



Impact on Health-Related Quality of Life (HRQOL) Using Direct Antiviral Agents (DAA) in Patients with Chronic Hepatitis C

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Abstract

Introduction: Measurement of patient's Health Related Quality of Life (HRQOL) is acquiring attention in medical research, as it used to gauge the influence of a long-lasting disease or surgery on patients' health. It has now become the principal goal of medical care and is a subjective multidimensional concept. In past, the treatment with Pegylated Interferon (PEG-IFN) had a negative impact on quality of life leading to lower treatment adherence. Therefore, we aim to evaluate satisfactory quality of life with Direct Acting Antiviral Agents (DAAs). The result of this study not only shed light on impact of DAAs on HRQOL but also helps physician assessment regarding prescribing these expensive medications.

Objective: To determine the frequency of satisfactory quality of life assessed on CLDQ in chronic hepatitis C patients treated with direct oral antiviral agents.

Setting: Department of Hepatogastroenterology, Sindh Institute of Urology and Transplantation Karachi (SIUT).

Duration: 6 months from October 2018 to March 2019.

Design: Longitudinal study.

Subject and Methods: A total of 168 Patient diagnosed as hepatitis C for last 6 months and has not been treated for HCV were included in this study. CLDQ score (Appendix-A). Data was collected and was transferred to pre-designed Performa. Mean score of >5 was associated with satisfactory HRQOL.

Results: Majority of patients were female 92 (54.76%) with average age of 44.58 ±10.69 years. Satisfactory quality of life was observed in 76.79% (129/168) in one month after completion of treatment. One-month post-treatment with direct oral antiviral agents, there was significant increase in mean CLDQ score (3.5 ± 1.16 vs. 5.4 ±1.76; p=0.0005 paired t-test applied).

Conclusion: This study revealed short-term positive impact on the HRQoL of the patients with chronic hepatitis C treated with sofosbuvir based direct acting antiviral agents.

Keywords: Chronic hepatitis C; CLDQ; Direct oral antiviral agents; Satisfactory quality of life; PEG-IFN

Introduction

Measurement of patient's Health Related Quality of Life (HRQOL) is acquiring attention in medical research [1], as it used to gauge the influence of a long-lasting disease or surgery on patients' health [2]. It has now become the principal goal of medical care and is a subjective multidimensional concept. The impact of Hepatitis C Virus (HCV) infection is not limited to cirrhosis and Hepatocellular Carcinoma (HCC) but also it is associated with reduced HRQOL, even in the absence of cirrhosis [3-6]. Chronic HCV is associated with symptoms comprising of fatigue and lethargy, nausea, anorexia, headache, irritability, abdominal discomfort, and muscle aches [7-8]. In past, the treatment with Pegylated Interferon (PEG-IFN) had a negative impact on quality of life leading to lower treatment adherence [9]. Not only patients with hepatitis C virus infection have low HRQOL as compared to general population but its impact is comparable to other chronic

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Received Date: 13 Nov 2021

Accepted Date: 03 Dec 2021

Published Date: 21 Dec 2021

Citation:

Khan SA, Khan RTY, Majid Z, Khalid MA, Hanif FM, Laeeq SM, et al. Impact on Health-Related Quality of Life (HRQOL) Using Direct Antiviral Agents (DAA) in Patients with Chronic Hepatitis C. *J Gastroenterol Hepatol Endosc.* 2021; 6(3): 1102.

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disease [7].

With the advent of oral Direct Acting Antiviral agents (DAAs), the treatment of hepatitis C has been revolutionized, even in patients with decompensated cirrhosis, for whom PEG-IFN is contraindicated and who otherwise have a poor prognosis, can now be cured safely and effectively [10]. A Chronic Liver Disease Questionnaire (CLDQ) was a particular tool, which was developed by Younossi et al., that has been validated for the utilization in all sort of liver diseases [11]. The questionnaire consisted of 29 items categorized into six different portions: Abdominal symptoms, fatigue, systemic symptoms, activity, emotional function, and worry. Parkash et al. [12] utilized above mentioned questionnaire (CLDQ) in Pakistani cirrhotic patients and has documented 69 percent of study population had poor quality of life. The study involved cirrhotics of multiple etiology and author had not documented response to treatment in study population. Although DAAs has shown greater than 90% of Sustained Virological Response (SVR) [13], there is no recent local study available on this topic and one study on Pakistani population was conducted in 2012 [12].

The new data is necessary to identify the current burden and baseline information for treatment with DAAs. Therefore, we aim to evaluate satisfactory quality of life with DAAs. The result of this study not only shed light on impact of DAAs on HRQOL but also helps physician assessment regarding prescribing these expensive medications.

Objective

To determine the frequency of satisfactory quality of life assessed on Chronic Liver Disease Questionnaire (CLDQ) in chronic hepatitis C patients treated with direct oral anti-viral agents.

Operation Definition

Quality of life

Quality of life was assessed through Chronic Liver Disease Questionnaire (CLDQ) Health survey scoring system (Appendix-A). This questionnaire includes the emotional, social, physical and mental health and is divided into 6 domains; Abdomen Symptoms (AS), Fatigue (FA), Systemic Symptoms (SS), Activity (AC), Emotional Function (EF) and Worry (WO). Scoring of each questions was done as per response and total mean score was calculated for each patient as shown in Appendix-A. Patient with mean score >5 was labeled as satisfactory quality of life. Pre score was assessed before 1 week of starting DAAs and post score was assessed one month after completion of treatment [11].

Chronic hepatitis C

Chronic Hepatitis C defined as the presence of detectable HCV RNA for at least six months [14].

Materials and Methods

Sample size

By using WHO sample size calculator taking statistics for poor quality of life as 69% [12] margin of error 7% and 95% confidence interval the calculated sample size came out as 168.

Sample selection

Inclusion criteria

- Age 18 to 65 years
- Either gender

- Patient diagnosed as hepatitis C for last 6 months and has not been treated for HCV

Exclusion criteria

- Patient non-compliant to prescribed medications.
- Previously treated for hepatitis C treatment with or without direct oral antiviral agents.
- Lost to follow-up.
- History of Cardiovascular diseases (i.e. Myocardial infarction or Angina or heart failure) assessed on medical record and history.
- Chronic Renal failure assessed on medical record.
- Malignancy (Hepatocellular carcinoma) assessed on medical record.
- Diabetes Mellitus assessed on medical record and history.
- History of neuropsychiatric disorder assessed on medical record and history.

Data collection procedure

Data collection was started after approval of synopsis from College of Physician & Surgeons Pakistan and institutional ethical review committee. All the chronic hepatitis C patients fulfilling the inclusion criteria were enrolled in the study. After explaining informed consent was taken. Quality of life was assessed on Chronic Liver Disease Questionnaire (CLDQ) score (Appendix-A). Patients was treated with Sofosbuvir 400 mg daily, Daclatasvir 60 mg daily and Ribavirin 400 mg twice daily for 24 weeks. The researcher recorded each question score by face to face interview and ticked the statement by asking the patient who describes their current status before 1 week and 1 month after completion of treatment. Data was collected and was transferred to pre-designed Performa by the researcher. Mean score was calculated of each segment in questionnaire. Then sum of total mean score of segments was calculated. Mean score of >5 was labeled as satisfactory quality of life.

Data analysis procedure

All the data was entered and analyzed using SPSS version 20. Mean and standard deviation was measured for continuous variable like age, duration of disease, pre and post CLDQ score while frequency and percentage was obtained for categorical variables like age, occupation, socioeconomic status and satisfactory quality of life. Paired t-test was applied to analyze pre and post treatment CLDQ score.

Frequency of satisfactory QOL was stratified with respect to age, gender, occupation, socioeconomic status and duration of disease. Post stratification chi square was applied. A p value ≤ 0.05 was taken as significant.

Results

A total of 168 patients diagnosed as hepatitis C for last 6 months and has not been treated for HCV were included in this study. Most of them, had age more than 40 years. The average age of the patients was 44.58 ± 10.69 years. There were 76 (45.24%) male and 92 (54.76%) females. Sixty-one (36.3%) of the patients were employed while unemployment was seen in 56 (33.3%) patients. Most of the patients belonged to lower or middle socio-economic status seen in 100 (59.52%) and 65 (38.6%) patients respectively. Regarding education

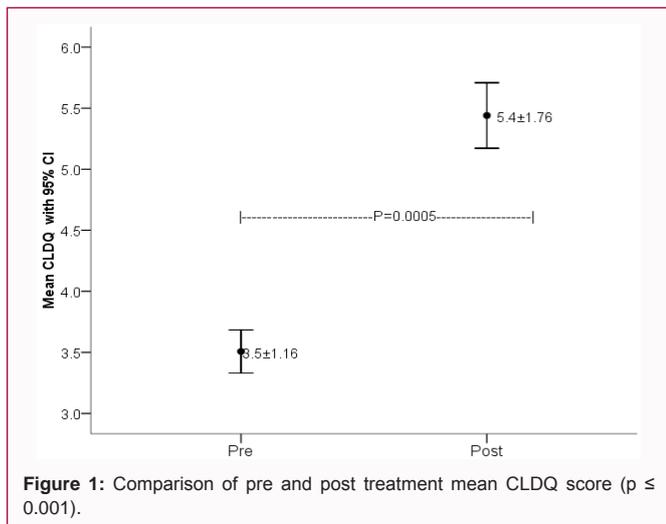


Figure 1: Comparison of pre and post treatment mean CLDQ score (p ≤ 0.001).

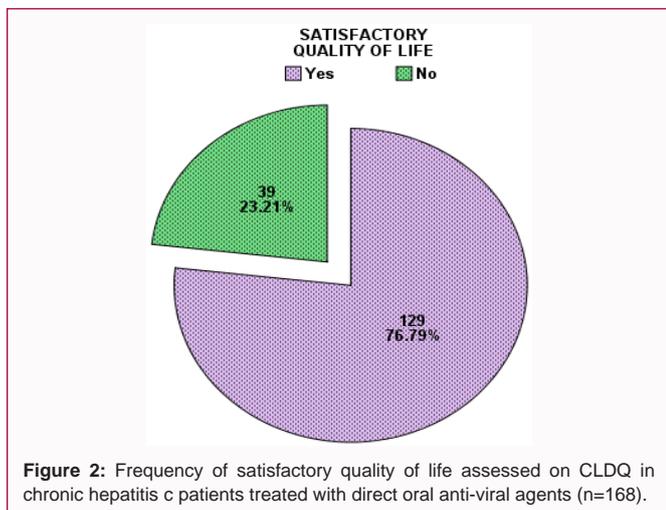


Figure 2: Frequency of satisfactory quality of life assessed on CLDQ in chronic hepatitis c patients treated with direct oral anti-viral agents (n=168).

status of the patients, 78 (46.43%) patients were illiterate, 75 (44.64%) had just primary education while others had higher qualification.

The mean duration of disease was 8.68 ± 1.26 months. Pre and post-mean CLDQ score were compared (Figure 1). Mean CLDQ score was significantly increased one month after completion of treatment with direct oral antiviral agents (3.5 ± 1.16 vs. 5.4 ± 1.76; p=0.0005 paired t-test applied). According to operational definition, patient with mean score >5 was labeled as satisfactory quality of life. After one month of treatment completion, satisfactory quality of life was observed in 129 (76.79%) patients (Figure 2).

Stratification analysis was also performed after treatment with DAA and it was observed that rate of satisfactory quality of life was high in all stratified groups but insignificant difference was observed between these groups. (p-value >0.05) (Table 1).

Discussion

Hepatitis C Virus (HCV) is a blood-borne organism and has a significant impact on global health [15]. Approximately around 71 million people are infected globally from this virus HCV resulting in increased morbidity and mortality from complications of chronic liver disease [16]. However, there is varied prevalence of this pathogen among the countries. There is approximately 5% prevalence of HCV in Pakistan which is quite alarming [17]. With

Table 1: Frequency of satisfactory quality of life assessed on CLDQ in chronic hepatitis c patients treated with direct oral anti-viral agents by different categorical variables (n=168).

Variable	Sub-variable	Satisfactory quality of life		p-value
		Yes	No	
Age	≤ 30	15 (68.2%)	7 (31.8%)	0.422
	31 to 40	32 (80%)	8 (20%)	
	41 to 50	46 (73%)	17 (27%)	
	>50	36 (83.7%)	7 (16.3%)	
Gender	Male	60 (78.9%)	16 (21.1%)	0.546
	Female	69 (75%)	23 (25%)	
Duration of disease	6-9	109 (77.3%)	32 (22.7%)	0.716
	>9	20 (74.1%)	7 (25.9%)	
Occupation	Employed	49 (80.3%)	12 (19.7%)	0.624
	Unemployed	43 (76.8%)	13 (23.2%)	
	Housewife	37 (72.5%)	14 (27.5%)	
Socioeconomic status	Low	77 (77%)	23 (23%)	0.916
	Middle	50 (76.9%)	15 (23.1%)	
	High	2 (66.7%)	1 (33.3%)	
Education	Uneducated	62 (79.5%)	16 (20.5%)	0.315
	Primary	57 (76%)	18 (24%)	
	Secondary	7 (58.3%)	5 (41.7%)	
	Higher Secondary	3 (100%)	0 (0%)	

the advent of Direct-Acting Antivirals (DAAs), a highly efficacious HCV treatment, HCV disease burden and ongoing transmission has been reduced [18]. In recent years, there has been a paradigm shift from the use of less efficacious and more toxic interferon to Direct Antiviral Agents (DAAs) which are highly effective and less toxic [19]. New Direct Acting Antiviral regimens (DAAs) have been the revolution in treatment of chronic hepatitis C. they are associated with higher efficacy, shorter period of treatment and an excellent safety profile [20,21]. Conversely, there has been little research concerning the effect of the new DAAs on HRQOL and comes from a few clinical trials, in which certain subpopulations are understated, such as psychiatric patients, those co-infected with HIV or those with addictive behaviors [22]. In order to gauge the economic and health influence of these new therapies, there is a need to assess HRQOL in real life from chronic hepatitis C patients [23]. To determine the frequency of satisfactory quality of life assessed on CLDQ in chronic hepatitis C patients treated with direct oral anti-viral agents, a total of 168 patient, of either gender, age 18 to 65 years, diagnosed as hepatitis C for last 6 months and has not been treated for HCV were included in this study with most of them aging above 40 years. Considering the age group distribution, the prevalence of HCV infection showed a gradual increase before 50 years. There is decreased prevalence of HCV infection after the age of 50 years, which likely results from impaired and decreased physical mobility and poor financial status resulting in decrease number of elderly patients undergoing screening for HCV. There is debatable prevalence of HCV in both genders. Certain studies reveal increased HCV incidence among men, while other surveys reveal slightly higher rates in women. However, further studies are required to validate the greater risk of HCV transmission in men [24]. The seroprevalence was higher in females in a study done by Rajesh N. Gacche et al. along with some other studies revealing similar results [25,26]. Similarly, there were 45.24% male and 54.76%

females in our study showing female preponderance.

There is significant improvement in HRQOL after treatment with DAAs in patients with chronic hepatitis C, which started immediately after the initiation of therapy and improved after achieving sustained virological response. However, in our study, the mean CLDQ score was significantly increase after one month of treatment of direct oral antiviral agents (3.5 ± 1.16 vs. 5.4 ± 1.76 ; $p=0.0005$ paired t-test applied). According to operational definition, patient with mean score >5 was labeled as satisfactory quality of life. Satisfactory quality of life was noted in 129 (76.79%) patients one month after treatment completion. In the first 4 weeks of treatment, the median VAS score increased up to 5 points along with improved health related aspects that were negatively affected with interferon treatments [27]. This early improvement in HRQOL has been described for DAAs [28], opposing to what happened with PEG-IFN+RBV and triple therapy with boceprevir or telaprevir [8,29], which appears to relate HRQOL deterioration during treatment to interferon and not to second generation DAAs. The patients cured with DAAs had vast improvement in QoL supporting the fact that chronic HCV infection, is clearly an important systemic component than can result in impaired HRQOL [30,31]. In clinical practice, patient reporting outcomes constitute useful tools in the evaluation and monitoring of health interventions, since they provide information on patient perception and needs [32]. There are no previous studies from this region emphasizing on improvement in QOL in patients undergoing treatment for HCV with DAA. In order to increase patient adherence to DAAs, it is important to understand the predictors resulting in improvement in HRQOL. The major limitation of our study is the small sample size which can be improved by doing further studies comprising of large number of HCV patients undergoing treatment with DAA.

Conclusion

This study showed a short-term positive impact on the health-related quality of life of patients with chronic hepatitis C treated with sofosbuvir based direct acting antiviral agents. However, further studies on a larger scale are required to see the impact of treatment with DAAs on QOL in HCV population.

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