe plus bempedoic acid.

Secondary Objectives

- To determine and compare the proportion of patients achieving the target LDL-C level of <55 mg/dL at 1 month and 3 months.
- To assess the comparative efficacy of dual and triple lipid-lowering therapy over statin monotherapy in achieving LDL-C targets after acute coronary syndrome.

MATERIALS AND METHODS

This single-center prospective study was conducted in the Department of Cardiology at KLES Dr. Prabhakar Kore Hospital and MRC, Belagavi, from July 1, 2024 to March 31, 2026. A total of 300 patients diagnosed with acute coronary syndrome, including ST-elevation myocardial infarction, non-ST-elevation myocardial infarction, and unstable angina, with elevated LDL-C levels and no prior lipid-lowering therapy were enrolled by consecutive sampling after obtaining written informed consent. Patients with known myositis or myopathy, previous intolerance to lipid-lowering therapy, prior use of statins or other lipid-lowering agents, severe systemic illness interfering with follow-up, or unwillingness to participate were excluded. The enrolled patients were divided equally into three groups: Group A received statin monotherapy (n=100), Group B received statin plus ezetimibe (n=100), and Group C received statin plus ezetimibe plus bempedoic acid (n=100). Treatment selection and dosage were determined according to prevailing clinical guidelines and treating physician discretion.

Baseline demographic and clinical characteristics,

cardiovascular risk factors, presenting ACS diagnosis, and laboratory parameters were recorded using a predesigned case record proforma. A complete lipid profile was obtained before initiation of therapy, along with routine investigations including fasting blood glucose, renal function tests, liver function tests, complete blood count, and cardiac biomarkers. Electrocardiography and echocardiography were performed as part of routine clinical evaluation. Patients were reassessed at 1 month and 3 months, when repeat lipid profiles were obtained. The primary outcome was percentage reduction in LDL-C from baseline at 1 month and 3 months. Secondary outcomes included the proportion of patients achieving an LDL-C target of <55 mg/dL and comparison of LDL-C reduction and target attainment among the three treatment groups.

Data were entered into Microsoft Excel and analyzed using SPSS version 27.0. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. Student's unpaired t-test and one-way analysis of variance were used for comparison of continuous variables, with Bonferroni post-hoc analysis following significant ANOVA results. Nonparametric tests were applied when data were not normally distributed. Categorical variables were analyzed using the Chi-square test, Fisher's exact test, or test of proportion, as appropriate. A p value <0.05 was considered statistically significant. The study was conducted after approval from the Institutional Ethics Committee, and confidentiality of all participant information was maintained throughout the study.

RESULTS

Table 1. Percentage Reduction in LDL-C from Baseline to 1 Month Among the Three Treatment Groups

Group	Baseline LDL-C (Mean ± SD)	One month LDL (Mean ± SD)	Mean % LDL-C Reduction (Baseline → 1 month)
Statin alone	110.9 ± 21.7	62.8 ± 21.8	43.4
Statin + Ezetimibe	113.6 ± 27.1	58.06 ± 22.2	50.1
Statin + Ezetimibe + Bempedoic acid	150.9 ± 45.8	46.6 ± 24.0	69.1

In the present study, LDL-C decreased from 110.9 ± 21.7 to 62.8 ± 21.8 mg/dL (43.4%) with statin alone, 113.6 ± 27.1 to 58.06 ± 22.2 mg/dL (50.1%) with statin + ezetimibe, and 150.9 ± 45.8 to 46.6 ± 24.0 mg/dL (69.1%) with triple therapy at 1 month.

Table 2. Percentage Reduction in LDL-C from Baseline to 3 Months Among the Three Treatment Groups

Group	Baseline LDL-C (Mean ± SD)	3 months LDL (Mean ± SD)	Mean % LDL-C Reduction (Baseline → 3 months)
Statin alone	110.9 ± 21.7	53.07 ± 16.61	52.0
Statin + Ezetimibe	113.6 ± 27.1	44.83 ± 14.19	60.6
Statin + Ezetimibe + Bempedoic acid	150.9 ± 45.8	36.60 ± 16.10	75.7

In the present study, LDL-C decreased from 110.9 ± 21.7 to 53.07 ± 16.61 mg/dL (52.0%) with statin alone, 113.6 ± 27.1 to 44.83 ± 14.19 mg/dL (60.6%) with statin + ezetimibe, and 150.9 ± 45.8 to 36.60 ± 16.10 mg/dL (75.7%) with triple therapy at 3 months.

Table 3. Achievement of Target LDL-C (<55 mg/dL) at 1 Month Among the Three Treatment Groups

Group	Patients achieving target LDL <55 mg/dL	Total patients	Percentage
Statin alone	36	100	36.0
Statin + Ezetimibe	53	100	53.0
Statin + Ezetimibe + Bempedoic acid	72	100	72.0

In the present study, target LDL-C <55 mg/dL at 1 month was achieved by 36/100 (36.0%) patients with statin alone, 53/100 (53.0%) with statin + ezetimibe, and 72/100 (72.0%) with statin + ezetimibe + bempedoic acid.

Table 4. Achievement of Target LDL-C (<55 mg/dL) at 3 Months Among the Three Treatment Groups

Group	Patients achieving target LDL <55 mg/dL	Total available follow-up	Percentage
Statin alone	52	81	64.2
Statin + Ezetimibe	67	83	80.7
Statin + Ezetimibe + Bempedoic acid	80	88	90.9

In the present study, target LDL-C <55 mg/dL at 3 months was achieved by 52/81 (64.2%) patients with statin alone, 67/83 (80.7%) with statin + ezetimibe, and 80/88 (90.9%) with statin + ezetimibe + bempedoic acid.

Table 5. Comparison of LDL-C Levels at 1 Month Among the Three Treatment Groups

Treatment Group	n	Mean LDL-C (mg/dL)	SD	F value	p value
Statin alone	100	62.78	21.8	13.51	<0.001*
Statin + Ezetimibe	100	58.06	22.2		
Statin + Ezetimibe + Bempedoic acid	100	46.6	24.0		

In the present study, mean LDL-C levels at 1 month were 62.78 ± 21.8 mg/dL (n=100) with statin alone, 58.06 ± 22.2 mg/dL (n=100) with statin + ezetimibe, and 46.6 ± 24.0 mg/dL (n=100) with triple therapy. The difference was statistically significant (F=13.51, p<0.001).

Table 6. Post-hoc Comparison of LDL-C Levels at 1 Month Among the Treatment Groups

Comparison	Mean Difference (mg/dL)	p value	Significance
Statin alone vs Statin + Ezetimibe	4.72	0.43	Not significant
Statin alone vs Triple therapy	16.22	<0.001*	Significant
Statin + Ezetimibe vs Triple therapy	11.50	0.001*	Significant

Bonferroni post-hoc test applied

In the present study, the mean differences were 4.72 mg/dL (p=0.43; not significant) between statin alone and statin + ezetimibe, 16.22 mg/dL (p<0.001; significant) between statin alone and triple therapy, and 11.50 mg/dL (p=0.001; significant) between statin + ezetimibe and triple therapy.

Table 7. Comparison of LDL-C Levels at 3 Months Among the Three Treatment Groups

Treatment Group	n	Mean LDL-C (mg/dL)	SD	F value	p value
Statin alone	81	53.07	16.61	23.43	<0.001*
Statin + Ezetimibe	83	44.83	14.19		
Statin + Ezetimibe + Bempedoic acid	88	36.60	16.10		

In the present study, mean LDL-C levels at 3 months were 53.07 ± 16.61 mg/dL (n=81) with statin alone, 44.83 ± 14.19 mg/dL (n=83) with statin + ezetimibe, and 36.60 ± 16.10 mg/dL (n=88) with triple therapy. The difference was statistically significant (F=23.43, p<0.001).

Table 8. Post-hoc Comparison of LDL-C Levels at 3 Months Among the Treatment Groups

Comparison	Mean Difference (mg/dL)	p value	Significance
Statin alone vs Statin + Ezetimibe	8.24	0.003*	Significant
Statin alone vs Triple therapy	16.47	<0.001*	Significant
Statin + Ezetimibe vs Triple therapy	8.23	0.02*	Significant

Bonferroni post-hoc test applied

In the present study, the mean differences were 8.24 mg/dL (p=0.003; significant) between statin alone and statin + ezetimibe, 16.47 mg/dL (p<0.001; significant) between statin alone and triple therapy, and 8.23 mg/dL (p=0.02; significant) between statin + ezetimibe and triple therapy.

DISCUSSION

In the present study, intensive lipid-lowering therapy produced a progressive reduction in LDL-C levels among patients with acute coronary syndrome, with the greatest reduction observed with statin plus ezetimibe plus bempedoic acid. At 1 month, LDL-C decreased by 43.4% with statin monotherapy, 50.1% with statin plus ezetimibe, and 69.1% with triple therapy. At 3 months, the corresponding reductions were 52.0%, 60.6%, and 75.7%, respectively. These findings demonstrate a stepwise improvement in LDL-C lowering with intensification of therapy. This is consistent with the principle emphasized by Mhaimeed et al. (2024) that greater and sustained LDL-C reduction is important for reducing atherosclerotic cardiovascular risk, particularly in high-risk patients (4).

Statin therapy remains the foundation of lipid-lowering treatment in patients with established cardiovascular disease. Jaam et al. (2023), in their systematic review and meta-analysis of high-intensity statins, demonstrated the substantial LDL-C-lowering efficacy of intensive statin therapy (6). In the present study, statin monotherapy reduced LDL-C from 110.9 ± 21.7 mg/dL at baseline to 62.8 ± 21.8 mg/dL at 1 month and 53.07 ± 16.61 mg/dL at 3 months, corresponding to reductions of 43.4% and 52.0% respectively.

Addition of ezetimibe resulted in greater LDL-C lowering compared with statin monotherapy. Phan et al. (2012) described ezetimibe as an effective cholesterol-lowering agent with a complementary mechanism of action to statins, while Vavlukis and Vavlukis (2018) highlighted the clinical value of adding ezetimibe when statin therapy alone is inadequate (7,8). In the present study, statin plus ezetimibe achieved LDL-C reductions of 50.1% at 1 month and 60.6% at 3 months. Target LDL-C <55 mg/dL was achieved by 53.0% of patients at 1 month and 80.7% of available patients at 3 months, compared with 36.0% and 64.2%, respectively, with statin monotherapy.

The most pronounced LDL-C reduction was observed with triple therapy incorporating bempedoic acid. At 1 month, LDL-C decreased from 150.9 ± 45.8 to 46.6 ± 24.0 mg/dL, representing a 69.1% reduction, while at 3 months it decreased to 36.60 ± 16.10 mg/dL, representing a 75.7% reduction. Similarly, Marazzi et al. (2024) evaluated the addition of bempedoic acid to statin-ezetimibe therapy in patients at high cardiovascular risk and supported treatment intensification with bempedoic acid when further LDL-C lowering was required (10). Albosta et al. (2023) also described bempedoic acid as an additional oral lipid-lowering option for cardiovascular disease prevention (9).

Target attainment further demonstrated the benefit of treatment intensification. LDL-C <55 mg/dL was achieved at 1 month by 36.0%, 53.0%, and 72.0% of patients receiving statin, dual, and triple therapy, respectively. At 3 months, the respective rates were 64.2%, 80.7%, and 90.9%. Nicholls et al. (2024) demonstrated that bempedoic acid significantly reduced LDL-C and the total burden of major cardiovascular events in high-risk patients, supporting the clinical importance of additional LDL-C lowering (11).

The intergroup comparisons further supported these findings. At 1 month, mean LDL-C differed significantly among the groups ($F=13.51$, $p<0.001$), with triple therapy significantly superior to statin monotherapy and dual therapy. At 3 months, the difference remained significant ($F=23.43$, $p<0.001$), and all pairwise comparisons were statistically significant. Overall, the present findings indicate that progressive intensification from statin monotherapy to dual and triple lipid-lowering therapy was associated with greater LDL-C reduction and higher achievement of the recommended LDL-C target, with statin plus ezetimibe plus bempedoic acid demonstrating the greatest efficacy.

CONCLUSION

The present prospective study demonstrated that intensification of lipid-lowering therapy resulted in progressively greater reductions in LDL-C levels among patients with acute coronary syndrome. Statin monotherapy was effective in lowering LDL-C, while the addition of ezetimibe produced a greater reduction and improved achievement of the target LDL-C level of <55 mg/dL. The greatest LDL-C reduction was observed with triple therapy comprising statin, ezetimibe, and bempedoic acid. At both 1 month and 3 months, triple therapy showed the highest percentage reduction in LDL-C and the highest proportion of patients achieving the recommended LDL-C target. Statistically significant differences in mean LDL-C levels were also observed among the treatment groups, particularly in favor of triple therapy. These findings suggest that early and progressive intensification of lipid-lowering treatment may be more effective than statin monotherapy alone in achieving optimal LDL-C control following acute coronary syndrome.

REFERENCES

1. Jain A, Singh A, Shah K, Grossman SA. Acute coronary syndrome. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2026.
2. Husted S. Antithrombotic therapy for long-term secondary prevention of acute coronary syndrome in high-risk patients. Ther Clin Risk Manag. 2015;11:263-77. doi:10.2147/TCRM.S75024.
3. Siegel PM, Katzmann JL, Weinmann-Menke J, Landmesser U, Schunkert H, Baldus S, et al. A practical guide to the management of dyslipidaemia. Clin Res Cardiol. 2026;115(2):185-97. doi:10.1007/s00392-025-02833-y.
4. Mhaimeed O, Burney ZA, Schott SL, Kohli P, Marvel FA, Martin SS. The importance of LDL-C lowering in atherosclerotic cardiovascular disease prevention: lower for longer is better. Am J Prev Cardiol. 2024;18:100649. doi:10.1016/j.ajpc.2024.100649.
5. Tanaka A, Oyama K, Yakushiji Y, Natsuaki M, Mizuno A, Saito Y, et al. Lipid management for secondary prevention in atherosclerotic cardiovascular disease: a scoping review and scientific report. J Atheroscler Thromb. 2026;33(3):336-64. doi:10.5551/jat.65908.

6. Jaam M, Al-Naimi HN, Haddad MM, Abushanab D, Al-Badriyeh D. Comparative efficacy and safety among high-intensity statins. Systematic review and meta-analysis. J Comp Eff Res. 2023;12(3):e220163. doi:10.57264/cer-2022-0163.
7. Phan BAP, Dayspring TD, Toth PP. Ezetimibe therapy: mechanism of action and clinical update. Vasc Health Risk Manag. 2012;8:415-27. doi:10.2147/VHRM.S33664.
8. Vavlukis M, Vavlukis A. Adding ezetimibe to statin therapy: latest evidence and clinical implications. Drugs Context. 2018;7:212534. doi:10.7573/dic.212534.
9. Albosta M, Grant JK, Michos ED. Bempedoic acid: lipid lowering for cardiovascular disease prevention. Heart Int. 2023;17(2):27-34. doi:10.17925/HI.2023.17.2.1.
10. Marazzi G, Caminiti G, Perrone MA, Campolongo G, Cacciotti L, Giamundo DM, et al. Addition of bempedoic acid to statin-ezetimibe versus statin titration in patients with high cardiovascular risk: a single-centre prospective study. J Cardiovasc Dev Dis. 2024;11(9):286. doi:10.3390/jcdd11090286.
11. Nicholls SJ, Nelson AJ, Lincoff AM, Brennan D, Ray KK, Cho L, et al. Impact of bempedoic acid on total cardiovascular events: a prespecified analysis of the CLEAR Outcomes randomized clinical trial. JAMA Cardiol. 2024;9(3):245-53. doi:10.1001/jamacardio.2023.5155.
12. Palloni MC, Farella T, Faggiano A, Vatri M, Fattirolli F, Angelino E, et al. LDL-cholesterol distance to target: a practical tool for guiding lipid-lowering treatment decisions. Atheroscler Plus. 2026;65:100574. doi:10.1016/j.athplu.2026.100574.

.