

Original Article

A comparison of clinical and patient-reported treatment outcomes in chronic hepatitis C patients treated with direct-acting antivirals with and without cirrhosis: a prospective cohort study

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Abstract

Managing patients with chronic hepatitis C and progressive liver conditions poses significant challenges for healthcare professionals. This research sought to evaluate and compare the clinical outcomes and patient-reported treatment experiences of individuals with chronic hepatitis C, differentiating between those with and without cirrhosis, all of whom were receiving standard direct-acting antiviral (DAA) therapy. This prospective cohort study enrolled outpatients who were diagnosed with hepatitis C virus (HCV) infection and who were recruited from a major public tertiary care hospital. The participants received a standard 12-week antiviral regimen consisting of 400 mg of sofosbuvir (SOF) and 60 mg of daclatasvir (DCV) once daily, with or without ribavirin (RBV) at a dose of 400 mg taken two to three times daily. The primary outcome was the cure rate, which was defined as an undetectable viral load at the end of the 12-week treatment period. The secondary outcomes included patient-reported outcomes (PROs), such as health-related quality of life (HRQoL), which were measured via the EuroQol 5-Dimensions 3-Levels (EQ-5D-3 L) questionnaire, and work productivity loss, which was assessed via the Work Productivity and Activity Impairment (WPAI) questionnaire. A total of 300 participants were assessed, comprising 150 cirrhotic and 150 noncirrhotic patients. Group B (cirrhosis) had a greater proportion of treatment-experienced patients and elevated aspartate aminotransferase (AST) levels (48 ± 22 vs. 131 ± 165 , $p < 0.001$), along with significantly lower platelet counts ($p = 0.024$). An end-of-treatment response (ETR) was observed in 92.7% of patients without cirrhosis, whereas a significantly lower rate of 52.7% was observed in those with cirrhosis ($p < 0.001$). A significant increase in HRQoL was noted in both groups across all the EQ-5D-3 L domains ($p < 0.001$); however, patients with cirrhosis experienced relatively smaller improvements in the areas of pain/discomfort and anxiety/depression. A small subset of noncirrhotic patients showed no improvement in mobility (-0.59 ± 0.62). Regarding work productivity, both groups experienced substantial reductions in overall impairment (43.0% in noncirrhotic patients, 32.3% in cirrhotic patients), absenteeism, and activity limitations ($p < 0.001$). However, presenteeism increased slightly in both groups, suggesting a return to work with residual functional limitations. The study concluded that SOF-based regimens were highly effective in noncirrhotic patients, who showed greater improvements in virological response, quality of life, and work productivity. In contrast, cirrhotic patients demonstrated lower treatment response rates and smaller gains in patient-reported outcomes despite receiving similar therapies.

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Keywords

Hepatitis C, Liver cirrhosis, Sofosbuvir, Daclatasvir, Patient-reported outcome measures, Clinical pharmacy, Quality of life

1. Introduction

Hepatitis C virus (HCV) remains a major contributor to chronic liver disease and related complications globally and continues to significantly impact morbidity, mortality, and healthcare expenditures [1,2]. If left untreated or inadequately managed, over time, HCV infection can progress to severe hepatic complications such as hepatocellular carcinoma, fibrosis, and cirrhosis [3,4]. HCV infection poses a major public health challenge, particularly in low- and middle-income countries (LMICs), where timely diagnosis and access to standardized care remain constrained [5,6]. Recent global estimates show that HCV has affected more than 185 million people worldwide—an increase of nearly 2.8% in the past decade and a half [7]. In Pakistan, where the national prevalence of chronic HCV exceeds 5%, the burden is particularly high. Punjab, the country's most populous province, has reported prevalence rates as high as 6.5% [8]. Transmission primarily occurs through unsafe injection practices, transfusions, needlestick injuries, and intravenous drug use [9].

The primary objective in managing HCV is to achieve a virological cure, either through a sustained virological response (SVR)—defined as undetectable viral levels at 12 weeks (SVR12) or 24 weeks (SVR24) posttherapy—or by achieving an end-of-treatment response (ETR) [10]. With the advent of treatment modalities such as direct-acting antivirals (DAAs), the clinical landscape of HCV management has undergone a paradigm shift. Compared with earlier interferon-based therapies, DAAs, such as sofosbuvir (SOF)-based regimens, offer high rates of SVR, shorter treatment durations, improved tolerability, and minimal adverse effects [11,12]. Current clinical guidelines aim for SVR12, which is widely accepted as a surrogate marker for virologic cure [13]. These therapies have been proven effective across a wide range of patient profiles, including naïve to treatment, experienced treatment, and those with compensated liver cirrhosis [14,15].

Nevertheless, while clinical outcomes such as SVR and liver function normalization are well documented, there remains a critical gap in understanding how these treatments influence patients' lived experiences, particularly in LMICs such as Pakistan [16,17]. Patient-reported outcomes (PROs), which highlight the perspectives of patients without clinician interpretation, are increasingly recognized as essential components of treatment evaluation [18,19]. While viral eradication remains the cornerstone of therapeutic success, it does not fully capture how patients perceive their recovery, nor does it reflect the treatment's influence on daily functioning, mental well-being, social participation, and work productivity [20,21].

Notably, advanced liver disease presents complex clinical challenges, and patients with cirrhosis may experience different therapeutic responses, symptom burdens, and quality-of-life outcomes than those without cirrhosis. There is a lack of empirical data from Pakistan exploring distinctions, especially concerning PROs. The lack of such data limits the development of evidence-based, patient-centered treatment strategies across healthcare systems globally. Therefore, this study compared both patient-reported treatment experiences and clinical outcomes among chronic hepatitis C patients with and without cirrhosis receiving standard DAA therapy. By integrating clinical indicators such as SVR12 with PROs assessed through the EuroQol 5-Dimensions 3-Levels (EQ-5D-3L) and Work Productivity and Activity Impairment (WPAI) instruments, this study aims to gen-

erate holistic, locally relevant evidence to inform treatment guidelines, clinical counseling, and public health strategies in Pakistan.

2. Methodology

2.1. Study design and duration

This prospective cohort study was carried out over a six-month period spanning from May to November 2020.

2.2. Ethics approval

This study obtained ethics clearance from the Services Institute of Medical Sciences (SIMS), Lahore (No. IRB/2020/734/SIMS), and was approved by the Institutional Review Board (IRB) of Lahore College for Women University (LCWU), Lahore.

2.3. Study settings

This study was conducted at the Services Hospital, Lahore, a 1325-bed tertiary care referral and teaching hospital located in Lahore, Pakistan [22]. The hospital has a specialized clinic for liver and hepatitis, offering outpatient services for diagnosing, treating, and managing hepatitis C and other chronic liver diseases.

2.4. Sample size and sampling technique

The study sample was obtained via the OpenEpi online sample size calculator (version 3.01) [23], with a minimum of 101 participants per group calculated on the basis of a 95% confidence level, a 5% margin of error, and an anticipated proportion of 93% [24]. To increase the study's statistical power, the sample size was expanded to 150 participants per group, totaling 300 chronic HCV patients—150 with cirrhosis and 150 without cirrhosis—selected through a nonprobability purposive sampling technique.

2.5. Selection criteria

The study recruited adults (≥ 18 years) diagnosed with chronic hepatitis C, verified through detectable levels of HCV ribonucleic acid (RNA). Both naïve to treatment and experienced patients for treatment were included, provided that they had not previously received DAA therapy. Patients with or without cirrhosis, as confirmed through clinical or radiological evaluation, were enrolled. All participants needed to be eligible for the standard antiviral regimen of daclatasvir (DCV) and SOF, with or without ribavirin (RBV), and had to provide informed consent for enrollment and follow-up assessments at baseline and 12 weeks posttreatment. Patients with hepatitis B virus (HBV) or human immunodeficiency virus (HIV) coinfection, hepatocellular carcinoma, decompensated liver disease, pregnancy, lactation, treatment with investigational or nonstandard HCV therapies, or psychiatric or cognitive impairments that could obstruct the completion of PRO questionnaires were excluded.

2.6. Data collection procedure

All patients with chronic hepatitis C were screened for cirrhosis via the aspartate aminotransferase-to-platelet ratio index (APRI). Laboratory values for platelet count and aspartate aminotransferase (AST) levels were obtained from patient records. An APRI score of ≥ 1.5 was used to classify patients as cirrhotic, whereas a score < 1.5 indicated noncirrhosis [25,26].

The patients were categorized into two groups: Group A included individuals with chronic hepatitis C without cirrhosis, whereas Group B included those with cirrhosis. All patients received a standardized treatment regimen consisting of SOF 400 mg once daily and DCV 60 mg once daily. RBV 400 mg was additionally administered either twice or three times daily on the basis of clinical judgment and the specific characteristics of each patient. The treatment protocol was the same for both naïve patients and experienced patients; the latter had previously received interferon-based regimens but not DAAs [27]. Participants were prospectively followed over the 12-week treatment course to monitor their clinical response and assess changes in PROs at baseline and posttreatment.

2.7. Data collection tools

The EQ-5D-3 L is a commonly used instrument for evaluating health-related quality of life (HRQoL) [28]. It consists of two primary sections: a descriptive system of health states and a self-rated health assessment. The descriptive system includes five areas: self-care, mobility, pain/discomfort, usual activities, and anxiety/depression. Participants assessed their overall health status via a visual analog scale (VAS) at the time of evaluation.

The WPAI questionnaire is a well-established tool for assessing disruptions in both work performance and daily activities [29]. In this study, participants provided insights into how the hepatitis C virus (HCV) affects their productivity at work and in routine daily tasks. The work impairment score reflects the combined impact of missed work (absenteeism) and reduced efficiency while on the job (presenteeism) and was evaluated only for those who identified as employed. Conversely, the activity impairment score captures limitations in nonwork-related daily functions and was assessed across all participants, irrespective of their job status. Notably, high scores on this instrument correspond to worse health-related outcomes.

Each domain was calculated as a percentage (%) via the standard WPAI scoring formula:

$$\text{Absenteeism} = (\text{Total hours scheduled to work} \div \text{Hours missed due to health}) \times 100 \quad (1)$$

$$\text{Presenteeism} = (\text{Self-rated impairment at work} \div 10) \times 100 \quad (2)$$

$$\text{Work productivity loss} = \text{Absenteeism} + [(1 - \text{Absenteeism}) \times \text{Presenteeism}] \quad (3)$$

$$\text{Activity impairment} = (\text{Self-rated activity impairment} \div 10) \times 100 \quad (4)$$

Individual scores were calculated for each patient via these formulas [30]. The mean percentage scores for each domain were then computed by averaging the individual values:

$$\text{Mean score (\%)} = (\text{Sum of all individual percentage scores}) \div (\text{Number of individuals}) \quad (5)$$

In addition to the five dimensions of the EQ-5D-3 L descriptive system, the study also assessed absenteeism, presenteeism, work productivity, and activity limitations before and after treatment. The instrument used for data collection was divided into five sections: informed consent from participants, demographic details, laboratory test results, self-reported patient outcomes, and the clinical management of hepatitis C.

2.8. Statistical analysis

Descriptive statistics were used to summarize the collected data via SPSS, version 25.0 (SPSS Inc., Chicago, IL, USA). An independent samples t test was applied to compare

the mean values between the cirrhotic and noncirrhotic groups. Paired samples t tests were conducted to assess within-group changes in PROs, including HRQoL, as measured by the EQ-5D-3 L, and work-related impairments, as measured by the WPAI questionnaire, before and after treatment.

3. Results

3.1. Participant characteristics

Among the 300 patients evaluated in this study, half ($n = 150$) did not have cirrhosis and were placed in Group A, whereas the other half ($n = 150$) had cirrhosis and were assigned to Group B. In Group A, 39 (26.0%) were aged 20–40 years, 98 (65.3%) were aged 41–60 years, and 13 (8.7%) were older than 60 years. In Group B, 44 (29.3%) were between 20–40 years, 93 (62.0%) were 41–60 years, and 13 (8.7%) were older than 60 years. The sex distribution in Group A was 50% male ($n = 75$), and that in Group B was 54.7% male ($n = 82$). Most participants in both groups were married: 95.3% and 97.4% in both groups, respectively. With respect to economic status, 72.7% and 80.0% of the respondents in both groups reported monthly incomes of less than 15,000 rupees. A smaller percentage earned between 15,000 and 50,000 rupees, 26.7% and 20% in both groups, respectively. Only one individual (0.7%) in Group A earned above this range. Employment was reported by 64 participants (42.7%) and 54 (36.0%) in the two groups, respectively.

In terms of clinical indicators, 107 (71.3%) noncirrhotic patients had HCV viral loads exceeding 10/IU/mL, whereas 115 (76.7%) patients in the cirrhotic group did. AST levels were elevated in 98.0% ($n=147$) of Group B patients compared with 51.3% ($n = 77$) of Group A patients ($p < 0.001$). Platelet counts were lower in cirrhotics, averaging 121 ± 56 versus 253 ± 73 in noncirrhotics ($p = 0.024$). Ultrasound findings revealed a coarse liver texture in 63.3% of the cirrhotic patients, whereas only 9.3% ($n = 14$) of the noncirrhotic patients had similar findings. The source of infection was unknown in 30.7% and 28.7% of patients in both groups, whereas nonoccupational or iatrogenic transmission accounted for 68.0% and 70.0%, respectively, in both groups. Drug abuse was reported in 1.3% of both groups. Additionally, 88.7% ($n = 133$) of the noncirrhotic patients were treatment naïve, whereas 70.0% ($n = 105$) of the cirrhotic patients were treatment naïve.

Table 1. Baseline sociodemographic and clinical features of the patients ($N = 300$).

Variables		Noncirrhotic Group A $n = 150$	Cirrhotic Group B $n = 150$
		Frequency (%)	Frequency (%)
Age	20 – 40 years	39 (26.0)	44 (29.3)
	41 – 60 years	98 (65.3)	93 (62.0)
	> 60 years	13 (8.7)	13 (8.7)
Male		75 (50.0)	82 (54.7)
Marital status (married %)		142 (95.3)	145 (97.4)
Income per month (in Pakistani rupees)	< 15,000	109 (72.7)	120 (80.0)
	15,000 – 50,000	40 (26.7)	30 (20.0)
	> 50,000	1 (0.7)	0 (0.0)
Employed		64 (42.7)	54 (36.0)
HCV viral load $n > 10^6$ (%)		107 (71.3)	115 (76.7)
AST > Upper limit normal (ULN) (Mean $\pm$ SD) *		48 $\pm$ 22	131 $\pm$ 165 **
n > ULN		77 (51.3)	147 (98.0)
Platelets $10^9/l$ (Mean $\pm$ SD) *		253 $\pm$ 73	121 $\pm$ 56 ***
Liver coarseness on ultrasonography		14 (9.3)	95 (63.3)

Variables		Noncirrhotic Group A n = 150	Cirrhotic Group B n = 150
		Frequency (%)	Frequency (%)
Source of Infection	Unspecified	46 (30.7)	43 (28.7)
	Nonoccupational/iatrogenic	102 (68.0)	105 (70.0)
	Drug abuse	2 (1.3)	2 (1.3)
	Treatment naïve	133 (88.7)	105 (70.0)

*Independent samples t test used to compare group means. ** p value < 0.001. *** p value = 0.024.

3.2. Prescribed treatment and cure rate

In the noncirrhotic patient group, 65.3% ($n = 98$) were treated with SOF/DCV, whereas the remaining 34.7% ($n = 52$) received a combination of SOF/DVC and RBV. In contrast, among the cirrhotic patients, 60.7% ($n = 91$) were administered SOF/DCV/RBV, and 39.4% ($n = 59$) were given SOF/DCV. ETR, marked by an undetectable viral load after 12 weeks, was achieved by 92.7% ($n = 139$) of individuals in the noncirrhotic patient group. Only 52.7% ($n = 79$) of the cirrhotic patients achieved this outcome, indicating a statistically significant difference ($p < 0.001$).

3.3. Effect of treatment on PROs (EQ-5D-3 L)

In the noncirrhosis group, the mean improvements in the EQ-5D-3 L domains from baseline to posttreatment were as follows: 0.58 (mobility), 0.11 (self-care), 0.43 (usual activities), 0.43 (pain/discomfort), and 0.69 (anxiety/depression). In the cirrhosis group, the corresponding mean improvements were 0.59, 0.24, 0.46, 0.16, and 0.46, respectively (all $p < 0.001$; Table 2).

In the cirrhosis group, the PRO scores significantly improved across all the domains ($p < 0.001$ for each). By the end of the 12-week treatment period, the noncirrhotic group demonstrated significant improvements in pain/discomfort, usual activities, and anxiety/depression. However, a subset of these patients showed no improvement in mobility (mean score: 0.59) (Table 2).

Table 2. Effect of treatment on PROs in noncirrhotic and cirrhotic patients who achieved ETR.

EQ-5D-3 L Domains	Noncirrhotic Group A			Cirrhotic Group B		
	MD ± SD	95% CI (difference)	<i>p</i> value *	MD ± SD	95% CI (difference)	<i>p</i> value *
		Lower – Upper			Lower – Upper	
Mobility	-0.58 ± 0.49	-0.67 to -0.49	< 0.001 *	-0.59 ± 0.62	-0.70 to -0.47	< 0.001 **
Self-care	-0.11 ± 0.32	-0.17 to -0.06	< 0.001 *	-0.24 ± 0.54	-0.35 to -0.14	< 0.001 **
Usual activities	-0.43 ± 0.64	-0.55 to -0.32	< 0.001 *	-0.46 ± 0.67	-0.85 to -0.33	< 0.001 **
Pain/discomfort	-0.43 ± 0.54	-0.52 to -0.33	< 0.001 *	-0.16 ± 0.45	-0.24 to -0.07	< 0.001 **
Anxiety/depression	-0.69 ± 0.50	-0.78 to -0.60	< 0.001 *	-0.46 ± 0.64	-0.58 to -0.34	< 0.001 **

* Paired samples t test. ** $p < 0.05$, statistically significant. *** Patients who achieved SVR12 were included in the analysis and completed both pre- and posttreatment EQ-5D-3 L assessments. **** Of the 150 patients initially enrolled per group, only 122 from Group A (noncirrhotic) and 62 from Group B (cirrhotic) were included due to incomplete data or missed assessment timelines. ***** The instrument's descriptive system covers five core dimensions, including self-care, mobility, pain/discomfort, usual activities, and anxiety/depression, denoted as SC, MB, PD, UA, and AD, respectively.

3.4. Effect of treatment on WPAI

Among noncirrhosis patients, significant improvements were observed across all WPAI domains following treatment. The mean work productivity impairment score de-

creased from 65% (95% CI: 57.3–72.7) at baseline to 22% (95% CI: 17–27) after 12 weeks of treatment, reflecting a 43.0% absolute improvement ($p < 0.001$). Similarly, absenteeism was significantly reduced from 15.4% (95% CI: 8.5–22.3) to 1.3% (95% CI: –0.7–3.3) ($p < 0.001$), representing a 14.1% absolute decrease. However, presenteeism increased slightly from 40.8% (95% CI: 31.9–49.7) to 52.0% (95% CI: 45.5–58.8) ($p < 0.001$), suggesting that patients remained at work but perceived reduced effectiveness. Notably, activity impairment significantly decreased from 55.0% (95% CI: 46.5–63.5) to 25.0% (95% CI: 22–28) ($p < 0.001$), indicating a 30.0% improvement in daily functioning. (Table 3).

In the cirrhosis group, similar patterns of improvement were observed. Work productivity impairment declined from 74.3% (95% CI: 67.4–81.2) to 42.0% (95% CI: 34.5–49.3), representing a 32.3% reduction ($p = 0.003$). Absenteeism decreased significantly from 22.9% (95% CI: 14.2–31.6) to 9.4% (95% CI: 4.6–14.1) ($p < 0.001$). However, presenteeism increased from 40.1% (95% CI: 30.2–49.9) to 51.9% (95% CI: 41.5–62.3) ($p < 0.001$), echoing findings in the noncirrhotic group. A marked improvement in activity impairment was observed, decreasing from 82.9% (95% CI: 79.8–85.9) to 54.0% (95% CI: 50.4–58.2) ($p < 0.001$), corresponding to a 28.9% absolute reduction (Table 3).

Table 3. Comparison of WPAI domains before and after 12 weeks of antiviral therapy in cirrhotic and noncirrhotic patients.

Domain	Group	Before Treatment	After 12 Weeks	Absolute Change (%)	p value
		Mean Score (%) 95% CI	Mean Score (%) 95% CI		
Work productivity impairment	Non-Cirrhosis	65.0 (57.3–72.7)	22.0 (17–27)	↓ 43.0	< 0.001 ***
	Cirrhosis	74.3 (67.4–81.2)	42.0 (34.5–49.3)	↓ 32.3	0.003 ***
Absenteeism	Non-Cirrhosis	15.4 (8.5–22.3)	1.3 (–0.7–3.3)	↓ 14.1	< 0.001 ***
	Cirrhosis	22.9 (14.2–31.6)	9.4 (4.6–14.1)	↓ 13.5	< 0.001 ***
Presenteeism	Non-Cirrhosis	40.8 (31.9–49.7)	52.0 (45.5–58.8)	↑ 11.2	< 0.001 ***
	Cirrhosis	40.1 (30.2–49.9)	51.9 (41.5–62.3)	↑ 11.8	< 0.001 ***
Activity impairment	Non-Cirrhosis	55.0 (46.5–63.5)	25.0 (22–28)	↓ 30.0	< 0.001 ***
	Cirrhosis	82.9 (79.8–85.9)	54.0 (50.4–58.2)	↓ 28.9	< 0.001 ***

* Paired samples t tests were used to assess within-group changes in WPAI scores before treatment and at SVR12. ** Mean percentage scores were calculated by averaging individual WPAI domain scores across each group. *** $p < 0.05$, statistically significant. **** A higher WPAI score indicates greater impairment in work or activity, whereas a lower score reflects improved functioning and less impairment. ***** Absolute change was calculated as the difference between the mean score before treatment and after 12 weeks: (before treatment mean – after treatment mean).

4. Discussion

This study examined three key aspects of hepatitis C in patients with or without cirrhosis. First, we assessed the cure rates after a 12-week antiviral therapy course. The results revealed that noncirrhotic patients had higher cure rates than did patients with cirrhosis. Second, the study evaluated PROs before and after treatment. Initial findings indicated that both groups experienced significant impairments in PROs, including lower HRQoL and decreased work productivity. However, treatment with DAAs resulted in substantial improvements in these areas, regardless of cirrhosis status. The standard regimen, which included SOF/DCV/RBV, played a major role in these improvements. Finally, the study compared the two groups. Cirrhotic patients had more severe impairments in HRQoL and work productivity at baseline. While both groups improved after treatment, noncirrhotic patients gained relatively greater benefits.

Our finding that outcomes are better in noncirrhotic patients is supported by research on hepatitis C virus-related hepatocellular carcinoma and indicates that the fibrosis patterns in noncirrhotic HCC patients differ on the basis of the underlying cause of

their liver disease. Furthermore, even patients with advanced hepatocellular carcinoma who do not have cirrhosis experience significantly longer survival than those with cirrhosis [31]. In a British study, the median survival of patients with cirrhotic hepatocellular carcinoma was 19.6 months, which was lower than the 24.5-month median survival for those with noncirrhotic HCC ($p = 0.05$) [32]. An American study indicated that HCV treatment significantly reduces the incidence of nonhepatic cancers among HCV-infected patients. These findings suggest that treating HCV can decrease the risk of extra-hepatic cancers associated with chronic HCV infection, despite differences among specific cancer types or HCV therapy subgroups [33]. However, a study conducted at the University Hospital in Bern reported no significant differences in complication rates between patients with cirrhosis and those without cirrhosis [34].

The literature has shown differences in treatment outcomes between patients with genotype 2 and genotype 3 disease, indicating that those with genotype 3 disease typically require a longer course of therapy to achieve a sustained virologic response [35]. A randomized controlled trial revealed high sustained virologic response rates with SOF in patients with genotypes 2 and 3, who had no further treatment options after interferon-based therapy failed [36]. A previous investigation involving HCV-infected individuals examined the impact of cirrhosis and related complications on PROs during therapy with newly introduced anti-HCV treatments. The findings indicated that both cirrhotic and noncirrhotic patients were generally able to tolerate treatment regimens containing SOF and RBV, with or without pegylated interferon-alpha, as reflected by their PRO scores. Following an SVR12 via an interferon-free regimen, individuals with cirrhosis demonstrated improvements in certain dimensions of their PROs [25]. Another study utilized four different instruments to assess HRQoL and functional outcomes: HRQoL, including the Short SF-36, FACIT-F, CLDQ-HCV, and WPAI questionnaires. Compared with the placebo, the use of SOF and velpatasvir, either alone or in combination with voxilaprevir, has been shown to increase PRO scores. These results highlight the broad therapeutic advantages of these regimens, both during the course of treatment and following the achievement of SVR [29].

A randomized phase III study evaluated a 12- to 16-week treatment course featuring a combination of SOF, DCV, and RBV for patients with genotype 3 HCV and advanced liver disease. These results suggest that combination therapy is effective and generally well tolerated in genotype 3 patients, irrespective of their treatment history, whether treatment-naïve or previously treated [27]. A prospective observational study demonstrated the effectiveness of DAAs on the HRQoL of patients with chronic hepatitis C. HRQoL was assessed via the EQ-5D-3 L questionnaire at the beginning and again after 12 weeks of treatment. The findings revealed notable enhancements in mobility, pain management, anxiety levels, daily activities, and self-care [37]. A prospective cohort study reported that patients receiving interferon-free antiviral therapies show notable improvements in PROs. However, comorbid conditions such as diabetes mellitus, cirrhosis, and HIV coinfection tend to negatively influence HRQoL before, throughout, and following hepatitis C treatment [38]. Furthermore, incorporating RBV into treatment regimens may adversely impact HRQoL scores during therapy [39].

This study provides valuable insights by integrating both clinical outcomes and PROs to assess the effectiveness of DAAs among individuals with chronic hepatitis C, regardless of cirrhosis status, particularly in low-resource settings. The prospective design, use of validated tools (EQ-5D-3 L and WPAI), and real-world data from a high-volume tertiary care liver clinic increase the study's applicability and relevance. However, the study is limited by its single-center design, which may affect generalizability, and the relatively short follow-up period was restricted to 12 weeks posttreatment, which may

not capture longer-term PROs. Additionally, potential recall bias in self-reported data and the lack of genotype-specific analysis could influence the results.

5. Conclusions

This study revealed that chronic hepatitis C patients without cirrhosis who received SOF/DCV/RBV standardized treatment experienced significantly greater improvements in HRQoL and other PROs than did patients with cirrhosis, who showed smaller gains and less improvement in clinical outcomes. In both groups, improved PROs were accompanied by better work productivity and reduced activity impairment.

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