Biological and Clinical Sciences Research Journal
eISSN: 2708-2261; pISSN: 2958-4728
www.bcsrj.com
DOI: https://doi.org/10.54112/bcsrj.v6i6.2075
*Biol. Clin. Sci. Res. J., Volume 6(6), **2025**: 2075*
Original Research Article

Effect of Carvedilol on Thrombocytopenia in Patients with Hepatitis C-Related Cirrhosis

Samiullah Douna[*1], Yasir Abbas Zaidi[1], Qasim Umar[1], Sohail Safdar[2]

[1]Department of Gastroenterology, Nishtar Hospital, Multan, Pakistan
[2]Nishtar Medical University, Multan, Pakistan
**Corresponding author`s email address:* samiullah.med14@gmail.com

(Received, 4th June 2025, Accepted 28th June 2025, Published 30th June 2025)

Abstract: *Thrombocytopenia is a frequent complication in hepatitis C virus (HCV)–related cirrhosis, contributing to heightened bleeding risk and complicating management. Carvedilol, a non-selective β-blocker with additional α_1-adrenergic blocking properties, may alleviate portal hypertension and thereby improve platelet counts.* ***Objective:*** *To evaluate the effect of carvedilol on thrombocytopenia in patients with HCV-related cirrhosis.* ***Methods:*** *This prospective cohort study was conducted in the Department of Gastroenterology at Nishtar Hospital, Multan, Pakistan, from December 2024 to May 2025. Adults aged 20–60 years with PCR-confirmed HCV infection and clinically diagnosed cirrhosis were consecutively enrolled after informed consent. Standard exclusion criteria were applied. Carvedilol was titrated to achieve a 25% reduction from baseline heart rate. Platelet counts and vital signs were recorded at baseline and two weeks after completing the target heart rate, following standardised procedures. The primary outcome was a >15% increase in platelet count from baseline to two weeks (Yes/No). Secondary outcomes included absolute and relative changes in platelet count, and changes in heart rate and blood pressure. Data were analysed using paired t-tests and subgroup comparisons.* ***Results:*** *A total of 176 patients were enrolled (mean age 48.4 ± 9.1 years; 58.0% male). Carvedilol titration achieved the target physiological effects (mean heart rate reduction of −21 bpm; systolic BP reduction of −6 mmHg; diastolic BP reduction of −2 mmHg). Platelet counts increased from 98.2 ± 22.4 to 121.0 ± 26.3 ×10³/mm³ (mean change +22.8 ×10³/mm³; p<0.001). The primary endpoint was met in 68.8% (95% CI 62.0–75.6). No significant effect modification was observed across subgroups defined by age, sex, obesity, Child–Pugh class, variceal grade, diabetes, residence, or disease duration.* ***Conclusion:*** *In patients with HCV-related cirrhosis, carvedilol titrated to a 25% heart-rate reduction was associated with a clinically significant improvement in platelet counts within two weeks in approximately two-thirds of patients, without major hypotensive events. The effect was consistent across major clinical subgroups, supporting its potential role in the management of portal hypertension–associated thrombocytopenia.*

Keywords: Carvedilol, Cirrhosis, Hepatitis C, Platelet Count, Portal Hypertension, Thrombocytopenia

[***How to Cite:*** Douna S, Zaidi YA, Umar Q, Safdar S. Effect of carvedilol on thrombocytopenia in patients with hepatitis C-related cirrhosis. *Biol. Clin. Sci. Res. J.*, **2025;** 6(6): 594-598. doi: https://doi.org/10.54112/bcsrj.v6i6.2075

Introduction

Liver cirrhosis, a progressive hepatic disease characterized by the replacement of standard liver architecture with scar tissue, is a prevalent consequence of chronic hepatitis C virus (HCV) infection. Globally, HCV is responsible for approximately 71 million chronic infections, leading to a significant burden of liver disease, notably cirrhosis, which presents a serious risk of complications such as hepatocellular carcinoma and liver failure (1, 2). In Pakistan, the prevalence of hepatitis C has escalated to alarming levels, affecting around 4.8% of the population, contributing significantly to the national healthcare crisis associated with chronic liver diseases (3, 2).

Cirrhosis results in multifaceted complications, including portal hypertension, variceal bleeding, and, notably, thrombocytopenia, defined as a reduction in platelet count. Thrombocytopenia in cirrhotic patients often stems from hypersplenism, decreased thrombopoietin production, and bone marrow suppression (4). This poses a challenging scenario, especially as thrombocytopenia complicates surgical interventions and increases the risk of bleeding [5]. Furthermore, patients who experience advanced liver disease are often at high risk of requiring therapeutic interventions, which can be exacerbated by low platelet counts (5).

Carvedilol, a non-selective beta-blocker with additional alpha-1 adrenergic blocking activity, has garnered attention for its potential benefits in managing portal hypertension and improving platelet counts through mechanisms such as decreasing portal hypertension and enhancing splenic blood flow (6,7). Recent studies have indicated that carvedilol may increase platelet counts and overall hepatic health in patients with HCV-induced cirrhosis, possibly by modulating systemic hemodynamics and the splenic microenvironment (8, 9). Specifically, carvedilol's role in reducing portal hypertension may counteract the underlying mechanisms responsible for thrombocytopenia (6,10).

The primary objective of this study is to evaluate the therapeutic effect of carvedilol on thrombocytopenia in patients with hepatitis C-related cirrhosis. This inquiry is particularly significant in the context of Pakistan, where hepatitis C is endemic, and cirrhosis consequently represents a significant healthcare challenge. Addressing thrombocytopenia may not only improve quality of life for these patients but also potentially optimise treatment pathways, thereby reducing the healthcare burdens associated with complications arising from thrombocytopenia and liver cirrhosis (6). Thus, given the dual burden of significant HCV prevalence and its resultant complications, such as thrombocytopenia in cirrhotic patients within Pakistan, there is a pressing need to explore novel therapeutic approaches. Carvedilol's potential to enhance platelet counts in this underserved population warrants rigorous investigation in our study.

Methodology

This was a prospective cohort study conducted in the Department of Gastroenterology at Nishtar Hospital, Multan, Pakistan, over three months following ethical approval. Participants were recruited consecutively from inpatient and outpatient services after written informed consent. Eligible patients were 20–60 years of age, of either sex, with Hepatitis C-related cirrhosis as defined in the synopsis (polymerase–chain–reaction–confirmed HCV infection and a diagnosis of cirrhosis by a senior consultant with more than ten years of experience). A minimum disease duration of six months was required. Patients were excluded for a

history of autoimmune disorders (including multiple sclerosis on MRI), chronic lung disease (COPD or interstitial lung disease), cardiac conditions such as valvular or congenital heart disease, co-infection with hepatitis B, pregnancy, pulmonary embolism, or connective-tissue disease. These criteria reflect the operational definitions and exclusions prespecified in the protocol.

After enrollment, baseline demographics and clinical variables were recorded on a structured pro forma, including age, sex, residential status (urban/rural), body mass index, classification of obesity, diabetes mellitus, Child–Pugh class, grade of oesophageal varices, and disease duration. Vital signs (blood pressure and pulse) were measured with a calibrated automated sphygmomanometer after five minutes of seated rest, taking the average of two readings. A venous sample was collected into an EDTA tube and analysed in the hospital's central laboratory for platelet count, which, per the synopsis, defined thrombocytopenia as <150,000/mm³. Carvedilol dosing was then titrated to achieve a 25% reduction in the individual's baseline heart rate. Two weeks following attainment of the heart-rate target, a repeat EDTA sample was analysed for platelet count in the same laboratory to limit inter-assay variability; blood pressure and pulse were re-measured using the same technique. All measurements were performed according to standard operating procedures, and the study investigators recorded the data.

The primary endpoint was efficacy, defined a priori as a >15% increase in platelet count from baseline to two weeks (Yes/No). Secondary within-patient endpoints included absolute and relative changes in platelet count, changes in heart rate and blood pressure from baseline to two weeks, and documentation of protocol adherence and physiologic response to carvedilol titration. The sample size of 176 was derived from the standard single-proportion formula using an expected efficacy of 66%, a precision (d) of 7%, and a two-sided 95% confidence level. Data were entered and analysed in SPSS v20. Categorical variables were summarised as counts and percentages; continuous variables as mean ± standard deviation or median with interquartile range where appropriate. For the primary analysis, we calculated the overall proportion that met the efficacy criterion, with 95% confidence intervals. We explored post-stratification across prespecified effect modifiers (age, sex, obesity, diabetes, Child–Pugh class, variceal grade, residence, and disease duration) using the chi-square test, with p-values ≤ 0.05 considered statistically significant. Paired t-tests assessed mean changes in heart rate, blood pressure, and platelet count; if normality was violated on inspection, non-parametric alternatives (Wilcoxon signed-rank) were planned. The analysis set included all enrolled patients with both baseline and two-week platelet counts available; quality assurance included calibrated devices, duplicate data checks, and adherence to the predefined measurement and recording procedures.

Results

A total of 176 adults with Hepatitis C-related cirrhosis meeting eligibility criteria were enrolled over six months at a tertiary public hospital in Multan. Mean age was 48.4 ± 9.1 years (range 20–60), 58.0% were male, and the median disease duration was 36 months (IQR 18–60). Most participants had compensated to moderately decompensated disease by Child–Pugh class, and oesophageal varices were standard. Carvedilol was titrated to achieve a 25% reduction in heart rate from baseline per protocol, with paired measurements of vital signs and platelets at baseline and two weeks post-titration. Platelet counts increased significantly from baseline; the prespecified efficacy criterion (>15% rise from baseline) was achieved in approximately two-thirds of patients, with consistent effects across key strata. (Table 1).

Most patients had compensated-to-moderately decompensated HCV cirrhosis (Child–Pugh A/B ≈ 88%) with common varices (grades I–II predominated) and notable metabolic comorbidity (obesity ~28%, diabetes ~24%), reflecting a typical tertiary-care Pakistani cohort. (Table 2)

The carvedilol protocol achieved the target ~25% reduction in heart rate (−21 bpm, p<0.001) with only modest blood pressure changes (SBP −6 mmHg, p=0.002; DBP −2 mmHg, p=0.084), indicating effective portal-flow surrogacy without clinically meaningful hypotension. (Table 3)

Platelets rose significantly from 98×10³/mm³ to 121×10³/mm³ (mean change +22.8×10³/mm³; p<0.001) within two weeks of titration, demonstrating a clear within-patient efficacy signal. (Table 4)

Overall response was high at ~69% (121/176), with no statistically significant effect modification by age, sex, obesity, Child–Pugh class, variceal grade, diabetes, residence, or disease duration; numerically higher response was observed in Child–Pugh A (Table 5).

The overall response rate was high (≈69%), with no statistically significant effect modification by age, sex, obesity, Child–Pugh class, variceal grade, diabetes, residence, or disease duration; numerically higher response rates were observed in Child–Pugh A.

In this study, adults with HCV-related cirrhosis, who were titrated to a 25% heart-rate reduction, experienced a clinically meaningful rise in platelet count in roughly two-thirds of patients within two weeks, with consistent effects across common clinical subgroups.

Table 1. Demographic characteristics (n = 176)

Measure	n	% / summary
Age, years (mean ± SD)	—	48.4 ± 9.1
Age group, n (%)		
• 20–29	12	6.8
• 30–39	28	15.9
• 40–49	56	31.8
• 50–60	80	45.5
Sex, n (%)		
• Male	102	58.0
• Female	74	42.0
Residence, n (%)		
• Urban	106	60.2
• Rural	70	39.8

Table 2. Disease profile and comorbidities at baseline

Measure	n	% / summary
Disease duration, months — median (IQR)	—	36 (18–60)
Child–Pugh class, n (%)		
• A	81	46.0
• B	74	42.0

• C	21	11.9
Oesophageal varices grade, n (%)		
• I	60	34.1
• II	69	39.2
• III	33	18.8
• IV	14	8.0
Obesity (BMI ≥30 kg/m²), n (%)	49	27.8
Diabetes mellitus, n (%)	42	23.9

Table 3. Hemodynamics and carvedilol titration target

Variable	Baseline	2 weeks	Mean change	p-value (paired t-test)
Heart rate, bpm	82 ± 9	61 ± 7	−21	<0.001
Systolic BP, mmHg	118 ± 13	112 ± 12	−6	0.002
Diastolic BP, mmHg	72 ± 9	70 ± 8	−2	0.084

Table 4. Platelet counts (primary efficacy readout)

Platelets (×10³/mm³)	Baseline	2 weeks	Mean change (95% CI)	p-value (paired t-test)
Mean ± SD	98.2 ± 22.4	121.0 ± 26.3	+22.8 (+19.7 to +25.9)	<0.001
Median (IQR)	97 (82–113)	120 (102–139)	—	—

Table 5. Proportion meeting efficacy criterion (>15% rise from baseline)

Cohort / Stratum	Responders n/N (%)	p-value (χ^2)
Overall	121/176 (68.8)	—
Sex		0.34
• Male	73/102 (71.6)	
• Female	48/74 (64.9)	
Age group		0.75
• 20–39	29/40 (72.5)	
• 40–49	39/56 (69.6)	
• 50–60	53/80 (66.3)	
Obesity		0.17
• BMI ≥30	30/49 (61.2)	
• BMI <30	91/127 (71.7)	
Child–Pugh		0.12
• A	61/81 (75.3)	
• B	48/74 (64.9)	
• C	12/21 (57.1)	
Varices grade		0.67
• I / II / III / IV	43/60 (71.7) / 45/69 (65.2) / 22/33 (66.7) / 11/14 (78.6)	
Diabetes		0.48
• Yes	27/42 (64.3)	
• No	94/134 (70.1)	
Residence		0.68
• Urban	74/106 (69.8)	
• Rural	47/70 (67.1)	
Disease duration		0.78
• 6–24 / 25–60 / >60 mo	42/58 (72.4) / 43/64 (67.2) / 36/54 (66.7)	

Discussion

This study highlights the effects of carvedilol on thrombocytopenia among adults with hepatitis C-related cirrhosis, providing essential insights into its role within this patient population. A total of 176 participants were evaluated, with a mean age of 48.4 years and a predominance of male patients. The study achieved significant results, demonstrating a statistically significant increase in platelet counts after two weeks of carvedilol titration, with 68.8% of participants meeting the pre-specified efficacy criterion of a> 15% increase from baseline. These findings support the role of carvedilol as a therapeutic option in managing thrombocytopenia, a common complication in patients with cirrhosis due to increased splenic sequestration and altered hematopoiesis (11, 12).

The results are consistent with recent literature that underscores carvedilol's effectiveness in improving hemodynamics and potentially enhancing liver function, owing to its dual-action mechanism as a non-selective β-blocker with α1-adrenergic antagonism (13, 14). Notably, prior studies have reported improvements in platelet counts and reductions in portal hypertension with carvedilol treatment (15). A systematic review reported carvedilol's significant superiority over propranolol in reducing hepatic venous pressure gradients (HVPG), a critical factor in determining the risk of variceal bleeding (11, 16). In our study, a 25% reduction in heart rate and the associated decrease in portal pressure reflect established physiological mechanisms that may explain the observed haematological improvements.

Most participants in our study had either Child-Pugh Class A or B cirrhosis, which was associated with a favourable safety profile and tolerability of carvedilol. This is consistent with findings from McDowell et al., who noted improved survival rates in patients treated with carvedilol along with an overall better-tolerated profile compared to

traditional β-blockers (17,18). While some variation was observed across demographic strata, no statistically significant differences were detected, suggesting that carvedilol's efficacy is relatively uniform across different age groups and clinical backgrounds. This aligns with Cheung et al.'s conclusions regarding the generalizability of carvedilol's benefits across varying patient demographics [15].

Additionally, the high response rate in our study reinforces previous evidence supporting carvedilol's ability to alleviate symptoms of portal hypertension (11, 17). Sharma et al. highlighted that the therapeutic advantages of carvedilol extend beyond hemodynamic benefits, as it may also exert anti-fibrotic effects, which are crucial in managing chronic liver diseases (14, 18). Given that 27.8% of our population exhibited obesity, an established risk factor for deteriorating liver function and disease progression, it is crucial to explore carvedilol's potential to mitigate these risks through further trials focusing on metabolic profiles (12).

In the context of Pakistan, where hepatitis C prevalence is notably high, the implications of our findings are particularly significant. The majority of our cohort faces compounded health challenges due to hepatopathies associated with multifactorial socio-economic burdens that often limit timely access to advanced medical care [3, 4]. The introduction of carvedilol as a feasible and effective treatment could represent a pivotal advancement in the therapeutic approaches available to clinicians managing patients with chronic liver disease in resource-limited settings. The promising results of this study pave the way for more extensive clinical trials in this local context, aimed at validating these outcomes and exploring the long-term benefits and safety profile of carvedilol in this demographic (8, 10, 18).

Thus, the results of our study provide strong evidence supporting the use of carvedilol to improve thrombocytopenia in cirrhotic patients with hepatitis C. Incorporating carvedilol's therapeutic potential into routine practice could significantly enhance patient outcomes, ultimately addressing the broader public health challenge posed by hepatitis C in Pakistan.

Conclusion

Carvedilol, titrated to a 25% reduction in baseline heart rate, improved thrombocytopenia in patients with HCV-related cirrhosis, with 68.8% achieving a >15% platelet increase at two weeks and significant mean platelet gains, while maintaining acceptable hemodynamics. The effect was broadly uniform across demographic and disease strata, supporting generalizability to routine care. Larger, controlled trials with longer follow-up are warranted to confirm durability, define optimal dosing windows, and assess clinical outcomes such as bleeding events and transfusion needs, particularly in high-burden settings like Pakistan.

Declarations

Data Availability statement

All data generated or analysed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department concerned. (IRBEC-2343/24)

Consent for publication

Approved

Funding

Not applicable

Conflict of interest

The authors declared no conflict of interest.

Author Contribution

SD (PGR)
Manuscript drafting, Study Design,
YAZ (Associate Professor)
Review of Literature, Data entry, Data analysis, and drafting an article.
QU (Senior Registrar)
Conception of Study, Development of Research Methodology Design
SS (Principal)
Study Design, manuscript review, and critical input.

All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the study's integrity.

References

1. Zhang Y., Wang H., Zhou N., Zhang Y., Lin Y., Wu L., et al. A multidisciplinary team approach to the treatment of liver cirrhosis. Journal of Inflammation Research 2021; Volume 14:5443-5450. https://doi.org/10.2147/jir.s328334
2. Iqbal J.. Liver dynamics of HCV infection amongst patients aged 50 years or older visiting a larger tertiary care centre of Hyderabad, Pakistan. Gastroenterology & Hepatology Open Access 2021;12(2):68-72. https://doi.org/10.15406/ghoa.2021.12.00458
3. Ahmad I., Majeed Z., & Iqbal J. Presence of cirrhosis in newly diagnosed hepatitis C patients without prior history of chronic liver disease. The Professional Medical Journal 2019;26(12):2095-2099. https://doi.org/10.29309/tpmj/2019.26.12.3161
4. Şahin T.. An unwanted side effect: giant hepatocellular carcinoma development after ledipasvir/sofosbuvir therapy in a chronic hepatitis C virus-induced cirrhotic patient. Demiroglu Bilim University Florence Nightingale Transplantation Journal 2020;3(1-2):6-8. https://doi.org/10.5606/fng.transplantasyon.2018.00
5. Lien H. and Dieu N. Assessment of the results of sofosbuvir/velpatasvir treatment in chronic HCV-infected patients at the National Hospital for Tropical Diseases. Tạp Chí Truyền Nhiễm Việt Nam 2023;4(32):21-25. https://doi.org/10.59873/vjid.v4i32.182
6. Asadi-Lari M., Sheidaei A., Khademi S., Gohari K., Delavari F., Delavari A.et al.. Liver cirrhosis mortality at national and provincial levels in Iran between 1990 and 2015: a meta-regression analysis. Plos One 2019;14(1):e0198449. https://doi.org/10.1371/journal.pone.0198449
7. Kanwal F., Mapaskhi S., Smith D., Taddei T., Hussain K., Madu S.et al.. Implementation of a population-based cirrhosis identification and management system. Clinical Gastroenterology and Hepatology 2018;16(8):1182-1186.e2. https://doi.org/10.1016/j.cgh.2018.01.041
8. Singal A., Bataller R., Ahn J., Kamath P., & Shah V. Acg clinical guideline: alcoholic liver disease. The American Journal of Gastroenterology 2018;113(2):175-194. https://doi.org/10.1038/ajg.2017.469
9. Sepanlou S., Safiri S., Bisignano C., Ikuta K., Merat S., Saberifiroozi M.et al.. The global, regional, and national burden of cirrhosis by cause in 195 countries and territories, 1990–2017: a systematic analysis for the global burden of disease study 2017. The Lancet Gastroenterology & Hepatology 2020;5(3):245-266. https://doi.org/10.1016/s2468-1253(19)30349-8
10. Morita A., Tamaki N., Kobashi H., Mori N., Tsuji K., Takaki S.et al.. Effect of treatment periods on efficacy of glecaprevir and pibrentasvir in chronic hepatitis C: a nationwide, prospective, multicenter study. JGH Open 2024;8(4). https://doi.org/10.1002/jgh3.13068
11. Dwinata M., Putera D., Adda'i M., Hidayat P., & Hasan I. Carvedilol vs endoscopic variceal ligation for primary and secondary prevention of variceal bleeding: systematic review and meta-analysis. World Journal of Hepatology 2019;11(5):464-476. https://doi.org/10.4254/wjh.v11.i5.464
12. Serper M., Kaplan D., Taddei T., Tapper E., Cohen J., & Mahmud N. Nonselective beta blockers, hepatic decompensation, and mortality in cirrhosis: a national cohort study. Hepatology 2022;77(2):489-500. https://doi.org/10.1002/hep.32737

13. Sharma M., Singh S., Desai V., Shah V., Kamath P., Murad M.et al.. Comparison of therapies for primary prevention of oesophageal variceal bleeding: a systematic review and network meta-analysis. Hepatology 2019;69(4):1657-1675. https://doi.org/10.1002/hep.30220
14. Turco L., Reiberger T., Vitale G., & Mura V. Carvedilol as the new non-selective beta-blocker of choice in patients with cirrhosis and portal hypertension. Liver International 2023;43(6):1183-1194. https://doi.org/10.1111/liv.15559
15. Cheung K., Mok C., Lam L., Mao X., Mak L., Seto W.et al.. Carvedilol versus other nonselective beta blockers for variceal bleeding prophylaxis and death: a network meta-analysis. Journal of Clinical and Translational Hepatology 2023;000(000):000-000. https://doi.org/10.14218/jcth.2022.00130s
16. Tosetti G., Degasperi E., Farina E., D'Ambrosio R., Soffredini R., Borghi M.et al. Decompensation in direct-acting antiviral-cured hepatitis C virus compensated patients with clinically significant portal hypertension: too rare to warrant universal β-blocker therapy. The American Journal of Gastroenterology 2021;116(6):1342-1344. https://doi.org/10.14309/ajg.0000000000001158
17. McDowell H., Chuah C., Tripathi D., Stanley A., Forrest E., & Hayes P. Carvedilol is associated with improved survival in patients with cirrhosis: a long-term follow-up study. Alimentary Pharmacology & Therapeutics 2020;53(4):531-539. https://doi.org/10.1111/apt.16189
18. Tevethia H., Pande A., Vijayaraghavan R., Kumar G., & Sarin S. Combination of carvedilol with variceal band ligation in prevention of first variceal bleed in child-turcotte-pugh b and c cirrhosis with high-risk oesophageal varices: the 'cavarly trial'. Gut 2024;73(11):1844-1853. https://doi.org/10.1136/gutjnl-2023-331181.