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DIRECTLY ACTING ANTIVIRALS (DAAS) THERAPY AND PLATELET COUNT IN CHRONIC HCV (CHCV) PATIENTS AT CHANDKA TEACHING HOSPITAL LARKANA

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OBJECTIVE
To assess the effect of Direct-Acting Antiviral (DAA) therapy on the change in platelet count (measured as an increase or decrease from baseline) in chronic HCV patients treated at Chandka Medical College Teaching Hospital, Larkana.
METHODOLOGY
This quasi-experimental study was conducted from January 30, 2024, to January 30, 2025, at Chandka Medical College Teaching Hospital, Larkana, using non-probability consecutive sampling. Patients aged 18–60 years with chronic HCV infection were enrolled and treated with Sofosbuvir plus Daclatasavir or Velpatasvir for 12 weeks. HCV RNA and platelet counts were recorded at baseline and post-treatment to assess changes based on sustained virological response (SVR). Data were analyzed using SPSS version 26, with significance set at $p \leq 0.05$.
RESULTS
In a cohort of 100 individuals diagnosed with chronic hepatitis C virus (HCV) infection (mean age 55.22 ± 4.98 years, 56% male), a statistically significant elevation in platelet count was observed subsequent to direct-acting antiviral (DAA) therapy, increasing from 125.59 ± 13.36 to 151.86±17.40 $\times 10^3/\mu L$ (mean change: 26.27±21.38; p=0.0001). A notable improvement was documented in 75% of the subjects, and was associated with lower bilirubin, and higher albumin levels (all p=0.0001), while gender, BMI and portal vein diameter showed no significant association.
CONCLUSION
The administration of Direct-Acting Antivirals (DAAs) has the potential to facilitate hematological restitution in a substantial proportion of individuals afflicted with chronic Hepatitis C Virus (HCV) infection, thereby markedly enhancing platelet counts. This improvement was associated with the amelioration in the liver functionality manifested by

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reduced spleen size and bilirubin levels and by increased albumin levels. These results underscore the extensive therapeutic advantages of DAA therapy in improving both hematologic and hepatic parameters, thereby reinforcing its continued application in the management of chronic HCV.

KEYWORDS
Antiviral Agents, Chronic Hepatitis C, Platelet Count, Sustained Virologic Response, Thrombocytopenia

INTRODUCTION

Hepatitis C virus infection is a major global public health concern. It affects more than 75 million people worldwide, with the prevalence being estimated to exceed 1% of the population [1]. The Eastern Mediterranean region has the highest prevalence of HCV infection globally at 2.3%. Egypt is the most affected country, followed by Pakistan. In Pakistan, approximately 11.55% of the adult population is infected with chronic HCV, which is predominantly genotype 3a [2,3].

Each year, nearly five million deaths are attributed to complications of HCV, many of which arise from extrahepatic manifestations such as thrombocytopenia (TCP), a common hematologic abnormality defined by a platelet count below 150,000/mm [3,4]. The pathogenesis of TCP in HCV involves reduced hepatic production of thrombopoietin (TPO), a key growth factor for megakaryocytes, as well as bone marrow suppression and hypersplenism [5]. These complications are particularly pronounced in cirrhotic patients and have historically limited the efficacy of antiviral therapies.

Among those with decompensated cirrhosis, treatment response remained low with sustained virologic response (SVR) rates as low as 30% [6] during the interferon era due to poor tolerability with conventional interferon. On the other hand, the breakthrough of Direct-Acting Antivirals (DAAs) has changed the scenario of treating chronic HCV. Direct acting antivirals (DAAs) including the combination of Sofosbuvir and Daclatasvir (SOF/DAC), with and without the use of Ribavirin, have increased SVR rates to greater than 95% [7,8]. In addition to high cure rates, DAAs have been associated with improvement in hematological parameters, including platelet counts. Saif-Al-Islam et al. reported a 73% platelet count improvement following DAA therapy [9]. Similarly, a study by Shaikh NT demonstrated that SVR-positive patients had significantly higher platelet counts (190 ± 94.55 $\times 10^3/mm^3$) compared to SVR-negative individuals (106.80 ± 13.25 $\times 10^3/mm^3$) [6].

In Pakistan, where HCV is highly prevalent, the World Health Organization has set a target to provide effective antiviral therapy to 80% of infected individuals by the year 2030, to mitigate disease burden and complications. However, treatment strategies must be informed by local clinical data, which remain scarce. This is especially relevant in rural areas, where the majority of cases are reported, yet structured evidence to guide clinical decisions is lacking [2,5]. Therefore, this study was designed to evaluate the effect of Sofosbuvir plus Daclatasvir (SOF/DAC) on platelet count in chronic HCV patients. The findings aim to contribute valuable local data, support optimized treatment strategies, and enhance patient outcomes in this high-burden population.

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METHODOLOGY

The research was conducted within the Medical Unit-III of Chandka Medical College Teaching Hospital, located in Larkana, over a duration of one year subsequent to the acquisition of synopsis approval from the Institutional Review Board (IRB) of Shaheed Mohtarma Benazir Bhutto Medical University, Larkana. All subjects involved in the study furnished written informed consent. Patients were enrolled using non-probability consecutive sampling. The inclusion criteria were: age 18–60 years, either gender, diagnosis of chronic HCV infection confirmed by PCR, and no prior antiviral treatment with interferon-containing regimens or DAAs. Exclusion criteria included pregnant females, liver transplant recipients, hepatocellular carcinoma (HCC), decompensated cirrhosis (Child-Pugh B or C), HIV or HBV co-infection, and other chronic liver diseases such as alcoholic or metabolic liver disease.

Eligible patients were assessed and categorized as cirrhotic or non-cirrhotic based on liver biopsy findings and ultrasound (presence of fibrosis/regenerating nodules or obliteration of central hepatic vein). Demographic and clinical variables including age, gender, height, weight, BMI, duration of disease, and Child-Pugh class were recorded. Baseline investigations included HCV RNA quantification, genotype, hepatic profile, and platelet count. Patients received a daily oral dose of Sofosbuvir 400 mg and Daclatasavir 60 mg (or Velpatasvir 100 mg) for 12 weeks. HCV RNA was measured at baseline, at 12 weeks (SVR12), and at 24 weeks post-treatment using the AMPLIQUALITY HCV-TS assay (AB Analitica, Italy) and PCR, with detection limit >50 IU/ml.

The primary outcome was to assess the effect of DAA therapy on change in platelet count (increase or decrease from baseline), stratified by SVR status (positive or negative). Platelet counts were categorized as normal, mild, moderate, or severe thrombocytopenia. Confounding variables were controlled according to predefined eligibility and clinical assessment criteria.

RESULTS

According to Table I, the cohort under investigation comprised 100 individuals, with an average age of 55.22 ± 4.98 years and a mean body mass index (BMI) of 25.81 ± 3.45 kg/m². The mean diameter of the portal vein was recorded at 11.09 ± 2.11 mm, whereas the average size of the spleen measured 13.05 ± 2.58 cm. The biochemical analyses indicated a mean total bilirubin level of 0.75 ± 0.18 mg/dL, serum albumin concentration of 3.65 ± 0.17 g/dL, aspartate aminotransferase (AST) level of 88.65 ± 24.01 IU/L, and alanine aminotransferase (ALT) level of 71.41 ± 18.89 IU/L. The analysis of gender distribution indicated that 56% of the cohort were male, while 44% were female. In the context of hepatic fibrosis staging, the majority were in stage F3 of hepatic fibrosis (71.0%), followed by stage F2 (15.0%), stage F0 (8.0%), and stage F1 (6.0%).

The influence of direct-acting antiviral (DAA) intervention on hematological parameters was evaluated in a cohort of 100 subjects. A notable elevation in the mean platelet count was observed, rising from 125.59 ± 13.36 at baseline to 151.86 ± 17.40 upon completion of the treatment, reflecting a mean alteration of 26.27 ± 21.38 (p = 0.0001). The mean white blood cell (WBC) count exhibited an increase from 5.66 ± 1.49 to 6.56 ± 1.49, corresponding to a

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mean change of 0.90 ± 2.13 (p = 0.0001). Conversely, the mean hemoglobin level at baseline was 13.47 ± 1.18 g/dL, which slightly increased to 13.56 ± 0.68 g/dL at the end of treatment. The mean change observed was 0.09 ± 1.44 g/dL, which was not statistically significant (p = 0.540). These observed modifications signify statistically significant variations in hematological parameters subsequent to DAA therapy, as delineated in TABLE II.

Among the 100 patients included in the study, 75 (75%) showed improvement in platelet count after antiviral therapy, while 25 (25%) did not. Patients with platelet improvement had a significantly lower mean age compared to those without improvement (54.57 ± 5.34 vs. 57.16 ± 3.02 years; p = 0.024). Spleen size was also markedly smaller in the improvement group (12.00 ± 1.64 vs. 16.20 ± 2.34 cm; p = 0.0001). Similarly, total bilirubin was significantly lower (0.71 ± 0.17 vs. 0.86 ± 0.16 mg/dL; p = 0.0001), whereas serum albumin was higher (3.70 ± 0.17 vs. 3.53 ± 0.11 g/dL; p = 0.0001) in patients with improvement. Liver enzymes also showed significant associations: AST was higher in the improvement group (90.93 ± 20.87 vs. 81.80 ± 31.15 IU/L; p = 0.0001), while ALT levels showed no meaningful difference between groups (71.19 ± 18.46 vs. 72.08 ± 20.50 IU/L; p = 0.0001, but clinically nonsignificant). In contrast, BMI (25.67 ± 3.38 vs. 26.21 ± 3.69 kg/m²; p = 0.507) and portal vein diameter (11.11 ± 2.01 vs. 11.04 ± 2.44 mm; p = 0.892) were not significantly associated with platelet count improvement. Regarding gender distribution, no significant difference was observed between males and females in relation to platelet count improvement (p = 0.352) in TABLE III.

DISCUSSION

This study examined the effects of DAA therapy on platelet counts among patients with chronic hepatitis C virus (HCV) infection at Chandka Medical College Teaching Hospital, Larkana. At 12 weeks after treatment with Sofosbuvir plus Daclatasvir/Velpatasvir, the platelet count increased from 125.59 ± 13.36 to 151.86 ± 17.40 ×10³/µL, for a mean change of 26.27 ± 21.38 ×10³/µL (p = 0.0001). This study supports the increasing amount of evidence that shows DAA therapy is effective not just for viral eradication but also for restoration of hematological features associated especially in patients who develop thrombocytopenia.

Comparable findings were documented by Saif-Al-Islam et al., who reported a mean platelet augmentation from 112.55 ± 30.19 to 146.91 ± 46.02 ×10³/µL (p = 0.001), thereby illustrating a consistent pattern in platelet resurgence subsequent to viral eradication [9]. Cheng et al. similarly noted a modest elevation in platelet counts within a cohort characterized by elevated baseline figures, ranging from 154.6 ± 64.0 to 157.9 ± 62.8 ×10³/µL, implying that the extent of enhancement may be associated with the severity of initial thrombocytopenia [16].

The mechanism behind platelet count improvement is likely multifactorial. As viral replication diminishes, hepatic synthetic function improves, and splenic sequestration often lessens. Soliman et al. noted that hematologic recovery following DAA treatment correlates with better clinical prognosis [11], while Mohamed et al. found that platelet elevation was associated with improved treatment outcomes [12]. Abd El Hafez and Kasemy further

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emphasized that reductions in systemic inflammation, as reflected in normalized platelet-to-lymphocyte ratios, support immune and marrow recovery [13].

Salama et al. expanded on the systemic impact of DAAs, stating that viral clearance ameliorates extrahepatic manifestations, including hematologic abnormalities such as thrombocytopenia [14]. Nevertheless, Kanwal et al. cautioned that despite successful treatment, patients with advanced fibrosis remain at long-term risk for hepatocellular carcinoma (HCC), highlighting the need for continuous surveillance post-SVR [15].

Thrombocytopenia due to chronic liver disease is often part of a multifactorial aetiology. Williamson et al. related to intensive care unit (ICU) conditions, e.g. infections, treatments or coagulopathies, might obscure the real impact of platelet variations as such a situation would require careful attention [10].

A notable advantage of this study is the implementation of standardized antiviral protocols (Sofosbuvir in combination with Daclatasvir or Velpatasvir) alongside objective PCR-based assessments to evaluate virological outcomes. Additionally, the inclusion of both cirrhotic and non-cirrhotic patients provides a broader perspective on treatment outcomes across disease severity. The study also maintained clear eligibility criteria and consistent baseline investigations, enhancing the internal validity of the findings.

However, several limitations must be acknowledged. The non-probability consecutive sampling technique may introduce selection bias and limit the generalizability of the results. The relatively small sample size and single-center design further restricts external validity. Moreover, factors such as spleen size, bone marrow function, and nutritional status—which could independently influence platelet count—were not evaluated. The absence of a control group also limits causal inference regarding DAA therapy's direct impact on platelet recovery.

A major limitation relates to the lack of extended longitudinal follow-up beyond SVR24 needed to assess whether any hematological improvements persist and whether this change is associated with clinical outcomes (ie, bleeding or liver decompensation). Also, more advanced techniques like transient elastography, which would allow for more accurate staging of fibrosis stages, could not be used due to lack of resources.

Future studies should include multi-center data, larger samples, and extended follow-up durations. Incorporating additional markers of liver and bone marrow function would further clarify the mechanisms underlying platelet count recovery post-DAA therapy.

CONCLUSION

The administration of Direct-Acting Antivirals (DAAs) has the potential to facilitate hematological restitution in a substantial proportion of individuals afflicted with chronic Hepatitis C Virus (HCV) infection, thereby markedly enhancing platelet counts. This improvement was associated with the amelioration in the liver functionality manifested by reduced spleen size and bilirubin levels and by increased albumin levels. These results underscore the extensive therapeutic advantages of DAA therapy in improving both hematologic and hepatic parameters, thereby reinforcing its continued application in the management of chronic HCV.

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Table I: Demographic Characteristics of Study Participants (n=100)	
(Mean ± SD)	
Age in years= 55.22 ± 4.98	
Body Mass Index in kg/m^2 = 25.81 ± 3.45	
Portal Vein Diameter in mm= 11.09 ± 2.11	
Spleen Size in cm = 13.05 ± 2.58	
Total Bilirubin in mg/dL= 0.75 ± 0.18	
Albumin in g/dl = 3.65 ± 0.17	
AST in IU/L= 88.65 ± 24.01	
ALT in IU/L = 71.41 ± 18.89	
Gender	
Male	56 (56.0)
Female	44 (44.0)
Stage of Hepatic Fibrosis	
F0	8 (8.0)
F1	6 (6.0)
F2	15 (15.0)
F3	71 (71.0)

Table II: Effect of DAA Therapy on Platelet Count and Blood Parameters (n=100)				
(Mean ± SD)	**Baseline**	**End of Treatment**	**Change**	**P-Value**
Platelet Count (×10^9/L)	125.59 ± 13.36	151.86 ± 17.40	26.27 ± 21.38	0.0001
WBCs (×10^9/L)	5.66 ± 1.49	6.56 ± 1.49	0.90 ± 2.13	0.0001
Hemoglobin (g/dL)	13.47 ± 1.18	13.56 ± 0.68	0.09 ± 1.44	0.540

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Table III: Factors Associated with Platelet Count Improvement After Antiviral Therapy (n=100)					
(Mean ± SD)		**Improvement of Platelet Count**		**95% C.I.**	**P-Value**
		Yes (n=75)	**No (n=25)**		
Age in years		54.57 ± 5.34	57.16 ± 3.02	-4.824---- -0.349	0.024
BMI in kg/m^2		25.67 ± 3.38	26.21 ± 3.69	-2.120----1.053	0.507
Portal Vein Diameter in mm		11.11 ± 2.01	11.04 ± 2.44	-0.909----1.042	0.892
Spleen Size in cm		12.00 ± 1.64	16.20 ± 2.34	-5.044---- -3.356	0.0001
Total Bilirubin in mg/dL		0.71 ± 0.17	0.86 ± 0.16	-0.227---- -0.071	0.0001
Albumin in g/dl		3.70 ± 0.17	3.53 ± 0.11	0.093----0.242	0.0001
AST in IU/L		90.93 ± 20.87	81.80 ± 31.15	-1.776----20.042	0.0001
ALT in IU/L		71.19 ± 18.46	72.08 ± 20.50	-9.595----7.808	0.0001
n (%)					
Gender	Male	40 (53.3)	16 (64.0)	0.253----1.636	0.352
	Female	35 (46.7)	9 (36.0)		

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REFERENCES

1. World Health organization. Global hepatitis report, 2017. Geneva: World Health organization, 2017.

2. Khan AQ, Mansoor FI, Iqbal J, Shahbaz RY, Fida S, Siddique M. Efficacy of first available direct-acting antiviral agent in treatment of chronic hepatitis C; results from a single centre in Pakistan. Pak Armed Forces Med J. 2020;70(6):1885-92.

3. Umer M, Iqbal M. Hepatitis C virus prevalence and genotype distribution in Pakistan: comprehensive review of recent data. World J Gastroenterol 2016;22(4):1684-700.

4. Salim A, Farooq MO, Mengal FUA, Malik K. Sofosbuvir-based treatment for HCV: a safe option in patients undergoing hemodialysis. J Coll Physicians Surg Pak. 2020;30(11):1230-1.

5. Mushtaq S, Akhter TS, Khan A, Sohail A, Khan A, Manzoor S. Efficacy and safety of generic Sofosbuvir plus daclatasvir and Sofosbuvir/Velpatasvir in HCV genotype 3-infected patients: real-world outcomes from Pakistan. Front Pharmacol. 2020;11:550205.

6. Sheikh NT, Shaukat MT, Hussain A, Alyan A, Iqbal A, Karim S, et al. SVR achievement in triple therapy treated hepatitis c induced cirrhosis: a dual center retrospective cohort study. Ann Med Surg (Lond).2022;80:104193.

7. Khaliq s, Raza SM. Current status of direct acting antiviral agents against hepatitis C virus infection in Pakistan. Medicina (Kaunas). 2018;54(5):80.

8. Smirne C, D'Avolio A, Bellan M, Gualerzi A, Crobu MG, Pirisi M. Sofosbuvir-based therapies in genotype 2 hepatitis C virus cirrhosis: a real life experience with focus on ribavirin dose. Pharmacol Res Perspect. 2021;9(4):e00811.

9. Saif-Al-Islam M, Abdelaal UM, Younis MA, Alghany Atgahlan HA, Khalaf S. Effect of direct-acting antiviral therapy on thrombocytopenic patients with hepatitis C virus-related chronic liver disease. Gastroenterol Res Pract. 2021;2021:8811203.

10. Williamson DR, Albert M, Heels-Ansdell D, Arnold DM, Lauzier F, Zarychanski R, et al. Thrombocytopenia in critically ill patients receiving thromboprophylaxis: frequency, risk factors, and outcomes. Chest. 2013;144(4):1201-15.

11. Soliman Z, El Kassas M, Elsharkawy A, Elbadry M, Hamada Y, ElHusseiny R, et al. Improvement of platelet in thrombocytopenic HCV patients after treatment with direct-

GLOBAL HEALTH & MEDICINE
ISSN / eISSN: 2434-9186 / 2434-9194
Volume 08, Issue 06.
https://ghsjournal.com/

acting antiviral agents and its relation to outcome. Platelets. 2021;32(3):383-90.

12. Mohamed HM, Bazeed SE, Osman HA, Fayed HM. Correlation between platelet count and outcome of chronic HCV patients treated with direct-acting antivirals. SVU Int J Med Sci. 2019;2(1):1-9.
13. Abd El Hafez MA, Kasemy ZA. Effect of direct-acting antivirals on platelet-to-lymphocyte ratio and neutrophil-to-lymphocyte ratio in patients with hepatitis C virus-related thrombocytopenia. Egypt J Intern Med. 2019;31:296-301.

14. Salama II, Raslan HM, Abdel-Latif GA, Salama SI, Sami SM, Shaaban FA, et al. Impact of direct-acting antiviral regimens on hepatic and extrahepatic manifestations of hepatitis C virus infection. World J Hepatol. 2022;14(6):1053.

15. Kanwal F, Kramer JR, Asch SM, Cao Y, Li L, El-Serag HB. Long-term risk of hepatocellular carcinoma in HCV patients treated with direct acting antiviral agents. Hepatology. 2020;71 (1):44-55.

16. Cheng CH, Chu CY, Chen HL, Lin IT, Wu CH, Lee YK, et al. Direct-acting antiviral therapy of chronic hepatitis C improves liver fibrosis, assessed by histological examination and laboratory markers. J Formosan Med Assoc. 2021;120(5):1259-68.