

# Comparison of Clinical and Patient Reported Outcomes of Treatment with Directly Acting Antivirals in Hepatitis C With and Without Cirrhosis: A Prospective Cohort Study

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## Research Article

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# Abstract

## *Background*

Chronic hepatitis C including liver cirrhosis poses challenges in treatment despite the availability of direct acting antivirals.

## *Aim*

To compare clinical and patient reported outcomes of routinely used pharmacotherapy in Hepatitis C infection (with or without cirrhosis).

## *Methods*

A prospective cohort study was undertaken recruiting outpatients from a large referral tertiary care hospital. Patients who were diagnosed of having Hepatitis C Virus (HCV) infection and presented with or without cirrhosis were included. A standard 12 weeks treatment comprising Sofosbuvir (SOF) 400mg O.D/ Daclatasvir (DCV) 60mg O.D with and without Ribavirin (RBV) 400mg B.D or T.I.D was used. The cure rate in terms of end-of-treatment response at the end of 12 weeks treatment and patient reported outcomes (PROs) in terms of health related quality of life using EQ-5D-3L and work productivity loss were determined.

*Results* The treatment regimen was found to be effective treatment in non-cirrhotic group in terms of cure rate compared to the cirrhotic patients (92.6 % vs 53%; p value<0.05). Cirrhotic patients showed significantly low score of PROs before initiating the treatment. After 12 weeks' treatment, significantly higher rate of improvement was observed in non-cirrhotic patients' PROs compared to cirrhotic group (p-value; <0.05).

## *Conclusion*

DAAs showed higher effectiveness in clinical outcomes and patient reported outcome measures in chronic hepatitis C patients without cirrhosis compared to those with cirrhosis. It is imperative to develop and optimize further effective treatment options for cirrhotic CHC patients.

## Impacts On Practice

- In real world setting, commonly utilised pharmacotherapy involving direct acting antivirals show higher effectiveness in clinical outcomes and patient reported outcome measures in chronic hepatitis C patients without cirrhosis compared to those with cirrhosis.
- There is a need to develop and optimize further effective treatment options for cirrhotic chronic hepatitis C patients.

## Introduction

Hepatitis C virus (HCV) is a major cause of chronic liver diseases globally and the leading cause of morbidity and mortality [1]. HCV is the main source of advanced and chronic liver diseases, carcinomas, and cirrhosis [2–4]. Hepatitis C (Hepatitis C) is a progressive disease and presents significant clinical issues worldwide [5]. The most recent disease burden shows an approximately 2.8% increase equalling to >185 million infections in the last 15 years [6].

Pakistan has the 2nd highest prevalence rate of chronic hepatitis and deaths due to liver failure in the World [3]. Hepatitis C in paediatric population prevalence is 2.1% (range 0.4-5.4%) while adult population prevalence is 3% (range 0.3-31.9%) [3]. The highest prevalence of Hepatitis C is found in Punjab, the largest Pakistan province. It is higher in males (15.1%) than in females (12.3%). Blood transfusions, drug abuse, injections in health care settings, occupational risks, and infected needle prick are the major cause of HCV infections [5]. Hepatitis C and viral clearance pathogenesis depends upon the immune response to viral antigens. The development of HCV infections occurs if associated with a weak immune response to viral antigens [7]. Anti HCV antibodies, enzyme immunoassay (EIA), and rapid diagnostic tests (RDTs) are used for detecting and diagnosing of HCV infection [8].

The goal of HCV treatment is to attain end-of-treatment (ETR) or a sustained virological response (SVR) measured as virus not-detected at 12 weeks or 24 weeks post end of treatment i.e; SVR12 and SVR24 [9]. Currently, Sofosbuvir, a newly licensed DAA, is being administered once daily with or without ribavirin for 12-24 weeks as a standard treatment in Hepatitis C [8]. Fatigue and headache are the most commonly observed side effects when given in combination with ribavirin [9]. However, treatment regimen comprising oral Direct Acting Antiviral (DAAs) have proven effective in Hepatitis C patients as higher cure were observed at SVR12 in non-complicated patients. All the treatment naïve and treatment-experienced patients were successfully treated and have no contraindication for this treatment [9–10]. The treatment of chronic Hepatitis C (CHC) with DAA has higher cure rates, fewer side effects, and shorter treatments duration. Nevertheless, the influence of these regimes on the lifestyle and quality of life (QOL) of the patients is infrequently monitored. The data on the efficiency of these regimes combined with patient-reported outcomes (PROs) such as health-related quality of life (HRQoL) and work productivity and activity impairment (WPAI) is scarce [11].

PROs are defined as measurements based on words that come from patients' health status directly without any interpretation by a clinician or anyone else. ETR and SVR are indicators of clinical outcomes, whereas PROs are used to evaluate patient experiences with disease and its treatments [11–12]. HRQoL includes patients' self-reports for their physical, mental, social, environmental, economic, and spiritual values. Work productivity is measured through presenteeism and absenteeism and is defined as the economic productivity of a workplace in which worker productivity is the main part of the overall productivity of the workplace [11]. Advanced treatment of Hepatitis C “DAA” shows high response rate and therapy goal is to improve liver functions and HCV symptoms [13].

Patients with CHC and advanced liver diseases as cirrhosis are a challenging population and urgently need appropriate, safe and effective treatment. Pakistan has second highest prevalence of CHC however,

lack data and practice related to newer therapies and PROs [14]. Currently, a standard combination of Daclatasvir (DCV), Sofosbuvir (SOF) with or without Ribavirin (RBV) is being administered in majority of clinical settings in Pakistan. However, there is a dearth of literature reported from Pakistan regarding PROs and effectiveness of this treatment regime.

## **Aim Of The Study**

This study aimed to compare clinical and patient reported outcomes of routinely used pharmacotherapy in Hepatitis C infection (with or without cirrhosis).

## **Ethics Approval**

Ethical approval for the use of the data collection form taken from the Ethical Review Board of the Lahore College for Women University, Lahore Pakistan and the other respective institutions. Permission to use EQ-5D-3L and WPAI was acquired from the European quality of life scale (EuroQol) department and Research and Development (RAND) healthcare centre. The research held in liver clinic Services hospital Lahore Pakistan. Institutional review board, Services institute of medical sciences, allowed the ethical permission with letter no. IRB/2020/734/SIMS to perform research in the institute. All patients were elaborated regarding the study prior to obtain the consent and administration of questionnaire.

## **Method**

### **Study Setting**

The study was conducted at a referral tertiary care hospital, the Services Hospital, Lahore Pakistan. This hospital is 1325 bedded teaching hospital and has a dedicated liver/ hepatitis clinic.

### **Study design**

A prospective cohort study was conducted, comparing CHC patients without cirrhosis (group A) and CHC patients with cirrhosis (group B) at the end of 12 weeks of standardized treatment. The standardized treatment regime included Daclatasvir (DCV) 60mg once a day and Sofosbuvir (SOF) 400mg once a day with or without Ribavirin 400mg twice a day or three times a day (RBV) for 12 weeks. Standardized treatment was prescribed to both treatment naïve and treatment-experienced patients [15]. All patients were followed up at the end of 12 weeks treatment. The treatment-experienced patients had taken interferons based treatments however, did not get this standardized treatment previously.

### **Sample size**

The sample size was calculated using the World Health Organization sample size calculator. The calculated sample size contained 300 patients; wherein 150 patients of chronic hepatitis C with cirrhosis

and 150 patients without cirrhosis, meeting the eligibility criteria, were included in the study through non-probability purposive sampling technique.

## **Participants and eligibility**

All adult outpatients diagnosed with chronic hepatitis C (any genotype), both treatment naïve and treatment-experienced (with or without cirrhosis), were included in the study.

Patients having current complaint or previous history of hepatic decompensation (e.g. ascites, jaundice, encephalopathy, or variceal haemorrhage), pregnant women, comorbidities, chronic illness, previous surgeries, and paediatric population were excluded.

All CHC patients were screened for the absence or presence of cirrhosis. The APRI scale was used to identify the presence of cirrhosis. The values of platelets and AST were collected from the reports of CHC patients. The patients were declared cirrhotic if APRI score  $\geq 1.5$  and non-cirrhotic if APRI score was found  $< 1.5$  [16].

## **Data collection of PROs**

PROs data was collected through face-to-face interview with the patients, The data were collected before and at the end of 12 weeks' treatment using standardized and validated data collection tools; the EQ-5D-3L (Euro QoL-5dimensions- 3levels) and WAPAI (work productivity and activity impairment questionnaire) through researcher administered survey. Data on detailed medical history was obtained before initiation and after completion of the standardized treatment.

## **Data sources and variables**

EQ-5D-3L is a widely used tool for health-related quality of life (HRQoL) evaluation. It has two components health state description and evaluation. Health state was measured in 5 dimensions: Mobility (MB), self-care (SC), usual activities (UA), pain/discomfort (PD), and anxiety/depression (AD). During assessment, respondents reported overall health status using a visual health scale [17].

WAPAI is another widely used and validated instrument to measure impairment in work and activities. In this study, patients were asked regarding the effect of HCV infection on work productivity and daily life activities. The work impairment domain is a sum of impairment in work productivity resulting from absenteeism and decreased productivity while working (presentism). The domain analysed only in those patients who reported being employee during administering the questionnaire. Activity impairment domain presents impairment in daily activities other than work and it was determined in all patients regardless of their employment status. In this instrument, a higher impairment score indicates poorer health status [18].

Total nine variables mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, presentism, absenteeism, activity impairment and work productivity impairment were analysed before and after the treatment. The data collection tool consisted of five parts, including patients consent,

patients' demographics, patients' lab reports value, patients reported outcome and management of hepatic C.

## **Statistical methods**

The data were analysed by using SPSS version 25.0. Simple descriptive and inferential statistics was applied. The descriptive data were represented as mean, frequency, standard deviation and percentages to summarize. An independent sample t-test was applied to compare the means. A paired sample t-test was applied to evaluate the patients' reported outcomes before and after the treatment. Pearson Chi-Square test was applied to check the association between the improvements of both groups i.e cirrhosis and non-cirrhosis groups.

## **Results**

### **Characteristics of the study participants**

Out of the 300 chronic hepatitis C patients enrolled for the study, 150 patients without cirrhosis and 150 patients with cirrhosis were enrolled and categorized as groups A and B respectively. Table 1 shows the patients' demographic profile and clinical lab report values. In non-cirrhosis group there were 100 patients aged 35 years or above, while in group B there were 124 participants. Non cirrhosis included 50% male and 50% female, while cirrhosis group included 54% male and 46% female (Table 1). Most of the patients 72-80% belonged to lower socio-economic strata, and their income was less than 15000 rupees (approximately 90 USD) per month. Almost 20-26.7% participants had monthly household income between 15000-50000 rupees (90-302.4 USD) per month. Only 1% of the patient income had a household income of more than 50000 rupees (302.4 USD) per month. There were 43% of participants who were employed in non-cirrhosis while 36% in cirrhosis.

**Table 1**  
**Demographic and baseline clinical characteristics of the study participants**

Parameters	Group A (Non-cirrhotic) (n=150)	Group B (cirrhotic) (n=150)
<b>Age (years)</b>		
20-40	39(26%)	44(29.3%)
41-60	98(65.3%)	93(62.0%)
>60	13(8.7%)	13(8.7%)
<b>Male n (%)</b>	75 (50%)	82 (54%)
<b>Marital status (married %)</b>	95.3%	97.4%
<b>Income per month</b>		
<15000	109(72.7%)	120(80%)
15000-50000	40(26.7%)	30(20%)
>50000	1(0.7%)	
<b>Employed n (%)</b>	43%	36%
<b>HCV viral load n&gt; 10<sup>6</sup> (%)</b>	107 (71%)	115(77%)
<b>AST &gt; ULN (M±S,D)</b>	48±22	131±165*
<b>(n&gt;ULN &amp;%)</b>	77(51%)	147(98%)
<b>platelets 10<sup>9</sup>/l (M±S.D)</b>	253±73	121±56**
<b>Coarse liver on USG</b>	14(9.3%)	95(63%)
<b>Mode of acquiring infections</b>	46(30.7%)	43(28.3%)
Unknown	102(68%)	105(70%)
Non-occupational/ iatrogenic	2(1.3%)	2(1.3%)
<b>Drug abuse</b>		
<b>Treatment naïve n (%)</b>	133 (88.6%)	105(70%)
<b>*P-value =0.000, **P-value=0.024</b>		

Treatment experienced patients had taken other than standardized treatments previously were less in non-cirrhosis (11.4%) than cirrhosis (30%). In cirrhosis 115 patients while in non-cirrhosis 107 have HCV viral load n>10<sup>6</sup>. AST values were found enormously increased (98%) in cirrhosis patients as compare to

non-cirrhotic patients (51%) (P-value=0.000). Platelets values were found lower in cirrhosis patients than no cirrhosis group (P-value=0.024). Nearly all the cirrhotic patients' liver was found fibrotic and coarse. The most common reason for mode of acquiring infection HCV was non-occupational or iatrogenic (68-70%) cases, while in 43-46% of cases, it was not known. (Table 1)

This descriptive analysis inferred that cirrhotic patients' group included relatively older population, more male and fewer treatment naïve patients. The AST values were very high and platelet count was very low in the cirrhosis group as shown in Table 1. High AST values reflected severe injury of hepatic cells and low platelet count likely to be due to two reasons: low thrombopoietin production and bone marrow suppression.

## Prescribed treatment for CHC patients with/ without cirrhosis and cure rate

In group A (non-cirrhotic), 65.3% of patients were given SOF/DCV, while 34.7% took SOF/DCV/RBV. In group B (cirrhotic), more patients (60.6%) were prescribed SOF/DCV/RBV and only 39.4% were prescribed SOF/DCV.

In non-cirrhotics, 92.6% of patients achieved ETR and PCR was found negative at the end of 12 weeks treatment. In cirrhotic patients, only approximately half of the patients (53%) achieved ETR (p-value=0.000). (Table 2)

**Table 2**  
Cure rate in chronic hepatitis C patients with and without cirrhosis

Group	ETR achieved n (%)	ETR not achieved n (%)
A	113 (92.6%)	9 (7.4%)
B	62 (53%)	52 (44.4%)

\*ETR= End-of-treatment response.

## Effect of treatment on Patient Reported Outcomes assessed by EQ-5D-3L scores

In non-cirrhotic group, mean score of mobility, self-care, usual activities, pain/discomfort, and anxiety were 0.58, 0.11, 0.43, 0.43 and 0.69 respectively whereas, in cirrhotic group the above domains scored as -.59, 0.24, 0.46, 0.16 and 0.46 respectively that inferred to be significant (p-value <0.05). The details of HRQoL scores as assessed by EQ-5D-3L are provided in Table 3.

**Table 3**  
Effect of treatment on Patient Reported Outcomes score (EQ-5D-3L)

Group A †					
EQ-5D	Mean (m)	Std. Deviation (S.D)	95% confidence interval of the difference		p-value*
			Lower	Upper	
Mobility	-0.58	0.49	-0.67	-0.49	<0.05
Self-care	-0.11	0.32	-0.17	-0.06	<0.05
Usual activities	-0.43	0.64	-0.55	-0.32	<0.05
Pain/discomfort	-0.43	0.54	-0.52	-0.33	<0.05
Anxiety/depression	-0.69	0.50	-0.78	-0.60	<0.05
Group B ‡					
EQ-5D	Mean (m)	Std. Deviation (S.D)	95% confidence interval of the difference		p-value*
			Lower	Upper	
Mobility	-0.59	0.62	-0.70	-0.47	<0.05
Self-care	-0.24	0.54	-0.35	-0.14	<0.05
Usual activities	-0.46	0.67	-0.58	-0.33	<0.05
Pain/discomfort	-0.16	0.45	-0.24	-0.07	<0.05
Anxiety/depression	-0.46	0.64	-0.58	-0.34	<0.05
*Paired sample t-test. Patients who achieved SVR 12; †Non cirrhosis (group A) (n=122)					
‡Cirrhosis (group B) (n=62)					

In cirrhotic group, PROs were improved markedly, and all *p*-values were significantly improved (*p*-value < 0.05). The statistical analysis also confirmed a significant improvement in PROs. In non-cirrhosis, at the end of 12 weeks' treatment, significant improvements were seen in pain/discomfort, usual activities, and anxiety/depression. There were few patients who showed less improvement 2(1.6%) and 13(10.7%) in self-care and mobility respectively post end of 12 weeks treatment. (Table 3)

## Effect of Treatment on PRO Score in Patients assessed by WAPAI scores

Only 26% of group A (non-cirrhotic) patients had employment to earn their livelihood. The percentage of productivity impairment and activity impairment was very high at baseline, while at the end of 12 weeks of treatment, both variables were improved (*p*-values < 0.001). Absenteeism was improved and decreased

from 15.4–1.3% ( $p$ -values < 0.001). Presentism was also improved and increased from 40 to 52% (Table 4).

**Table 4**  
Effect of treatment on PRO score in patients of group A (non-cirrhotic) and B (cirrhotic) who achieved end-of-treatment response (ETR).

WAPAI	Group A	Group B						
Currently Employed	39(26%)	36(24%)						
WAPAI	Group A			Group B			p-value (%)*	
	Before treatment			At end of 12 weeks treatment				
	N	%	95% CI	N	%	95% CI		
Work Productivity Impairment	39	65	4.73-6.35	29	22	1.7-2.7	<0.001(43.0%)	
Absenteeism	39	15.4	8.5-22.3	29	1.3	-0.7-3.3	<0.001(14.1%)	
Presentism	39	40.8	31.9-49.7	29	52	45.5-58.8	<0.001(11.2%)	
Activity Impairment	150	55	6.15-6.87	122	25	2.2-2.7	<0.001(30.0%)	
WAPAI	Group A			Group B			p-value*	
	Before treatment			At end of 12 weeks treatment				
	N	%	95% CI	N	%	95% CI		
Work Productivity Impairment	36	74.3	67.4-81.2	31	42	34.5-49.3	0.003(32.3%)	
Absenteeism	36	22.9	14.2-31.6	29	9.4	4.6-14.1	<0.001(13.5%)	
Presentism	36	40.1	30.2-49.9	29	51.9	41.5-62.3	<0.001(11.8%)	
Activity Impairment	150	82.9	79.8-85.9	113	54	50.4-58.2	<0.001(28.9%)	
*Paired sample t-test								

*Association between the PROs of Hepatitis C patients in Group A and Group B who achieve ETR (EQ-5D & WAPAI).*

Changes in all of the nine variables included in EQ-5D and WAPAI tools were compared between the groups non-cirrhosis and cirrhosis. Table 5 shows the assessment of the association between the PROs of chronic Hepatitis C patients with and without cirrhosis who achieve ETR (EQ-5D & WAPAI). There is association between mobility, self-care, usual activities, pain and depression problem improvements between the two groups. (P value =0.478). Mobility improvements in both the groups are nearly equivalent -0.59 in group B and -0.58 in group A. Similarly, usual activity improvements were also of similar readings in both groups (-0.46 in group B and -0.43 group A). Self-care was improved more in cirrhotic patients because they were in miserable condition at baseline while self-care was well improved in non-cirrhotic patients at baseline, therefore improvement values were less marked in this group. More pain and discomfort improvements were observed in group A compared to group B.

**Table 5**  
**Assessment of the association between the PRO's of hepatitis c patients with cirrhosis and those without cirrhosis who achieve ETR (EQ-5D & WAPAI)**

EQ-5D	Pearson Chi- square value	p-value*
Mobility	17.89	<0.05
Self-care	31.99	<0.05
Usual activities	36.22	<0.05
Pain/discomfort	53.53	<0.05
Anxiety/depression	56.03	<0.05
WAPAI	Pearson chi-square value	p-value
Work productivity impairment	39.96	<0.05
Absenteeism	23.25	<0.05
Presentism	29.37	0.0525
Activity impairment	124.72	<0.05
*Pearson Chi-Square test		

The improvements in mobility, absenteeism, presenteeism, and activity impairment between the two groups were found associated. The improvements in the presenteeism, absenteeism, and activity impairment were nearly equal and associated. Work productivity was also found improved in both groups.

Graphical presentation figure 1 (a) shows association in improvements in quality of life in both the groups. Mobility and usual activities improvements were nearly similar in both groups. Self-care, pain, and anxiety were more improved in cirrhotic patients. This is because at baseline, cirrhotic patients were suffering with more discomfort, pain anxiety and depression and were unable to perform self-care. In

figure 1 (b), both the groups show association having improved work productivity and activity impairment.

## Discussion

### Statement of key findings

This study explored three important aspects of patients' related outcomes in cirrhotic and non-cirrhotic conditions. Firstly, cure rate with available regimens at the end of 12 weeks treatment was determined. The cure rate was high in non-cirrhotic patients as 122 patients out of 124 were cured to ETR whereas 62 patients out of 117 were cured in cirrhotic group showing cure rate of 92.5% and 53% respectively.

Secondly, PRO's of hepatitis C patients in cirrhotic and non-cirrhotic patients before and after the treatment were analysed. Baseline data shows severe impairment in PRO's and compromised HRQoL and work productivity in hepatitis C patients both in cirrhotic and non-cirrhotic patients. After the anti-hepatitis C treatment with DAAs, significant improvement in HRQoL and work productivity was observed in hepatitis C patients both with and without cirrhosis. The standard treatment regimen comprising SOF/DCV/RBV combination showed significant improvement in PROs.

Thirdly, the researchers determined the association between the groups. The cirrhotic group showed more impairment in HRQOL and work productivity at baseline than the non-cirrhotic group. After the hepatitis C treatment, improvement in PRO's of both groups was evaluated. More improvement was observed in the non-cirrhotic patients.

### Strengths and weaknesses

The actual data of the patients was collected from a tertiary care hospital directly by the researcher. The study addressed the three main aspects related to the patients reported outcomes, response rate of direct acting antivirals and association between cirrhosis and non-cirrhosis groups before and after the standardizes treatment. Despite the study setting serves a large population every year, one study site is a limitation of this study. More assessment of PRO's using multiple instruments must be conducted for the variety of information collection necessary for hepatitis C patients.

### Interpretation

Previous studies have compared differences in treatment response between genotype 2 and 3 patients with an observation that a longer duration of therapy is required in genotype 3 to achieve a sustained virologic response [15]. Similar findings were reported by Jacobson et al, 2015 after the interferon therapy's failure to find another treatment option successfully [19]. One earlier study by Younossi et al, 2014 have determined whether cirrhosis influences PRO during treatment with newly available anti-HCV regimes. The pool of CHC patients with or without cirrhosis was administered SOF plus RBV. The cirrhotic patients who were treated with interferon free therapy experienced a decline in PRO score during treatment. However, this study lacked the follow up of PRO data after 4 weeks of treatment relapsed [20].

They used four different instruments; the HRQOL including Short Form-36 [SF-36], Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), Chronic Liver Disease Questionnaire-HCV (CLDQ-HCV) and work productivity and activity impairment [16]. While in our study, all the patients with and without cirrhosis was included irrespective of the genotype specificity. We analyse three main objectives. The PROs evaluation at baseline and post anti HCV treatment of SOF with or without RBV in both cirrhosis and no cirrhosis group. The association in both the groups at baseline and post-treatment was evaluated. The response rate with SOF / RBV therapy was analysed, and efficacy was proved to achieve ETR at the end of 12 weeks of therapy [16].

A similar study conducted amongst hepatitis C patients aimed to determine the efficacy of SOF and RBV with or without interferon. They reported high cure rates with this triple therapy in genotype 3 hepatitis C patients compared to interferon-free therapy. Furthermore, treatment-experienced genotype 2 patients also have high cure rates. Their study provided clear evidence to use SOF and RBV with interferon for 12 weeks is a treatment option or SOF with RBV for 24 weeks [13].

Leroy et al, in 2016 conducted a study on advanced treatments on DCV/SOF/RBV for 12 to 16 weeks. It was found that this combination of treatment is effective and well-tolerated by the genotype 3 patients with compensated and advanced liver diseases irrespective of the treatment naïve or experienced [15]. Juanbeltz et al, 2018 demonstrated the DAA's efficacy on the HRQoL of CHC patients. The HRQoL was measured by using EQ-5D-3L at baseline and after 12 weeks. The cure in mobility, pain, anxiety, usual activities, and self-care was evident [21].

## Further research

Patients with decompensated liver were excluded from the study. Although it was a large study measuring the PROs of patients with and without cirrhosis, further studies should be conducted to include the patients with decompensated liver. Further studies should be conducted to include the patients with decompensated liver.

More assessment of PROs using multiple instruments must be conducted for the variety of information collection necessary for hepatitis C patients.

## Conclusion

This study has found that non-cirrhotic CHC patients receiving SOF/DCV/RBV standardized treatment experienced significantly more improvements in health-related quality of life (HRQOL) and decrease in patient-reported outcomes (PROs) scores compared to cirrhotic patients who showed less improvements in clinical outcomes. The improvements in both the groups were associated with work productivity and activity impairment.

## Abbreviations

Chronic hepatitis C (CHC), Daclatasvir (DCV), Direct-acting antivirals (DAAs), Health-related quality of life (HRQOL), Hepatitis C virus (HCV), Patients reported outcomes (PRO's), Quality of life (QOL), Ribavirin (RBV), Sofosbuvir (SOF), Work productivity and activity impairment (WAPAI).

## Declarations

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### Conflicts of interest

The authors declare that there exists no conflict of interest for this study.

### Availability of data and materials

All the statistical analysis sheets and datasets available on demand from corresponding author at [fatimalcwu@gmail.com](mailto:fatimalcwu@gmail.com).

### Author Contribution

IA made the study concept and design, acquisition of data, statistical analysis and interpretation of data. FA contributed in study supervision, administrative support, final review of the manuscript and correspondence. SA contributed to support in data collection, Critical review of the manuscript, editing and final approval of the article publication. YA contributed in verification of statistical analysis and critical review of the manuscript. AH and VP contributed to Critical review of the manuscript. All the authors approved the final manuscript for submission.

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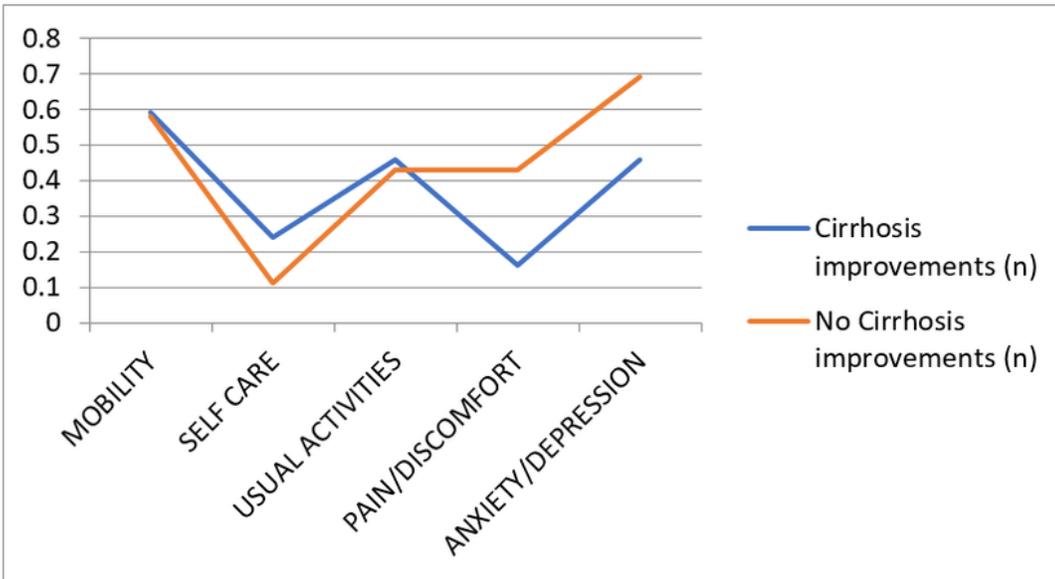
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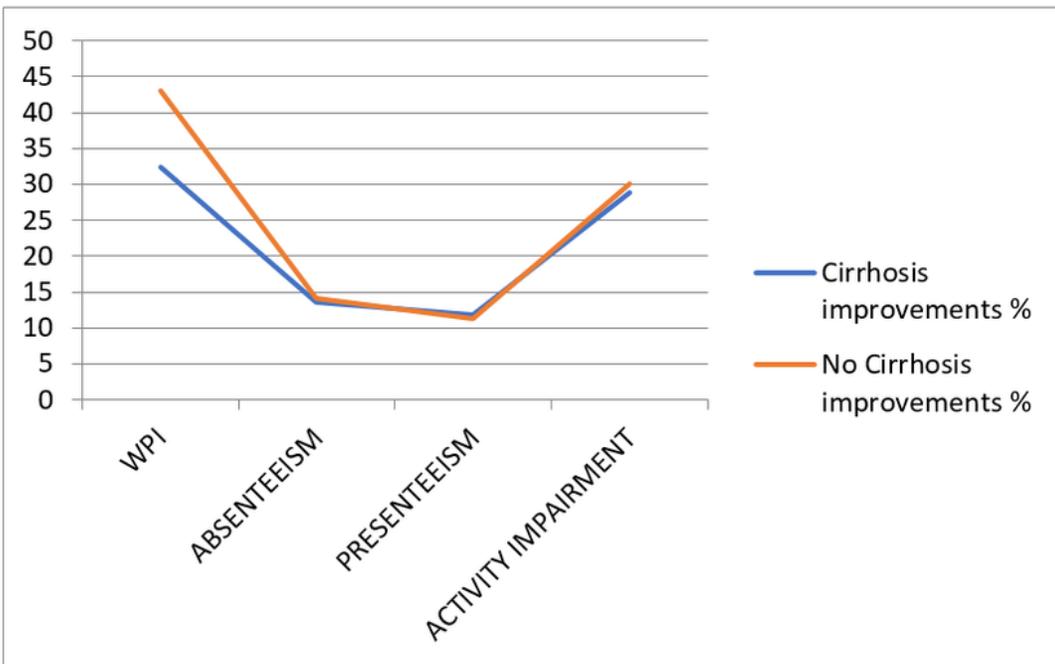
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## Figures



**A**



**B**

Figure 1

(a). Assessment of the association between the PROs of Hepatitis C patients with cirrhosis and without cirrhosis who achieve end-of-treatment response (EQ-5D). (b). Assessment of the association between the PRO's of hepatitis C patients with cirrhosis and without cirrhosis who achieved end-of-treatment response (WAPA).