JPSIM Journal of Pakistan Society of Internal Medicine

Original Article

Atorvastatin as Adjunctive Therapy in Hepatitis C-Induced Cirrhosis: Impact on Portal Hypertension via Doppler Damping Index

Muhammad Kamran,[1] Ali Asad Khan,[2] Muhammad Arshad Khan,[3] Bilal Aziz,[4] Tazeen Nazar,[4] Nouman Hameed[5]

[1]Pak Red Crescent Medical College, DinaNath, [2]Narowal Medical College, Narowal, [3]Rahbar College of Dentistry, Lahore, [4]King Edward Medical University Lahore, [5]Mayo Hospital Lahore

Abstract

Objective: To evaluate the effectiveness of adding atorvastatin to non-selective beta-blocker (NSBB) therapy to reduce portal hypertension, as measured by the damping index, in patients with hepatitis C virus (HCV)-related liver cirrhosis over a three-month period.

Methods: This randomized controlled trial was conducted over six months, from February 21, 2022 to August 20, 2022. A total of 70 patients with HCV-related cirrhosis who met the inclusion criteria were enrolled and randomly assigned into two equal groups (n = 35). Group A received carvedilol in combination with atorvastatin 20 mg once daily at night, while Group B was treated with carvedilol alone. All participants were followed for a duration of three months. Portal hypertension was assessed non-invasively using Doppler ultrasound, with measurements focused on portal vein diameter (PVD) and hepatic vein damping index (DI) as surrogate markers of portal pressure.

Results: The mean age was 47 ± 10.46 years in Group A and 49 ± 9.91 years in Group B. Baseline PVD was 16 ± 1.72 mm in Group A and 16 ± 1.99 mm in Group B. After three months, PVD decreased to 12 ± 2.17 mm in Group A and 14 ± 1.79 mm in Group B (p = 0.000). The mean DI at baseline was 0.83 ± 0.12 in Group A and 0.85 ± 0.13 in Group B, which decreased to 0.50 ± 0.05 and 0.70 ± 0.04, respectively (p = 0.047).

Conclusion: The addition of atorvastatin to NSBB therapy significantly reduced portal hypertension—as reflected by both portal vein diameter and damping index—compared to NSBB alone in patients with HCV-induced cirrhosis.

Keywords: Atorvastatin, Cirrhosis, Portal hypertension, Damping index.

How to cite this:

Kamran M, Khan AA, Khan MA, Aziz B, Nazar T, Hameed N. Atorvastatin as Adjunctive Therapy in Hepatitis C-Induced Cirrhosis: Impact on Portal Hypertension via Doppler Damping Index. J Pak Soc Intern Med. 2026;7(1): 33-37

Corresponding Author: Dr. Ali Asad Khan, **Email:** asad.kemcolian@yahoo.com

Received: 23-10-2025 **Revised:** 12-01-2026 **Accepted:** 18-02-2026 **DOI:** https://doi.org/10.70302/jpsim.v7i1.2607

Introduction

Portal hypertension (PHT) is a major contributor to the progression of decompensated cirrhosis, resulting in life-threatening complications including ascites, variceal bleeding and hepatic encephalopathy. Each episode of variceal hemorrhage carries a mortality rate of approximately 20–30%, with risk increasing in tandem with advancing Child-Pugh class.[1] Non-selective β-blockers (NSBBs), the cornerstone of medical therapy, effectively mitigate hyperdynamic splanchnic circulation but have limited impact on intrahepatic resistance. Consequently, their efficacy diminishes in early stages of portal hypertension, before the development of significant portosystemic collateralization.[2]

Statins have emerged as promising adjuncts in the management of cirrhosis-associated PHT due to pleiotropic effects, including enhancement of sinusoidal endothelial function, increased nitric oxide (NO) bioavailability, inhibition of Rho-kinase–mediated vasoconstriction, and antifibrotic properties—achieved without inducing systemic hypotension.[3] However, recent meta-analyses of randomized controlled trials (RCTs) indicate that statins may not significantly reduce hepatic venous pressure gradient (HVPG) which is the gold-standard marker of portal pressure.[4] Notwithstanding, observational studies consistently associate statin use with reduced rates of hepatic decompensation and all-cause mortality in liver cirrhosis patients.[5]

While HVPG remains the diagnostic benchmark, its

invasive nature limits routine application, particularly in resource-constrained settings. In contrast, the Doppler-based hepatic vein damping index (DI)—with DI > 0.6 suggestive of severe PHT—provides a non-invasive surrogate that demonstrates good correlation with HVPG.

Given the high burden of hepatitis C virus (HCV)-related cirrhosis in Pakistan, estimated to affect nearly 5% of the population, and the limited availability of invasive hemodynamic assessment tools, this study aims to evaluate whether adjunctive atorvastatin therapy can reduce portal hypertension—as measured by hepatic vein DI—in patients with HCV-induced cirrhosis.

Methods

This randomized controlled trial was conducted at the East Medical Ward, Mayo Hospital, Lahore, over a six-month period from February 21, 2022, to August 20, 2022, following ethical approval. A total of 70 patients with HCV-induced liver cirrhosis were enrolled through non-convenience random sampling using the lottery method and allocated equally into two groups (n=35 each). Sample size was calculated with a 95% confidence level and 90% power, based on previously reported means of portal vein diameter (13.44 ± 2.204 mm in the statin group vs. 14.27 ± 2.209 mm in the control group).

Adult patients aged 18–70 years, diagnosed with cirrhosis clinically, radiologically, and biochemically, and having evidence of portal hypertension (e.g., ascites, splenomegaly, varices) were included. Only Child-Pugh class A or B patients on the maximum tolerable dose of carvedilol (6.25–25 mg/day, defined by HR ≥55 bpm and systolic BP ≥90 mmHg) were eligible. Exclusion criteria included pregnancy or lactation, ischemic heart disease, recent variceal band ligation, hepatocellular carcinoma, hepatic encephalopathy grade 2–4, renal impairment (serum creatinine >1.5 mg/dL), contraindications to statins (including hypersensitivity and elevated transaminases), vascular thrombosis, pre- or post-hepatic causes of portal hypertension, history of surgical shunts or TIPS, and insulin-dependent diabetes mellitus.

After obtaining informed consent, patients were randomized into Group A (intervention: atorvastatin 20 mg at night plus carvedilol) or Group B (control: carvedilol only). Baseline investigations included complete blood count, renal and liver function tests, INR, prothrombin time, abdominal Doppler ultrasound, and upper GI endoscopy; these were repeated at 3 months. Liver function was monitored monthly in the statin group, and any deterioration led to exclusion. The primary endpoints were reduction in portal hypertension as measured by hepatic vein Doppler damping index (DI), portal vein diameter, and hepatic venous waveform pattern, with DI <0.6 considered significant. Secondary endpoints included clinical improvements such as change in variceal grade, absence of new variceal bleeding, resolution or improvement of ascites, and incidence of spontaneous bacterial peritonitis.

All data were analyzed using SPSS version 24. Quantitative variables (e.g., DI, portal vein diameter) were expressed as mean ± SD and compared using the independent samples t-test. Qualitative variables (e.g., gender, waveform type) were presented as frequencies and percentages, with a p-value ≤0.05 considered statistically significant.

Results

A total of 70 patients were enrolled and randomized equally into two groups (35 patients each). The mean age of participants in Group A (atorvastatin + carvedilol) was 47 ± 10.46 years, while in Group B (carvedilol alone) it was 49 ± 9.91 years. The overall gender distribution included 40 males (57%) and 30 females (43%).

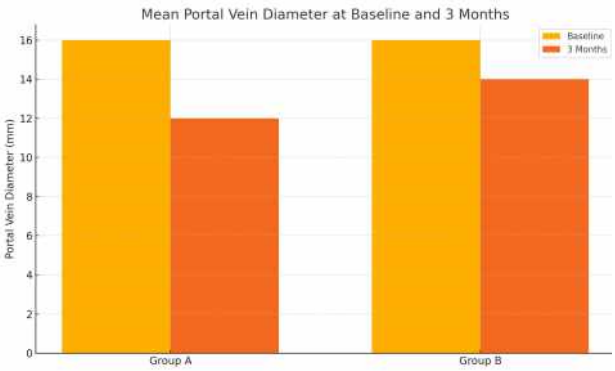

Figure I. *Portal Vein Diameter (PVD) at Baseline and 3 Months*

Figure I shows the mean portal vein diameter at baseline and at 3 months in both groups. At baseline, the mean portal vein diameter (PVD) was similar in both groups: 16 ± 1.72 mm in Group A and 16 ± 1.99 mm in Group B. After 3 months, the mean PVD significantly reduced in Group A to 12 ± 2.17 mm, compared to 14 ± 1.79 mm in Group B. This difference was statistically significant (t = –3.897, p = 0.001) (Table 1). The baseline mean damping index (DI) of the hepatic vein waveform was 0.83 ± 0.12 in Group A and 0.86 ± 0.13 in Group B. At 3 months, DI decreased significantly in Group A to 0.50 ± 0.05, compared to 0.70 ± 0.04 in Group B (t = –2.023, p = 0.047) (Tables 2 & 3). The hepatic venous waveform pattern at baseline was predominantly monophasic in both groups: 60% in Group A and 57.1% in Group B. After 3 months, waveform improved to triphasic in 65.8% of patients in Group A versus 48.6% in Group B (Figure II); however, the difference was not statistically significant (p = 0.294) .

Table 1: *Independent t-Test: Mean Portal Vein Diameter at 3 Months*

Group	Mean± SD (mm)	t-value	p-value
A	12 ± 2.17	-3.897	0.001
B	14 ± 1.79		

Table 2: *Damping Index (DI) at Baseline and 3 Months*

Time Point	Group	N	DI ± SD
Baseline	A	35	0.83 ± 0.12
	B	35	0.86 ± 0.13
3 Months	A	35	0.50 ± 0.05
	B	35	0.70 ± 0.04

Table 3: *Independent t-Test: Damping Index at 3 Months*

Group	DI ± SD	t-value	p-value
A	0.50 ± 0.05	-2.023	0.047
B	0.70 ± 0.04		

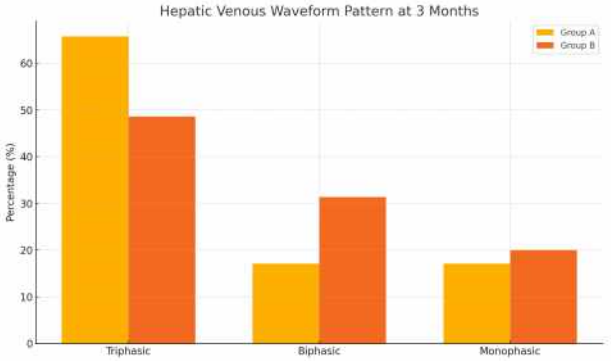

Figure II. *Hepatic Venous Waveform Pattern at 3 Months*

Table 4: *Clinical Outcomes at 3 Months (N = 35 in each group)*

Outcome	Group		p-value
	A n (%)	B n (%)	
Improvement in variceal grade	22 (62.9)	16 (45.7)	0.150
New variceal bleed	4 (11.4)	7 (20)	0.324
Resolving ascites	25 (71.4)	24 (68.6)	0.794
Worsening ascites	10 (28.6)	11 (31.4)	
SBP occurrence	3 (8.6)	5 (14.3)	0.452

Improvement in variceal grade was observed in 62.9% of patients in Group A and 45.7% in Group B, a difference that did not reach statistical significance (p = 0.150). New variceal bleeding episodes occurred in 11.4% of Group A and 20% of Group B (p = 0.324). Ascites resolved in 71.4% of patients in Group A and in 68.6% in Group B. Worsening ascites occurred in 28.6% and 31.4%, respectively, with no significant difference (p = 0.794). Spontaneous bacterial peritonitis (SBP) occurred in 3 patients (8.6%) in Group A and 5 patients (14.3%) in Group B (p = 0.452) (Table 4).

Discussion

This randomized controlled trial demonstrated that adjunctive atorvastatin significantly improved portal hemodynamics in patients with HCV-related cirrhosis. Specifically, the atorvastatin group exhibited a greater reduction in mean portal vein diameter (PVD) and hepatic vein damping index (DI), compared to carvedilol monotherapy. However, these hemodynamic improvements did not translate into statistically significant differences in clinical outcomes, such as variceal grade regression, variceal bleeding, ascites, or spontaneous bacterial peritonitis during the 3-month follow-up.

Non-selective β-blockers (NSBBs), such as carvedilol and propranolol, remain the cornerstone of portal hypertension (PHT) management. However, less than 50% of patients achieve a meaningful hemodynamic response, and approximately 30% are either intolerant or have contraindications to their use.[6,7] Therefore, interest has grown in therapies that target intrahepatic resistance without adversely affecting systemic circulation. Statins, particularly HMG-CoA reductase inhibitors such as simvastatin and atorvastatin, have shown promise due to pleiotropic actions including upregulation of endothelial nitric oxide synthase (eNOS), improved sinusoidal endothelial function, Rho-kinase inhibition, and antifibrotic effects.[8,9]

In our study, a statistically significant improvement in hepatic vein DI (to <0.6) and reduction in PVD support the hypothesis that statins ameliorate intrahepatic vascular tone and portal flow. These findings are consistent with prior trials demonstrating that statins improve hepatic vascular resistance. For example, the addition of simvastatin to NSBB therapy resulted in a significantly greater hepatic venous pressure gradient (HVPG) reduction than NSBBs alone in patients with cirrhosis (mean reduction: 4.81 ± 2.82 vs. 2.58 ± 1.88 mmHg; p = 0.041).[10,11] Hussein et al. similarly reported superior HVPG reduction when atorvastatin was combined with propranolol[12]. Abraldes et al. also confirmed enhanced hepatic perfusion and synthetic function with simvastatin, without significant systemic hypotension.[13]

Unlike these studies, which used the invasive HVPG technique, our trial utilized Doppler ultrasound-derived DI and PVD as non-invasive surrogates for portal

pressure. While HVPG remains the gold standard, emerging data support the validity of DI, particularly in resource-limited settings where HVPG measurement is not feasible[14,15]. The significant PVD reduction after 3 months of atorvastatin therapy contrasts with earlier studies—such as Elwan et al.—that found no measurable PVD change after 1 month, suggesting that vascular remodeling may require longer durations to become apparent.[16]

Despite favorable hemodynamic effects, clinical outcomes remained statistically indistinguishable between the groups. This observation is in line with prior research indicating that reductions in portal pressure precede measurable changes in clinical decompensation events.[17,18] Moreover, a recent meta-analysis confirmed moderate HVPG reductions with statin therapy, with pooled relative risks of 2.20 for simvastatin and 1.82 for atorvastatin, but highlighted variability in translating these effects to clinical endpoints.[19]

Our study adds to the evidence supporting the use of statins in cirrhosis. Retrospective cohort studies have reported associations between statin use and reduced risks of hepatic decompensation, hepatocellular carcinoma, and liver-related mortality.[20,21] Furthermore, long-term statin use has been shown to reduce portal pressure, lower systemic inflammation, and improve transplant-free survival in compensated cirrhosis.[22,23]

Nevertheless, there are some limitations that must be acknowledged. First, the study had a relatively small sample size and this was conducted at a single center, limiting the external validity of the findings. Second, the study population was restricted to patients with HCV-induced cirrhosis, and results may not be generalizable to other etiologies such as NASH or alcoholic liver disease. Third, although non-invasive measures like DI and PVD correlate with portal hypertension, they lack the precision of HVPG and may be operator-dependent. However, in low-resource settings, these surrogates remain clinically valuable, especially when validated through robust methodology.[14,15,23]

Conclusion

Atorvastatin as an adjunct to carvedilol significantly improved portal hemodynamics as assessed by damping index and portal vein diameter. While short-term clinical outcomes were unaffected, these findings support the use of statins as promising agents in the management of portal hypertension. Further large-scale, multicenter trials with longer follow-up and diverse patient populations are warranted to validate these results and assess long-term clinical benefits.

Ethical Approval: The IRB/EC approved this study via letter no. 5233/REG/KEMU/22 dated February 04, 2022.

Conflict of Interest: None

Funding Source: None

Authors' Contribution

AAK: Conception.

MK, MAK: Design of the work.

BA, TN, NH: Data acquisition, analysis, or interpretation.

MAK, BA, TN, NH: Draft the work.

MK, AAK: Review critically for important intellectual content.

All authors approve the version to be published.

All authors agree to be accountable for all aspects of the work.

References

1. Tantai X, Wang Y, Dong Q. Risk factors and outcomes of variceal bleeding in cirrhosis: A multicenter prospective study. J Hepatol. 2021;75(2):299–307.
2. Bosch J, Abraldes JG, Berzigotti A, García-Pagán JC. The clinical use of HVPG measurements in chronic liver disease. Nat Rev Gastroenterol Hepatol. 2009; 6(10): 573-82.
3. Wan S, Huang C, Zhu X. Systematic review with a meta-analysis: clinical effects of statins on the reduction of portal hypertension and variceal haemorrhage in cirrhotic patients. BMJ open. 2019;9(7):e030038.
4. Kim RG, Loomba R, Prokop LJ, Singh S. Statins and portal hypertension: A systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2020; 18(8): 1741 – 52.
5. Krawczyk M, Bonfrate L, Portincasa P. Statins in liver disease: Evidence and challenges. J Clin Med. 2022; 11(1):182.
6. Villanueva C, Albillos A, Genescà J, Garcia-Pagán JC, Calleja JL, Aracil C, et al. β-blocker failure in patients with advanced cirrhosis: A multicenter prospective study. Hepatology. 2022;75(4):1051–63.
7. Suk KT. Hepatic venous pressure gradient: clinical use in chronic liver disease. Clinical and molecular hepatology. 2014;20(1):6-14.
8. Trebicka J. Statins and cirrhosis: More than lipid lowering. Hepatol Int. 2020;14(3):474–85.
9. Krawczyk M, Bonfrate L, Portincasa P. Statins in liver disease: Evidence and challenges. J Clin Med. 2022; 11(1):182-90.
10. Pelusi S, Tovoli F, Casadei-Gardini A, Ravaioli F, Conti F. Pleiotropic effects of statins in liver disease. Eur J Intern Med. 2021;84:30–36.

11. Tripathi DM, Vilaseca M, Lafoz E, Garcia-Caldero H, Haute GV, Fernandez-Iglesias A, et al. Simvastatin prevents progression of acute on chronic liver failure in rats with cirrhosis and portal hypertension. Gastroenterol. 2018;155(5):1564-77..
12. Bishnu S, Ahammed SM, Sarkar A, Hembram J, Chatterjee S, Das K, et al. Effects of atorvastatin on portal hemodynamics and clinical outcomes in patients with cirrhosis with portal hypertension: a proof-of-concept study. Eu J Gastroenterol Hepatol. 2018;30(1):54-9..
13. Shanti I, Samardali M, Abdeen AM, Joshi T, Ikram H, Frandah W, et al. S2819 A Meta-Analysis About the Efficacy of Statins on Hepatic Venous Pressure Gradient (HVPG) in Cirrhosis Disease. J Am Coll Gastroenterol. 2025;120(10S2):S605.
14. Tarantino G, Citro V, Conca P. Doppler ultrasonographic assessment of portal hypertension: Non-invasive surrogate of HVPG? Ultrasound Med Biol. 2021;47(4): 1097 – 106.
15. Mandorfer M, Hernández-Gea V, García-Pagán JC, Reiberger T. Noninvasive diagnostics for portal hypertension: a comprehensive review. Thieme Medical Publishers. InSeminars Liver Disease. 2020; 40(03); 240-55).
16. Elwan NM, Said MA, Shabana SS. Effect of simvastatin on portal hemodynamics in cirrhosis. Arab J Gastroenterol. 2020;21(2):74–78.
17. Nader ND, Mosquera D, Burgos LG. Delayed clinical benefits of hemodynamic response to statins in cirrhosis: A longitudinal study. Liver Int. 2021;41(9):2073-82.
18. Bai M, Qi XS, Yang ZP, Yang M, Fan DM, Han GH. Statins for portal hypertension: A meta-analysis of randomized controlled trials. Eur J Gastroenterol Hepatol. 2022;34(2):170–76.
19. Simon TG, Duberg AS, Aleman S. Statin use and risk of cirrhosis and hepatocellular carcinoma in chronic hepatitis B or C: A nationwide study. Lancet Gastroenterol Hepatol. 2020;5(10):892–900.
20. Kamal S, Khan MA, Seth A. Role of statins in reducing hepatocellular carcinoma risk in chronic liver disease: A meta-analysis. J Gastroenterol Hepatol. 2020; 35(8): 1330–38.
21. Pose E, Trebicka J, Mookerjee RP. Statins: Old drugs as new therapy for liver diseases? J Hepatol. 2021; 74(3): 734-48.
22. Di Pascoli M, Berzigotti A, Caraceni P. Statins in liver cirrhosis: Ready for prime time? JHEP Rep. 2021; 3(6): 1003-15.
23. Watanabe A, Wakabayashi H, Uchiyama T. Accuracy of Doppler ultrasound in estimating portal hypertension severity. Clin Imaging. 2023;94:44-49.