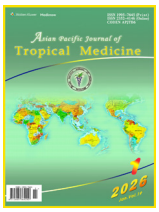

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Outcomes and predictors of treatment failure following direct-acting antiviral therapy in chronic hepatitis C: A retrospective cohort study

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ABSTRACT

Objective: To evaluate the effectiveness of direct-acting antivirals (DAAs) in patients with chronic hepatitis C, assess changes in liver function and hepatic fibrosis following treatment, and identify independent predictors of treatment failure.

Methods: This retrospective cohort study included patients who received DAA therapy at Hospital Kuala Lumpur between January 2020 and December 2023. Sustained virologic response (SVR) was assessed at least 12 weeks post-treatment by reverse transcription-polymerase chain reaction for hepatitis C virus (HCV) RNA. Demographic, clinical, and laboratory data were collected and analyzed. Multiple logistic regression analysis was performed to identify independent predictors of treatment failure.

Results: A total of 335 patients in the study. The overall SVR rate was 89%. After achieving SVR, significant improvements were observed in liver enzyme levels and non-invasive liver fibrosis scores, whereas the overall Model for End-Stage Liver Disease (MELD) scores remained unchanged.Significant independent predictors of treatment failure included non-compliance with DAA therapy [adjusted odds ratio (a*OR*) 68.3; 95% confidence interval (95% *CI*) 16.3-285.0; *P*<0.001], treatment with sofosbuvir/velpatasvir (a*OR* 6.1; 95% *CI* 1.4-26.5; *P*=0.015), MELD score of 10-15 (a*OR* 4.6; 95% *CI* 1.1-18.2; *P*=0.031), HCV genotype 3 infection (a*OR* 4.5; 95% *CI* 1.1-17.6; *P*=0.031), and elevated serum total bilirubin level (a*OR* 1.1; 95% *CI* 1.0-1.1; *P*=0.003).

Conclusions: DAA therapy yielded a high SVR rate, and treatment failure was strongly associated with non-adherence to therapy and advanced liver disease. These findings underscore the necessity of adherence support, early diagnosis, and individualized clinical management to optimize treatment outcomes in patients with chronic hepatitis C.

KEYWORDS: Chronic hepatitis C; Direct-acting antiviral agent; Liver function; Cirrhosis; Treatment compliance; Hepatitis elimination

Summary

Question: How effective are direct-acting antivirals (DAAs) in achieving sustained virologic response (SVR) in chronic hepatitis C patients, and what factors predict treatment failure?

Findings: In this retrospective cohort study of 335 patients, the overall SVR rate was 89%. Treatment failure was primarily associated with non-compliance with the therapy, genotype 3 infection, and advanced liver disease indicators. The liver enzyme levels and fibrosis scores improved post-treatment for patients who achieved SVR.

Meaning: DAA therapy is highly effective, but optimizing outcomes requires addressing patient adherence and managing advanced liver disease through early diagnosis.

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1. Introduction

According to the World Health Organization, approximately 50 million people worldwide are affected by chronic hepatitis C, with around one million new cases reported annually and a mortality rate of 242 000 deaths per year, primarily attributable to liver cirrhosis and hepatocellular carcinoma[1].

The primary goal of hepatitis C treatment is to achieve a sustained virological response (SVR), which is defined as an undetectable hepatitis C virus (HCV) ribonucleic acid (RNA) viral load following the completion of treatment. Achievement of SVR is associated with attenuated liver fibrosis, a reduced risk of liver failure and hepatocellular carcinoma, decreased healthcare expenditure, and improved quality of life. The advent of oral direct-acting antivirals (DAAs) has broadened treatment options, with these agents exhibiting efficacy rates of over 95% and a favorable safety profile in clinical trials. DAAs target viral proteins essential to multiple stages of the HCV life cycle, thereby inhibiting viral replication[2].

Although the percentage of SVR is above 95% in clinical trials, variable results have been obtained from several population-based studies, ranging from 71% to 95%. Treatment failure still occurs despite the high efficacy of antivirals. Several studies have reported factors associated with SVR after DAA treatment, which can be categorized into host, viral, and treatment factors[3-8]. However, data are limited in our region. This study aims to investigate the outcomes of DAA treatment in terms of SVR rate and changes in hepatic function, as well as the predictive factors based on demographic characteristics, baseline laboratory tests related to liver function and viral investigation profiles, and DAA treatment regimens, to develop optimal management strategies for patients with chronic hepatitis C.

2. Methods

2.1. Cohort description

Universal sampling included 382 patients identified *via* archived Pharmacy Department records of chronic HCV patients aged ⩾18 years who received DAA treatment in Hospital Kuala Lumpur, with complete demographic data and baseline laboratory profiles available in the Laboratory Information System. Of these, 309 patients were evaluated for virological outcomes and constituted the efficacy population. Among the 309 patients, 11 failed to

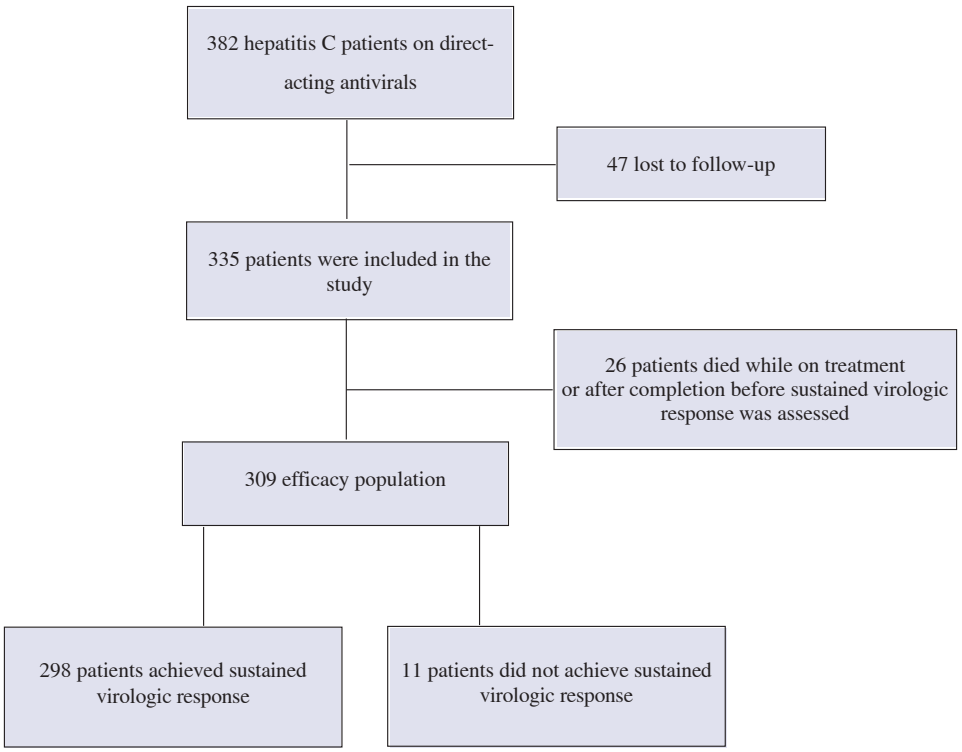

Figure 1. Patient disposition chart.

achieve SVR. Additionally, 26 patients died either during or after treatment completion, with no SVR data documented; this group was classified as treatment 'failures' when assessing therapeutic efficacy[9,10]. These patients were included in the efficacy group as 'failure to achieve SVR' in the statistical analysis (Figure 1).

This single-center retrospective study utilized data from patients with chronic hepatitis C who received DAA treatment between 2020 and 2023. For DAA treatment outcomes, we assessed the SVR rate and changes in liver function parameters before and after SVR achievement. SVR was defined as undetectable HCV RNA (below the limit of quantification) *via* real-time polymerase chain reaction at least 12 weeks following completion of DAA treatment. Patients who achieved SVR (n=298) were further analyzed to determine changes in hepatic function parameters pre- and post-DAA treatment.

Additional data collected included non-invasive fibrosis scores and prognostic markers. The Fibrosis-4 Index (FIB-4) and aspartate aminotransferase (AST) to Platelet Ratio Index (APRI) are validated non-invasive tests used to assess liver fibrosis in patients with chronic liver disease, including chronic hepatitis C[11]. In this study, patients with cirrhosis were classified using an APRI score of ⩾1.5 and/or a FIB-4 score of ⩾3.25[2,12]. Further stratification was performed to categorize patients into four distinct fibrosis stages according to their scores, as detailed in Supplementary Table 1. The Model for End-Stage Liver Disease (MELD) score was used as the prognostic marker, which is a well-established reliable indicator of short-term survival in patients with end-stage liver disease. A MELD 3.0 score of >10 is associated with a 3-month mortality rate of at least 6% in patients with chronic liver disease, with mortality risk increasing as the score rises[13–15].

For viral investigation profiles, data on baseline HCV RNA load, genotype, and co-infection with hepatitis B virus (HBV) and human immunodeficiency virus (HIV) were recorded. According to national clinical practice guidelines, genotype testing is not mandatory for all chronic hepatitis C patients prior to pan-genotypic DAA treatment, except for high-risk patients as assessed by clinicians[12]. In line with these guidelines, genotype testing in this study was primarily performed in cirrhotic patients and those with prior treatment failure, to guide the selection of treatment regimens and duration.

2.2. Statistical analysis

All data were collected using a standardized proforma and analyzed with IBM SPSS Statistics Version 29.0. Significant predictors of SVR were identified using odds ratios (*OR*) derived from multiple logistic regression analysis. For comparisons of liver function parameters between pre-treatment and post-SVR assessment, a paired t-test was used for normally distributed data and the Wilcoxon signed-rank test for skewed data.

2.3. Ethical statement

Ethical approval was waived by the National Medical Research Register, the Medical Research and Ethics Committee at the National Institute of Health Malaysia [NMRR ID-23-01664-VNC (IIR)] in view of the retrospective nature of the study and all the procedures being performed were part of the routine care. The site of study, the Clinical Research Centre of Hospital Kuala Lumpur (CRCHKL-2023-07-164) approved this study.

3. Results

3.1. Demography and baseline laboratory profile

The median age of the study population was 53 (IQR 46-61) years. Most participants were male (254/335, 75.8%). Median AST, alanine aminotransferase (ALT), and total bilirubin levels were elevated, while the mean albumin level was below the normal reference range, indicative of underlying liver injury. Approximately 28.1% (94/335) of patients had stage 3 or higher chronic kidney disease (CKD), and 13.4% (45/335) were receiving dialysis for end-stage renal failure (ESRF). Additionally, 34.9% (117/335) of patients had cirrhosis, as defined by an APRI score ⩾1.5 and/or a FIB-4 score ⩾3.25 (Supplementary Table 1).

3.2. Viral investigation profiles

Genotype testing was performed in 31.6% (106/335) of patients, with genotype 3 being the most prevalent (78/335, 23.3%), followed by genotype 1a (21/335, 6.3%). A single case of mixed genotypes 3 and 4 was identified in a patient with stage 3a CKD. Additionally, concurrent HIV and HBV co-infections were present in 4.2% (14/335) and 6.0% (20/335) of patients with chronic hepatitis C, respectively.

3.3. DAA treatment regimens for patients with chronic hepatitis C

The majority of patients (87.5%) received sofosbuvir/daclatasvir (SOF/DAC), while smaller cohorts received sofosbuvir/velpatasvir

(SOF/VEL) (8.1%)-this regimen was predominantly administered to cirrhotic patients-or sofosbuvir/ravidasvir (4.5%). High-risk patients (*e.g.*, those with genotype 3 infection and cirrhosis) were treated with ribavirin combination therapy and an extended treatment duration of 24 weeks. Treatment adherence rate was 90.7%, as detailed in Table 1.

Table 1. Direct-acting antiviral treatment for the chronic hepatitis C patients (n=335).

Treatment	Frequency (%)
Sofosbuvir/Daclatasvir (SOF/DAC)	293 (87.5)
Sofosbuvir/Ravidasvir	15 (4.5)
Sofosbuvir/Velpatasvir (SOF/VEL)	27 (8.1)
Ribavirin used	
Yes*	59 (17.6)
No	276 (82.4)
Treatment duration	
12 weeks	193 (57.6)
24 weeks**	142 (42.4)
Treatment compliance	
Yes	304 (90.7)
No	31 (9.3)

*Patients with HCV genotype-3 and liver cirrhosis (24/59, 40.7%); **Patients with HCV genotype-3 and liver cirrhosis (43/142, 30.3%). SOF/VEL: sofosbuvir/velpatasvir.

3.4. Sustained virological response (SVR) rates in chronic hepatitis C patients receiving DAA therapy

The overall treatment efficacy rate was 89.0% (308/335) (95% *CI* 85.1-92.1), with mortalities classified as treatment failures (failure to achieve SVR). For patients with available virological outcomes, 96.4% (298/309) (95% *CI* 93.7-98.2) achieved SVR, which was assessed at least 12 weeks following completion of DAA therapy.

3.5. Predictive factors for DAA treatment failure in patients with chronic hepatitis C

Logistic regression analysis was performed to calculate odds ratios (*OR*) for treatment failure. Multiple logistic regression analysis incorporated variables with a *P*-value <0.05 derived from univariate analysis (Supplementary Table 2). The primary predictor of SVR failure was non-adherence to DAA therapy, which conferred a 68.3-fold increased risk of treatment failure [adjusted odds ratio (a*OR*) 68.3; 95% confidence interval (95% *CI*) 16.3-285.0; *P*<0.001]. Other significant predictors included a MELD 3.0 score of 10-15 (*vs*. <10) (a*OR* 4.6; 95% *CI* 1.1-18.2; *P*=0.031), HCV genotype 3 (*vs*. other genotypes) (a*OR* 4.5; 95% *CI* 1.1-17.6; *P*=0.031), and treatment with the SOF/VEL regimen [*vs*. sofosbuvir/daclatasvir (SOF/DAC)] (a*OR* 6.1; 95% *CI* 1.4-26.5; *P*=0.015). Additionally, each unit increase in total bilirubin level was associated with an 8% increased odds of SVR failure (a*OR* 1.1; 95% *CI* 1.0-1.1; *P*=0.003)

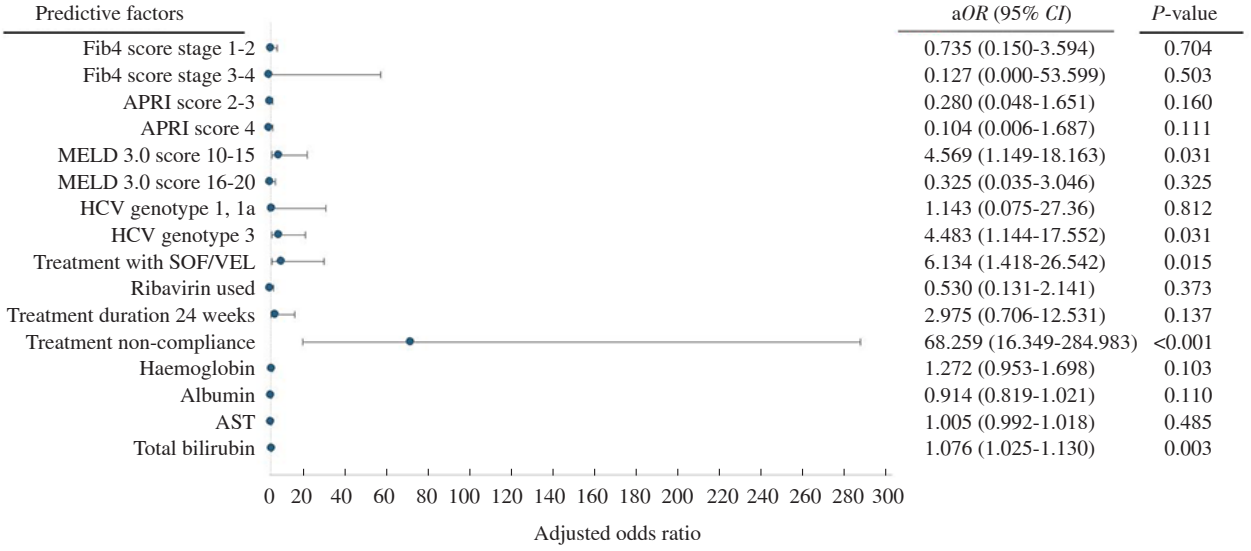

Figure 2. Forest plot on the predictive factors of treatment failure with direct-acting antiviral in chronic hepatitis C. FIB-4: Fibrosis-4 Index; AST: aspartate aminotransferase; APRI: aspartate aminotransferase to Platelet Ratio Index; MELD: Model for End-Stage Liver Disease; HCV: hepatitis C virus; SOF/VEL: sofosbuvir/velpatasvir.

Table 2. Laboratory parameters for liver function before and after direct-acting antiviral treatment (n=298).

Variables	Before treatment	After treatment	Z statistic	P-value*
ALT, U/L	41 (24-82)	17 (12-25)	-13.444	<0.001
Cirrhosis	56 (30-107)	19 (15-31)	-7.709	<0.001
Non-cirrhosis	40 (22-69)	15 (12-23)	-11.041	<0.001
AST, U/L	45 (30-73)	25 (19-34)	-12.445	<0.001
Cirrhosis	86 (48-121)	32 (24-46)	-7.387	<0.001
Non-cirrhosis	38 (27-52)	21 (17-29)	-10.023	<0.001
Total bilirubin, μmol/L	12 (8-15)	10 (6-14)	-3.784	<0.001
Cirrhosis	17 (12-28)	14 (10-26)	-2.783	0.005
Non-cirrhosis	10 (7-12)	8 (6-11)	-2.444	0.015
AFP, ng/mL	4.65 (2.48-8.14)	3.28 (2.25-5.20)	-8.076	<0.001
Cirrhosis	7.86 (3.91-16.70)	4.07 (2.64-6.44)	-5.141	<0.001
Non-cirrhosis	3.79 (2.28-5.61)	2.82 (1.99-4.40)	-6.173	<0.001
INR	1.0 (1.0-1.1)	1.0 (1.0-1.1)	-0.878	0.380
Cirrhosis	1.1 (1.1-1.2)	1.1 (1.0-1.2)	-1.471	0.141
Non-cirrhosis	1.0 (0.9-1.0)	1.0 (1.0-1.1)	-1.871	0.061

*Wilcoxon Signed-Rank test. ALT: alanine aminotransferase; AST: aspartate aminotransferase; AFP: alpha-fetoprotein; INR: international normalized ratio.

Table 3. Laboratory parameters for liver function before and after direct-acting antiviral treatment (n=298).

Variables	Before treatment	After treatment	Mean difference (95% *CI*)	t statistic (*df*)	P-value*
Platelet, 10^9/L	184.0±82.5	191.0±85.4	-6.77 (-12.06--1.48)	-2.517 (297)	0.012
Cirrhosis	103.0±41.6	109.0±48.5	-6.78 (-14.42-0.85)	-1.764 (96)	0.081
Non-cirrhosis	223.0±67.2	230.0±70.4	-6.76 (-13.72-0.21)	-1.912 (200)	0.057
Albumin, g/L	34.0±5.8	36.0±5.6	-1.46 (-1.99--0.94)	-5.476 (297)	<0.001
Cirrhosis	30.0±5.6	33.0±5.7	-2.91 (-3.79--2.03)	-6.540 (96)	<0.001
Non-cirrhosis	36.0±5.1	37.0±5.2	-0.77 (-1.40--0.13)	-2.377 (200)	0.018

Data are presented as mean±SD. *Paired t-test.

(Figure 2). In contrast, age, sex, CKD, HIV or HBV co-infection, and baseline HCV RNA viral load were not significantly associated with treatment outcomes (Supplementary Table 2).

3.6. Changes of liver function parameters before and after treatment with DAA

Hepatic function parameters assessed included ALT, AST, albumin, total bilirubin, international normalized ratio (INR), platelet count, alpha-fetoprotein (AFP), APRI score, FIB-4 score, and MELD 3.0 score, measured pre- and post-DAA therapy in patients with chronic hepatitis C. The median follow-up duration after SVR achievement was 17 (IQR, 12-33) weeks. Our findings demonstrated that SVR attainment following DAA therapy was associated with a significant reduction in median ALT, AST, total bilirubin, and AFP levels, irrespective of cirrhotic status (Table 2).

Table 3 shows that platelet counts were associated with a statistically significant increase following treatment (P=0.012); however, this difference was not significant following stratification by cirrhotic status. Additionally, albumin levels were significantly improved post-treatment in both cirrhotic and non-cirrhotic patients. The Wilcoxon signed-rank test demonstrated a significant improvement in APRI and FIB-4 scores among patients with chronic hepatitis C following DAA therapy. In contrast, no significant difference was observed in the overall median MELD 3.0 score pre- and post-treatment (P=0.857). However, our findings revealed a significant change in median pre-treatment MELD 3.0 scores for patients with scores of 6-9, 10-15, and ⩾20, as detailed in Table 4.

Table 4. Laboratory parameters for liver fibrosis before and after direct-acting antiviral treatment (n=298).

Variables	Before treatment	After treatment	Z statistic	P-value*
APRI score	0.70 (0.40-1.48)	0.30 (0.20-0.70)	-11.220	<0.001
Stage 0-1	0.40 (0.30-0.50)	0.20 (0.10-0.30)	-6.425	<0.001
Stage 2-3	0.90 (0.75-1.30)	0.40 (0.30-0.70)	-6.984	<0.001
Stage 4	3.30 (2.50-5.00)	1.10 (0.65-1.80)	-5.895	<0.001
FIB-4 score	2.12 (1.18-4.76)	1.62 (0.97-3.28)	-7.035	<0.001
Stage 0	1.00 (0.73-1.17)	0.86 (0.62-1.27)	-0.273	0.785
Stage 1-2	2.05 (1.70-2.49)	1.60 (1.22-2.24)	-4.490	<0.001
Stage 3-4	6.09 (4.60-9.84)	4.27 (2.88-6.27)	-5.488	<0.001
MELD 3.0	9.00 (7.00-15.00)	9.00 (7.00-14.00)	-0.484	0.629
Score 6-9	7.00 (6.00-8.00)	7.00 (6.00-9.00)	-3.044	0.002
Score 10-15	11.00 (10.00-13.00)	11.00 (9.00-13.00)	-2.476	0.013
Score 16-20	18.00 (18.00-19.00)	18.50 (18.00-20.00)	-0.422	0.422
Score >20	22.00 (21.00-24.00)	19.50 (17.50-21.00)	-2.698	0.007

*Wilcoxon Signed-Rank test. FIB-4: Fibrosis-4 Index; APRI: aspartate aminotransferase to Platelet Ratio Index; MELD: Model for End-Stage Liver Disease.

4. Discussion

In this real-world retrospective study of 335 patients with chronic hepatitis C who received direct-acting antiviral therapy at our center, an overall sustained virological response rate of 89% was observed. The most significant predictor of treatment failure was non-adherence to DAA therapy, with an a*OR* of 68.3. Other independent predictors included HCV genotype 3 infection, a MELD score of 10-15, elevated total bilirubin levels, and treatment with the SOF/VEL regimen.

Our SVR rate is comparable to those reported in other real-world studies in Asia and globally, where SVR rates typically range from 85% to 95% depending on population characteristics and comorbidities[2,12]. While controlled clinical trials report higher SVR rates (>95%), real-world studies often face challenges such as delayed diagnosis, treatment interruptions, and advanced liver disease at presentation[16,17]. The association between HCV genotype 3 infection and lower SVR rates is consistent with existing literature indicating that genotype 3 is more difficult to treat, particularly in cirrhotic patients[2,12,18].

The strong association between treatment non-adherence and treatment failure highlights an urgent need to implement adherence support strategies within hepatitis C treatment programmes[6]. Interventions including patient education, reminder systems, and close clinical follow-up can significantly improve treatment success rates. Conversely, non-modifiable factors such as elevated MELD scores and total bilirubin levels reflect underlying disease severity, underscoring the importance of early diagnosis and intervention prior to the development of advanced liver damage[19,20].

SOF/VEL use was independently associated with treatment failure in our study cohort. Although this pan-genotypic regimen demonstrates favourable overall efficacy, it is frequently prescribed for patients with more complex or advanced disease[12,21], a factor that may confound this observed association. Implementation of a treatment cascade with various DAA regimens stratified by disease severity is cost-effective, which optimizes healthcare expenditure control while expanding treatment coverage[21]. Further prospective studies are warranted to evaluate the real-world effectiveness of specific DAA regimens across different patient subgroups.

Encouragingly, significant improvements in liver function tests and non-invasive fibrosis scores were observed following SVR attainment. These findings corroborate previous research demonstrating hepatic recovery subsequent to viral eradication[22,23]. However, MELD scores remained largely unchanged in the overall cohort, indicating that advanced hepatic dysfunction may persist despite virological cure, particularly among patients with decompensated cirrhosis[22]. Notably, a significant improvement was observed in the subgroup with a MELD 3.0 score of $\geqslant$20. Nevertheless, caution should be exercised when interpreting improvements in MELD scores, as the phenomenon of MELD purgatory has been documented in patients with decompensated cirrhosis. Such patients may exhibit biochemical improvements with DAA therapy but still require liver transplantation to mitigate ongoing complications and improve survival outcomes[24,25].

This study has several limitations. Genotype data were incomplete owing to the use of pan-genotypic DAA regimens,

which limited subgroup analyses and comparisons. Additionally, the retrospective study design and single-center setting may restrict the generalizability of our findings. Long-term follow-up data—including data on hepatocellular carcinoma risk and SVR durability—were unavailable for analysis.

Nevertheless, this study's strengths lie in its large patient cohort, diverse study population, and real-world clinical context, which provide valuable insights into the real-world effectiveness of DAAs in our region. As we progress toward national hepatitis C elimination targets, our findings underscore the critical importance of adherence support and early therapeutic intervention to optimize treatment outcomes. Integration of these strategies into national clinical protocols may further improve treatment success rates, particularly among high-risk patient groups such as those with HCV genotype 3 infection or advanced liver disease.

DAA therapy achieved high SVR rates in this real-world cohort, with significant improvements in hepatic function parameters and non-invasive fibrosis scores. Strengthening adherence support and initiating treatment at an earlier stage—particularly in patients with advanced liver disease or HCV genotype 3 infection—are key strategies to optimize treatment outcomes and support national hepatitis C elimination initiatives.

Conflict of interest statement

The authors have no competing interests to declare that are relevant to the content of this article.

Ethical statement

Ethical approval was waived by the National Medical Research Register, the Medical Research and Ethics Committee at the National Institute of Health Malaysia [NMRR ID-23-01664-VNC (IIR)] in view of the retrospective nature of the study and all the procedures being performed were part of the routine care. The site of study, the Clinical Research Centre of Hospital Kuala Lumpur (CRCHKL-2023-07-164) approved this study.

Data availability

The datasets generated during and/or analysed during the current study are not publicly available due to reasons of sensitivity but are available from the corresponding author on reasonable request.

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Authors' contributions

NBH, NIKR, NMT, MM, NZ, ZS and SNM contributed to the study concept; NBH and NIKR were responsible for data acquisition and statistical analysis; NBH, NIKR, NMT, MM, NZ, ZS and SNM drafted the initial manuscript; NMT, MM, NZ, ZS and SNM provided critical review and expert opinion for the manuscript; NBH and SNM take responsibility for the integrity of the work as a whole. All authors have reviewed and approved the final version of the manuscript.

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Publisher's note

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Supplementary Table 1. Demography and baseline laboratory investigation profile (n=335).

Parameter	Mean[#](±SD)	Median[#] (IQR)	Frequency (%)	Reference range
Age (years)		53 (46-61)		
Sex				
Male			254 (75.8)	
Female			81 (24.2)	
Haemoglobin (g/dL)	13.1 (±2.3)			13.0-17.0
Platelet (10^9/L)	183 (±85)			150-410
AST (U/L)		47 (31-80)		<41
ALT (U/L)		43 (24-81)		<42
Total Bilirubin (µmol/L)		11 (8-16)		<22
Albumin (g/L)	33 (±7)			35-52
Creatinine (µmol/L)		86 (71-110)		59-104
eGFR (mL/min/1.73m^2)		79 (54-96)		45-84
CKD (≥Stage 3)				
Yes			94 (28.1)	
No			241 (71.9)	
ESRF on dialysis			45 (13.4)	
International Normalised Ratio (INR)		1.0 (1.0-1.1)		
Fib-4 score		2.14 (1.18-4.78)		
Fibrosis stage by Fib-4 score[a]				
Stage 0			108 (32.2)	
Stage 1-2			113 (33.7)	
Stage 3-4			114 (34.0)	
APRI score		0.7 (0.4-1.4)		
Fibrosis stage by APRI score[b]				
Stage 0-1			157 (46.9)	
Stage 2-3			117 (34.9)	

Stage 4	61 (18.2)	
MELD 3.0 score	8 (6-12)	
MELD 3.0 score[c]		
Score <10	182 (54.3)	
Score 10-15	76 (22.7)	
Score 16-20	61 (18.2)	
Score >20	16 (4.8)	
Cirrhosis[d]		
Yes	117 (34.9)	
No	218 (65.1)	
Alpha Fetoprotein (AFP) (ng/mL)	4.43 (2.52-9.45)	≤7
Baseline HCV RNA (IU/ml)	813342 (78955-2113708)	

[#]Mean values are provided when the data is normally distributed, while median values are used for skewed data. [a]The fibrosis stage was determined as follows: FIB-4 index <1.45 indicated stage 0 (minimal or no fibrosis), 1.45-3.25 indicated stage 1-2 (significant fibrosis), and >3.25 indicated stage 3-4 (advanced fibrosis/cirrhosis)[2,26-28]. [b]The fibrosis stage was determined as follow: APRI <0.7 indicated stage 0-1 (no or minimal fibrosis), 0.7-2.0 indicated stage 2-3 (significant fibrosis), and >2.0 indicated stage 4 (advanced fibrosis/cirrhosis)[2,28,29]. [c]MELD 3.0 score of more than 10 is associated with a 3-month mortality rate of at least 6% among patients with chronic liver disease and the rate is increasing as the score increases[13-15]. [d]Based on APRI score≥ 1.5 and/or Fib-4 score≥ 3.25[12].

Supplementary Table 2. Association between demographic profile, laboratory investigation profile, virological profile, and treatment with SVR in chronic hepatitis C patients receiving DAA (*n*=335).

Variables		Crude OR for fail to achieve SVR (95% CI) [#]	*P*-value	Adjusted OR for fail to achieve SVR (95% CI)[#]	*P*-value
Age	<50	1			
	≥50	2.2 (0.9-4.9)	0.07		
Sex	Male	1			
	Female	0.58 (0.2-1.4)	0.24		
CKD	Yes	1			
	No	1.47 (0.6-3.3)	0.36		
Cirrhosis	No	1		1	
	Yes	2.4 (1.2-4.9)	0.011*	2.7 (0.01-841.7)	0.735
Fib-4 score	Stage 0	1		1	
	Stage 1-2	1.5 (0.5-4.1)	0.38	0.7 (0.2-3.6)	0.704
	Stage 3-4	2.8 (1.1-7.1)	0.02*	0.1 (0.0-53.6)	0.503
APRI score	Stage 0-1	1		1	
	Stage 2-3	0.8 (0.3-2.0)	0.77	0.3 (0.05-1.7)	0.160
	Stage 4	2.3 (1.0-5.2)	0.04*	0.1 (0.01-1.7)	0.111
MELD 3.0	Score <10	1		1	
	Score 10-15	9.4 (3.9-22.3)	<0.001*	4.6 (1.1-18.2)	0.031*
	Score 16-20	1.9 (0.6-6.1)	0.26	0.3 (0.04-3.0)	0.325
	Score >20	1.4 (0.1-12.3)	0.73		
HCV genotype	Others**	1		1	
	1, 1a	0.5 (0.1-4.0)	0.52	1.4 (0.1-27.4)	0.812
	3	2.4 (1.2-5.1)	0.01*	4.5 (1.1-17.6)	0.031*
HIV coinfection	Yes	1			
	No	0.7 (0.1-3.4)	0.69		
HBV coinfection	Yes	1			
	No	0.6 (0.1-2.4)	0.56		
Treatment regimen	Sofosbuvir/Daclatasvir	1		1	
	Sofosbuvir/Ravidasvir	0.7 (0.1-5.5)	0.73	0.02 (0.0-3.6)	0.140
	Sofosbuvir/Velpatasvir	4.9 (2.0-12.0)	<0.001*	6.1 (1.4-26.5)	0.015*
Ribavirin used	No	1		1	
	Yes	2.2 (1.0-4.8)	0.044*	0.5 (0.1-2.1)	0.373
Treatment duration	12 weeks	1		1	
	24 weeks	4.2 (2.0-9.2)	<0.001*	3.0 (0.7-12.5)	0.137

Treatment compliance	Yes	1		1	
	No	47.0 (18.5-119.7)	<0.001*	68.3 (16.3-285.0)	<0.001*
Haemoglobin, g/dL		0.8 (0.7-0.9)	0.04*	1.3 (1.0-1.7)	0.103
Platelet, 10^9/L		0.9 (0.9-1.0)	0.46		
Albumin, g/L		0.8 (0.8-0.9)	<0.001*	0.9 (0.8-1.0)	0.110
AST, U/L		1.0 (1.0-1.0)	0.006*	1.0 (0.9-1.0)	0.485
ALT, U/L		1.0 (0.9-1.0)	0.200		
Total bilirubin, µmol/L		1.0 (1.0-1.1)	<0.001*	1.1 (1.0-1.1)	0.003*
Creatinine, µmol/L		0.9 (0.9-1.0)	0.070		
eGFR, mL/min/1.73m^2		1.0 (0.9-1.0)	0.180		
INR		4.1 (0.7-21.7)	0.090		
Baseline HCV RNA, IU/mL		0.9 (0.9-1.0)	0.300		
AFP, ng/mL		1.0 (1.0-1.0)	0.070		

*Significant at P<0.05. #A value of 1 indicates the reference group. **Genotype 1 (n=1), Genotype 1,1b (n=6), Genotype 4 (n=1), and patients with no genotype record were grouped into others. Multiple logistic regression analysis incorporated variables with a P-value <0.05 derived from univariate analysis, was performed to determine the independent variables associated with the failure to achieve SVR.