SSR Institute of International Journal of Life Sciences
ISSN (O): 2581-8740 | ISSN (P): 2581-8732
Vasu and Deepak, 2025
doi: 10.21276/SSR-IIJLS.2025.11.2.20

Original Article

open access

Prospective Study on the Impact of Carvedilol on Lipid Profiles and Oxidative Stress in Hypertensive Patients

Prathibha Vasu[1], Karuturi Deepak[2]*

[1]Assistant Professor, Dept of General Medicine, Dr.B.R. Ambedkar Medical College and Hospital, Bengaluru, India
[2]Senior Resident, Dept of General Medicine, Dr. B.R. Ambedkar Medical College and Hospital, Bengaluru, India

***Address for Correspondence:** Dr. Karuturi Deepak, Senior Resident, Dept of General Medicine, Dr. B.R. Ambedkar Medical College and Hospital, Bengaluru, India
E-mail: karuturideepak@gmail.com

Received: 06 Oct 2024/ Revised: 05 Dec 2024/ Accepted: 08 Feb 2025

ABSTRACT

Background: Arterial hypertension, a significant predisposition for cardiovascular problems, affects about one billion persons worldwide. Carvedilol, a third-generation β-blocker, has antihypertensive properties and offers metabolic benefits. This treatment, especially in hypertension and heart failure, demonstrates better results, such as enhanced vascular function, reduced inflammation, and increased antioxidant qualities, which may be ascribed to the heightened activity of HDL and PON1. This study examines the effects of the antioxidant qualities of carvedilol on individuals with mild to moderate hypertension in prospective open-label research.

Methods: The clinical study proceeded from Aug 2022 to Jul 2023, seventy hypertensive patients were examined in depth as part of a comprehensive clinical investigation at our university hospital. Several medical issues and drug abuse were among the covered exclusions. The effects of carvedilol on physiological markers in mild to moderate essential hypertension were studied by administering the drug to eligible participants after a 10-day run-in period. Serum samples were taken before and after treatment to examine parameters like PON-1, LDL, HDL, MDA, and sLOX-1.

Results: Hypertensive patients' blood pressure, lipid profiles, and oxidative markers were markedly improved with carvedilol medication. Total cholesterol and apolipoprotein B levels went up, PON1 activity went up, and ARE went down. The presence of negative associations between oxidative stress indicators and HDL enzyme activity, especially PON1, highlights the significance of HDLs in protecting against oxidative damage.

Conclusion: Carvedilol efficiently cures mild to moderate hypertension, unlike other β-blockers. It improves lipid profiles, HDL, and antioxidant activity by increasing PON-1 activity, making it a viable hypertension medication with metabolic advantages.

Key-words: Carvedilol, Arterial hypertension, High blood pressure, HDL, Primary risk factor

INTRODUCTION

Hypertension is a major risk factor for heart attacks, strokes, and kidney failure. Approximately one billion adults and 70 million people reside in the US. Hypertension is a worldwide health problem for me. Patients with known hypertension who are not receiving therapy, have never had their blood pressure (BP) measured, or do not follow lifestyle and antihypertensive drug guidelines are to blame for these poor statistics [1].

How to cite this article
Vasu P, Deepak K. Prospective Study on the Impact of Carvedilol on Lipid Profiles and Oxidative Stress in Hypertensive Patients. SSR Inst Int J Life Sci., 2025; 11(2): 7133-7138.

Access this article online
https://iijls.com/

To achieve blood pressure normalcy, the European Society for Cardiology and Hypertension recommends monotherapy for patients with baseline first-degree artery hypertension, mild to moderate global risk for cardiovascular disease, or a goal blood pressure of under 140/90 mmHg. With a goal blood pressure of less than 130/80 mmHg, moderate to extremely high global risk factors for cardiovascular disease, or baseline second-degree or worse arterial hypertension, combination therapy may be appropriate. Monotherapy fails to meet blood pressure targets or in people with significant cardiovascular risk, combined treatment is recommended [2,3].

β-blockers have been used to treat hypertension for over 40 years. Clinical research shows these medicines reduce

crossref doi: 10.21276/SSR-IIJLS.2025.11.2.20

cardiovascular mortality. The European Society for Hypertension/European Society of Cardiovascular and JNC-7 advocate using β-blockers as first- or second-line antihypertensive medicines based on these findings [4].

Recently, there has been debate and controversy over the use of β-blockers for treating uncomplicated hypertension. Meta-analyses and clinical trials indicate that β-blockers are less effective than placebo or other antihypertensive medications. Later, β-blockers were degraded. UK guidelines recommend fourth-line hypertension medicine after first-line treatments. Updated guidelines from the National Institute in Excellence in Health Care recommend against commencing hypertension treatment with β-blockers. [5,6].

Celiprolol, carvedilol, and nebivolol are examples of third-generation vasodilating β-blockers that lack some side effects frequently connected to other β-blocker drugs. Compared to other antihypertensive medications, these more recent medications lower blood pressure just as well, if not more so. Vasodilating β-blockers also have a better metabolic and tolerability profile than the more established conventional β-blockers [7,8].

Carvedilol offers antihypertensive and ancillary advantages. When compared to other antihypertensive drugs, carvedilol has been shown to lower blood pressure more effectively in hypertensive patients when used alone (25 mg/day) or with another antihypertensive drug, like a diuretic. Carvedilol also improves coronary flow reserve in hypertensives at risk of heart disease, is advised in the context of myocardial infarction, and protects the kidneys in diabetics and patients with metabolic syndrome [9,10].

In hypertensives, dyslipidemia and oxidative stress are major independent predictors of cardiovascular death. Evidence-based guidelines recommend initiating hypertension treatment in non-black individuals with an antagonist of the angiotensin-converting enzyme, a calcium channel blocker, a thiazide-type diuretic, or a receptor blocker [11]. The Joint National Committee-8 report identified no superior RCTs for Mantilol compared to the four recommended classes. Thus, it should not be the first-line treatment. Third-generation, nonselective β-/α1-blocker. Carvedilol lacks the adverse effects of traditional β-blockers. It improves heart failure patients' myocardium and inhibits remodeling. Carvedilol reduces blood pressure by reducing peripheral vascular resistance and vasodilation. Carvedilol's antioxidant, anti-inflammatory, and anti-apoptotic properties make it beneficial [12].

The extensive variety of anti-inflammatory and antioxidant activities and artery wall lipid absorption make HDL antiatherogenic. HDL naturally contains proteins and enzymes that deliver these benefits. Paraoxonase 1 (PON1) is only found in HDL. HDL's hydrophobic environment promotes PON1 activation binding and secretion. PON1, like phospholipase A2 and lactonase, removes oxidized lipid molecules from low-density lipoprotein (LDL) and HDL structures, which are anti-inflammatory and antioxidant. PON1, a biomarker for vascular diseases, showed an inverse connection with CAD risk in serum. [11,12].

MATERIALS AND METHODS

Research design- A clinical study evaluated the effects of carvedilol on mild to moderate essential hypertension. The sample size was 70 hypertensive patients, determined based on the standard deviation of paraoxonase-1 (PON-1) in prior studies. The study was conducted at our university hospital from August 2022 to July 2023. A professional cardiologist performed physical exams, blood testing, electrocardiography, and transthoracic echocardiography. Patients with diabetes, dyslipidemia, cardiovascular, cerebrovascular, hepatic, renal, thyroid, or mental disorders were excluded. Alcohol, tobacco, and other medication users were also excluded. A 10-day run-in phase included dietary modifications, particularly salt restriction, and ambulatory blood pressure (BP) monitoring. Subjects with mean systolic BP >130 mmHg and/or diastolic BP >85 mmHg were included. Patient demographics such as age, sex, weight, and BMI were recorded after informed consent. BP was measured thrice using a mercury sphygmomanometer with 5-minute intervals after a 10-minute rest. Under cardiologist supervision, 12.5 mg of carvedilol was taken twice daily. Serum samples were collected before and after two months and stored at -70°C. Triglycerides, total cholesterol, LDL, HDL, apo A-1, and apo B were analyzed using test kits and an autoanalyzer. Enzyme tests measured PON and arylesterase activity, while a colorimetric assay measured MDA. Soluble LOX-1 (sLOX-1) was assessed via ELISA. This study evaluates carvedilol's effects on physiological markers in hypertensive patients.

doi: 10.21276/SSR-IIJLS.2025.11.2.20

Inclusion criteria

- ✓ Mild to moderate essential hypertension must be diagnosed.
- ✓ There are no age or gender limits, ensuring a diverse population.
- ✓ Participants must consent to the clinical study.
- ✓ Participants should comprehend the research and agree.

Exclusion criteria

- ✓ People with diabetes are excluded from study.
- ✓ Primary dyslipidemia patients cannot participate.
- ✓ We excluded thyroid patients from the research.
- ✓ Excludes chronic conditions other than essential hypertension.

Statistical Analysis- The data, provided as mean±SD (n=40), was analyzed using a paired t-test with a significance level (α) of 0.05 (two-tailed) and a power (β) of 0.2 to compare pre-and post-carvedilol Furthermore, the significance of inter-variable correlations was determined by P-values using Pearson's correlation analysis. A significance level of $p<0.05$ was used. Data analysis was made easier with the help of IBM SPSS 22.

RESULTS

Table 1 compares factors before and after carvedilol therapy in detail. After therapy, blood pressure significantly improved, with systolic pressure lowering from 159±09 to 131±11 mmHg and diastolic pressure decreasing from 88±7 to 75±4 mmHg (both P-values=0). Carvedilol raises total cholesterol (p=0.031) and Apolipoproteins B (p=0.010). The enzyme activity indicates enhanced PON1 (p=0) and reduced ARE (p=0.005). Specifically, oxidative indicators show decreased MDA (p=0.001). Carvedilol improves blood pressure, lipid profiles, and oxidative indicators, suggesting therapeutic effectiveness.

Table 1: Comparisons of variables before and after carvedilol treatment

Variable	Before treatment	After treatment	p-value
Blood pressure (mmHg)			
Systolic	159±09	131±11	0
Diastolic	88±7	75±4	0
Lipid profiles (mg/dL)			
Total cholesterol	179.3±39.7	189.3±39.7	0.031
TG	161.8±70.6	159.7± 104.1	0.059
LDL-C	110.1±37.7	109.5±29.8	0.180
HDL-C	49.7±11.8	49.8±15.5	0.02
Apolipoproteins A-I	119.5±10.5	120.6±16.1	0.081
Apolipoproteins B	79.8±14.8	90.2±13.2	0.010
Apolipoproteins A-I/B ratio	1.50±0.4	1.39±0.2	0.159
Enzymes activity (U/L)			
PON1	111.3±29.5	130.2±29.6	0
ARE	60.4±7.9	59.3±9.8	0.005
Oxidative markers			
MDA (µM)	2.10±1.3	1.39±0.6	0.001
SLOX-1 (pg/ml)	870.6±619.8	1049.1±7880.2	0.090

LDL-C: Low-Density Lipoprotein Cholesterol; HDL-C: High-Density Lipoprotein Cholesterol; PON1: Paraoxonase 1; ARE: Antioxidant Response Element; Oxidative markers; MDA (µM): Malondialdehyde; SLOX-1 (pg/ml): Selenoprotein P

doi: 10.21276/SSR-IIJLS.2025.11.2.20

In Table 2, HDL enzyme activity is correlated with oxidative stress indicators including MDA, SLOX-1, and PON1. The negative association between MDA and PON1 (-0.261, p=0.040) suggests that PON1 activity increases when MDA levels fall. Insignificant negative connection between SLOX-1 and MDA (-0.09, p=0.29). MDA and SLOX-1 have no significant relationships with the antioxidant response element (ARE). These findings demonstrate that HDL enzymes, notably PON1, may influence oxidative stress indicators, highlighting their function in oxidative damage mitigation.

Table 2: Coefficients of correlation between high-density lipoprotein enzyme activities and markers of oxidative stress

	MDA(P)	SLOX-1(P)
PON1	-0.261* (0.040)	-0.09 (0.29)
ARE	-0.02 (0.91)	0.160 (0.159)

MDA(P): Malondialdehyde (Plasma); SLOX-1(P): Selenoprotein P (Plasma); PON1: Paraoxonase 1; ARE: Antioxidant Response Element

Fig. 1 shows a scatter plot of Pearson's correlation between serum paraoxonase 1 (PON-1) and MDA levels at 50, 100, 150, 200, and 250 U/L drug concentrations. Correlation analysis shows a significant connection ($p<0.05$). PON-1 activity increases as MDA levels fall, indicating an inverse connection. This suggests that Carvedilol affects MDA levels and PON-1 activity. Due to its antioxidant properties, the medication may reduce oxidative stress, especially in hypertension management.

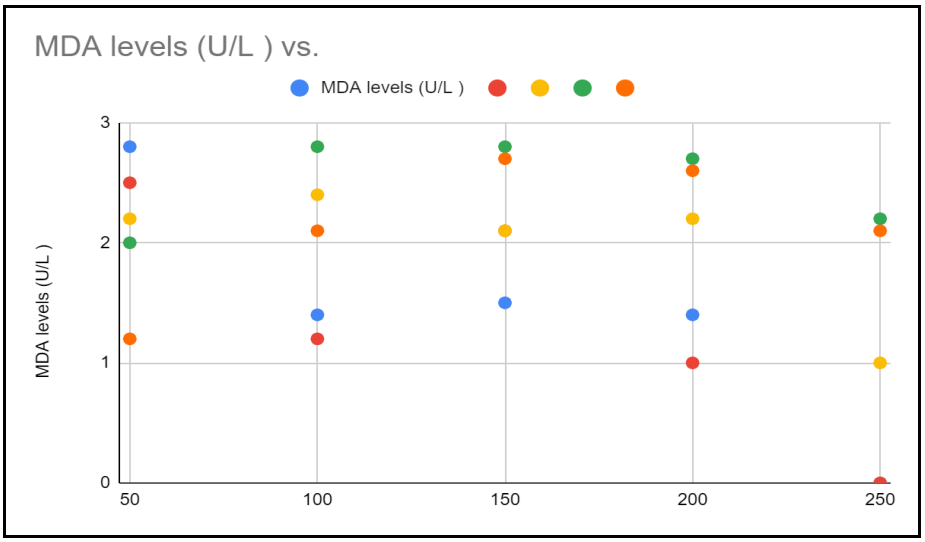

Fig. 1: Scatter plot of Pearson's correlation between values of serum paraoxonase-1

DISCUSSION

Unlike Caringilol, it is an additional generation non-select β-blocker, similar to traditional β-blockers. That has no side effects. Given that the special metabolic, anti-inflammatory, & antioxidant qualities of carvedilol are similar to those of HDL and PON1, a study aimed to explore how carvedilol treatment affects MDA and sLOX-1, a lipid profiles, apoproteins, as PON1 function in hypertensive patients as markers of oxidative stress in connection to soluble lectin-like ox-low-density ldl (LDL) receptor. The study validated the drug's ability to reduce hypertension and improve metabolism by raising HDL & PON1 activity. According to the study, carvedilol's antioxidant benefits may be partly explained by elevated PON-1 activity [13].

A novel β-blocker antihypertensive drug, carvingilol, has secondary vasodilating effects due to its α1-blocking action. Regarding the metabolism of lipids and glucose, carvingilol has no effect. When carvedilol and a diuretic are combined, the percentage of responders rises. This agent has several special qualities. It has been shown that carvingilol inhibits the growth of smooth muscle cells and neutralises oxygen-free radicals *in vitro* and *in vivo,* in addition to its antihypertensive properties.

crossref doi: 10.21276/SSR-IIJLS.2025.11.2.20

Compared to vitamin E, this molecule has far stronger antioxidant qualities. Carvedilol may be more effective than other β-blockers in improving postinfarction survival, slowing the atherogenesis process, and reducing infarct size in animal models. Carvedilol lowers morbidity and death in congestive heart failure individuals who are already on diuretics, digitalis, and angiotensin-converting enzyme inhibitors, according to recent studies [14].

Atherosclerosis and hypertension both have oxidative and inflammatory stressors as key players in their aetiology. By activating transcription factors that promote inflammation, oxidative stress also contributes to the production of inflammation. Since oxidative and inflammatory stress have a major part in the pathogenesis of atherosclerosis, understanding the processes causing oxidative stress and strategies for lowering it is essential to managing difficulties associated with atherogenesis. The ineffectiveness of chemical antioxidants, such as vitamins E and C, at scavenging reactive oxygen species (ROS) has prompted additional research into the potential ROS-suppressive effects of medications used to treat cardiovascular disease. It has been demonstrated that carvingilol use reduces oxidative stress because of its dual ROS-scavenging and ROS-suppressive qualities [15].

Individuals with decreased coronary flow reserve (CFR) suffer hypertensive left ventricular hypertrophy (LVH). It is unknown if carvedilol can help patients with hypertensive LVH with their CFR. Our goal was to find out how carvedilol affected CFR in individuals with hypertensive LVH. With six months of carvedilol medication, the CFR of individuals with hypertensive LVH but not coronary artery disease may rise [16].

Strong antioxidants like carvingilol and a few of its metabolites may contribute to the medication's cardioprotective properties in laboratory models for acute myocardial ischemia. These antioxidants may also help shield patients' hearts from oxidative stress in conditions like congestive heart failure, hypertension, and coronary artery disease. Carvedilol's antioxidant properties may prevent reactive oxygen radicals from directly inducing cell cytotoxicity and activating transcription factors and genes linked to inflammatory and remodelling processes [17].

As a result, carvedilol suppresses the expression of the gene encoding the polymorphonuclear leukocyte attachment molecule-1 (ICAM-1). This binding molecule normally invades the heart during acute ischemia and might worsen ischemia-induced damage. Low-density lipoprotein (LDL) oxidation has been inhibited by carvedilol's antioxidant action in vitro, reducing the development of this kind of LDL that is atherogenic and cytotoxic [18].

Thus, carvedilol has been demonstrated to maintain endothelial integrity and function while attenuating the accumulation of aortic lipids and reducing the number of monocytes & foam cells in the aorta in animal models of hyperlipidemia. Other beta-blockers and medications now used to treat Congestive heart failure, coronary artery disease, and hypertension do not have the same effects as carvedilol. The pharmacological rationale behind carvedilol's multiple actions could be found in its application to managing congestive heart failure and coronary artery disease. These deeds could also be partially responsible for the drug's ability to reduce mortality in congestive heart failure patients participating in clinical trials [19].

CONCLUSIONS

This study shows that the medication alone can cure mild to moderate hypertension. By raising HDL and PON-1 activity, carvingilol exhibits positive metabolic effects rather than adversely affecting lipid profiles like traditional β-blockers do. The decrease in serum MDA and rise in PON-1 activity suggest Carvedilol may be an antioxidant. This may explain the drug's antioxidant benefits by increasing PON-1 activity. These findings suggest that Carvedilol is a promising alternative to standard β-blockers for hypertension control, offering metabolic benefits. The study on carvedilol's antioxidant activities in mild to moderate hypertension individuals fills a major gap in the literature by checking physiological markers. Short-term study limits long-term effects and safety, hence more research is needed. Lack of direct comparisons with other β-blockers highlights the need for more research on carvedilol's efficacy and metabolic benefits.

CONTRIBUTION OF AUTHORS

Research concept- Prathibha Vasu
Research design- Karuturi Deepak
Supervision- Prathibha Vasu
Materials- Karuturi Deepak
Data collection- Prathibha Vasu

doi: 10.21276/SSR-IIJLS.2025.11.2.20

Data analysis and interpretation- Karuturi Deepak
Literature search- Prathibha Vasu
Writing article- Karuturi Deepak
Critical review- Prathibha Vasu
Article editing- Prathibha Vasu
Final approval- Prathibha Vasu

REFERENCES

[1] Chobanian AV, Bakris GL, Black HR, et al. The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood pressure: the JNC 7 report. JAMA, 2003; 289(19): 2560-72.

[2] Mancia G, De Backer G, Dominiczak A, et al. ESH-ESC Practice guidelines for the management of arterial hypertension: ESH-ESC Task Force on the Management of Arterial Hypertension. J Hypertens., 2007; 25(9): 1751-62.

[3] Mancia G, Laurent S, Agabiti-Rosei E, et al. Reappraisal of European guidelines on hypertension management: a European Society of Hypertension Task Force document. J Hypertens., 2009; 27(11): 2121-58.

[4] Wolf-Maier K, Cooper RS, Kramer H, et al. Hypertension treatment and control in five European countries, Canada, and the United States. Hypertension. 2004;43(1):10-17.

[5] Sarafidis PA, Bakris GL. State of hypertension management in the United States: confluence of risk factors and the prevalence of resistant hypertension. J Clin Hypertens (Greenwich)., 2008; 10(2): 130-39.

[6] Sarafidis PA, Bakris GL. Antihypertensive treatment with betablockers and the spectrum of glycaemic control. QJM.,. 2006; 99(7): 431-36.

[7] Frishman WH. A historical perspective on the development of betaa-drenergic blockers. J Clin Hypertens., 2007; 9(3): 19-27.

[8] Messerli FH, Grossman E. Beta-blockers in hypertension: is carvedilol different? Am J Cardiol., 2004; 93(1): 7-12.

[9] Briones AM, Touyz RM. Oxidative stress and hypertension: Current concepts. Curr Hypertens Rep., 2010; 12: 135-42.

[10] James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: Report from the panel members appointed to the Eighth Joint National Committee (JNC 8) JAMA, 2014; 311: 507-20.

[11] Leonetti G, Egan CG. Use of carvedilol in hypertension: An update. Vasc Health Risk Manag., 2012; 8: 307-22.

[12] Dandona P, Ghanim H, Brooks DP. Antioxidant activity of carvedilol in cardiovascular disease. J Hypertens., 2007; 25: 731-41

[13] Kontush A, Chapman MJ. Antiatherogenic function of HDL particle subpopulations: Focus on antioxidative activities. Curr Opin Lipidol., 2010; 21: 312-28.

[14] Ayashi S, Assareh AR, Jalali MT, Olapour S, Yaghooti H. Role of antioxidant property of carvedilol in mild to moderate hypertensive patients: A prospective open-label study. Indian J Pharmacol., 2016; 48(4): 372-76. doi: 10.4103/0253-7613.186206.

[15] Moser M, Frishman W. Results of therapy with carvedilol, a beta-blocker vasodilator with antioxidant properties, in hypertensive patients. Am J Hypertens., 1998; 11(1): 1-10. doi: 10.1016/s0895-7061(97)00424-x.

[16] Dandona P, Ghanim H, Brooks DP. Antioxidant activity of carvedilol in cardiovascular disease. J Hypertens., 2007; 25(4): 731-41. doi: 10.1097/HJH.0b013e3280127948.

[17] Ruffolo RR Jr, Feuerstein GZ. Pharmacology of carvedilol: rationale for use in hypertension, coronary artery disease, and congestive heart failure. Cardiovasc Drugs Ther., 1997; 1: 247-256. doi: 10.1023/a:1007735729121.

[18] Stafylas PC, Sarafidis PA. Carvedilol in hypertension treatment. Vasc Health Risk Manag., 2008; 4(1): 23-30. doi: 10.2147/vhrm.2008.04.01.23.

[19] Messerli FH, Grossman E. beta-Blockers in hypertension: is carvedilol different? Am J Cardiol., 2004; 93(9): 7B-12B. doi: 10.1016/j.amjcard.2004.01.020.