

ORIGINAL ARTICLE**Health-Related Quality of Life in Egyptian Patients with Chronic Hepatitis C Before and After Treatment with Direct Acting Antivirals**Waleed A. Ismail¹, Asmaa H. Nosair^{3*}, Ghada M. Salem², Emad F. Hamed¹*1 Assistant Professor in Internal Medicine department, Zagazig University.**2 Assistant Professor in community department, Zagazig University.**3 Post graduate in Internal Medicine department, Zagazig University.**** Corresponding author:**Asmaa Haroun Nosair
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asmaa_nosair@yahoo.com**Submit Date:** 07-07-2019**Revise Date:** 06-10-2019**Accept Date:** 08-10-2019**ABSTRACT**

Background: According to World Health Organization (WHO) estimates, the prevalence of HCV in Egypt is 4.5% to 6.7%, which is the uppermost prevalence of HCV in the world causing a substantial burden of mortality and morbidity. Health related quality of life [HRQoL] has been assessed in diabetes, arthritis and a wide variety of cancers, Until now, there is no sufficient report about HRQoL related to direct acting antiviral agents (DAAs) on Egyptian patients with chronic HCV. This prospective cohort study aimed to assess the health related quality of life in Egyptian patients with chronic HCV treated with daclatasvir (DAC) and sofosbuvir (SOF) ± ribavirin (RBV). **Methods:** One hundred HCV patients were classified according to the supreme council and national committee for control of HCV (NCCVH) into two groups: Group 1 (easy to treat) included 35 patients treated with SOF+DAC for 12 weeks, and group 2 (difficult to treat) included 65 patients treated with SOF+DAC+RBV for 12 weeks. The short form 36 scale (SF-36) was used to assess the health related quality of life in two groups. **Results:** Sustained virological response (SVR12) in patient received DAC/SOF was 83.3 % and in patient received DAC/SOF/RBV was 100% (Total 93%). The patients reported significant improvement in all HRQoL domains after therapy, group 1 reported higher improvement. **Conclusion:** Sofosbuvir and Daclatasvir with or without ribavirin are effective in treatment of chronic HCV infections with low adverse actions and better improvement in HRQoL. Sofosbuvir and Daclatasvir have better improvement in HRQoL than Sofosbuvir and Daclatasvir plus ribavirin.

Key words: HCV, Daclatasvir, Sofosbuvir, Health related quality of life, SF-36 scale

INTRODUCTION

The prevalence of HCV in Egypt according to World Health Organization, decrease to be around (4.5% to 6.7%) in 2016 [1].

Direct acting antiviral agents (DAAs) have changed the treatment of HCV infection over the last 5 years. DAAs have been proven to be harmless and in effect in clearing the hepatitis C virus from the body, so preventing lethal complications [2].

Antiviral therapies can eradicate the virus resulting in improvements in liver histology which prevent liver related mortality and enhances health related quality of life

(HRQoL)[3]. HRQoL uses to measure debilities related to specific diseases and also efficacy of treatment. HRQL Studies concentrate on quality of life components that can be impacted by specific diseases[4]. Short-form 36 (SF-36) which is one of short-form HRQoL measures is widely used [5].

The use of RBV free regimens and interferon free regimens for HCV is associated with better patients practice and work efficiency during treatment [6].

DAAs, sofosbuvir and daclatasvir are well accepted with slight adverse effects, have little pill burden and shows nominal drug interactions [7].

In our study, SF-36 is used to assess HRQL in Egyptian patient treated with Sofosbuvir and daclatasvir ± ribavirin.

METHODS

Patients

The prospective cohort study was conducted at (**Internal Medicine department, Zagazig University and Dumyat fever hospital**) according to the international guidelines of Strengthening the Reporting for Observational Studies in Epidemiology; STROBE [8]. Using the WHO Manual for Sample Size Determination in Health Studies [9], the minimal sample size calculated for the study was 92 patients based on an average previous estimate of 2.5 HCV infection among patients from different Egyptian regions [10], and with an absolute precision of 2% and at a 95% confidence interval. To avoid loss of participants, a total sample of 100 chronic HCV patients was included in the present study. All patients volunteered to participate in the study and were prospectively followed up for the full duration of the study, which was 6 months, from April 2018 to October 2018.

All patients were Exposed to clinical valuation before treatment and at 4,8,12 weeks and 12 weeks after treatment by laboratory studies including liver function tests, kidney function tests, complete blood count, alpha fetoprotein, pregnancy test for females at child bearing age and abdominal ultrasonography. Exclusion criteria included patients with Child Pugh score C, Pregnant and lactating female, HBV, HIV patients, diabetic patients and hypertensive patients, History of current psychiatry problems, auto immune diseases, kidney diseases, heart diseases, HCC and extra hepatic malignancy.

Study design

The work has been carried out in accordance with the code of Ethics of the world Medical Association (Declaration of Helsinki) for studies involving humans. Written informed consent was obtained from all participants and the study was approved by research ethical committee of faculty of medicine, Zagazig university. The study included Adult patients (male and female) >18 years, Positive HCV RNA by PCR, child-pugh score A or B,

group 1 (Treatment naïve, Total serum bilirubin ≤ 1.2 mg/dl, serum albumin ≥ 3.5 g/dl, INR ≤ 1.2 , Platelet count ≥ 150.000 /mm³). group 2 (Peg-INF treatment experienced, Total serum bilirubin ≥ 1.2 mg/dl, Serum albumin ≤ 3.5 g/dl, INR ≥ 1.2 , Platelet count < 150.000 /mm³).

Assessment of Health related quality of life

HRQoL was assessed before and after therapy using SF-36 scale and The Liver Disease Symptoms Index-2.0.

Statistical analysis

Statistical analysis was performed using the software Statistical Package for the Social Sciences [SPSS] version 20 (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0 Armonk, NY: IBM Corp). To compare quantitative data between groups the *Independent sample t test* and *Mann Whitney test* were used with parametric distribution or nonparametric distribution, respectively. *Paired sample t test* (for normally distributed data) and *Wilcoxon signed rank test* (for not normally distributed data) were used. The level of statistical significance was set at 5% ($P < 0.05$). Highly significant difference was present if $p \leq 0.001$.

RESULTS

This study included 100 patients with Hepatitis C virus positive, 35 patients received DAC/SOF and 65 patients received DAC/SOF/ RBV, Sustained virological response (SVR12) in patient received DAC/SOF was 83.3% and in patient received DAC/SOF/RBV was 100% (Total 93%) Figure 1.

The patients reported significant improvement in all HRQoL domains after therapy, Table 1, and group 1 reported higher improvement.

Table 2 shows statistically significant differences in ALT, AST, serum albumin, platelet count, TLC, bilirubin before and after treatment in all patients.

In Figure 2 there are significant differences regarding percent change in physical and mental summary scores where the group 2 receiving DAC/SOF/RBV had higher percent change in physical score while those receiving DAC/SOF therapy reported higher improvement.

Table 1. Comparison of HRQoL of studied patients before and after treatment

	Before treatment	After treatment	Wx	P
	Mean ± SD	Mean ± SD		
Physical functioning	44.75 ± 27.19	83.55 ± 10.85	8.609	<0.001**
Role physical	15.75 ± 33.46	99.5 ± 3.52	8.957	<0.001**
Body pain	49.02 ± 4.6	59.82 ± 19.61	4.774	<0.001**
General health	43.56 ± 7.59	57.98 ± 12.62	t (12.376)	<0.001**
Vitality	52.4 ± 7.67	55.15 ± 6.45	t (2.572)	<0.001**
Social functioning	48.63 ± 12.67	50.25 ± 3.54	t (1.237)	0.012*
Role emotional	26.87 ± 41.63	98.64 ± 9.47	8.226	<0.001**
Mental health	47.96 ± 20.92	77.76 ± 6.15	8.336	<0.001**
Physical summary score	38.27 ± 13.3	75.21 ± 5.74	8.657	<0.001**
Mental summary score	43.95 ± 14.12	70.39 ± 3.52	t (18.18)	<0.001**

WX Wilcoxon signed rank test

t paired sample t test

*p<0.05 is significant

**p<0.001 is highly significant

Table 2. Laboratory data changes of all patients before and after therapy.

	Before	After	Paired t	P
	Mean ± SD	Mean ± SD		
Hemoglobin (g/dl)	12.1 ± 2.05	12.1 ± 1.85	Paired t 0.028	0.978
ALT(IU/L)	27.98 ± 12.44	20.16 ± 7.44	Wx (7.535)	<0.001**
AST(IU/L)	27.37 ± 11.76	20.11 ± 6.91	Wx(-7.524)	<0.001**
S. Albumin (g/dl)	4.1 ± 0.34	4.16 ± 0.3	-5.353	<0.001**
Platelet(thousands/cmm)	179.58 ± 51.93	179.96 ± 48.82	2.203	<0.001**
WBC (thousands/cmm)	6.97 ± 2.81	6.63 ± 2.08	Wx (2.943)	0.003*
Bilirubin(mg/dL)	0.73 ± 0.25	0.61 ± 0.19	Wx (4.970)	<0.001**
S.Creatinine(mg/dL)	0.93 ± 0.19	0.93 ± 0.19	0	1
HCV RNA (6 Non responder)	236970.71 ±169139.73	288459.71 ±214389.99	Wx (0.582)	0.582

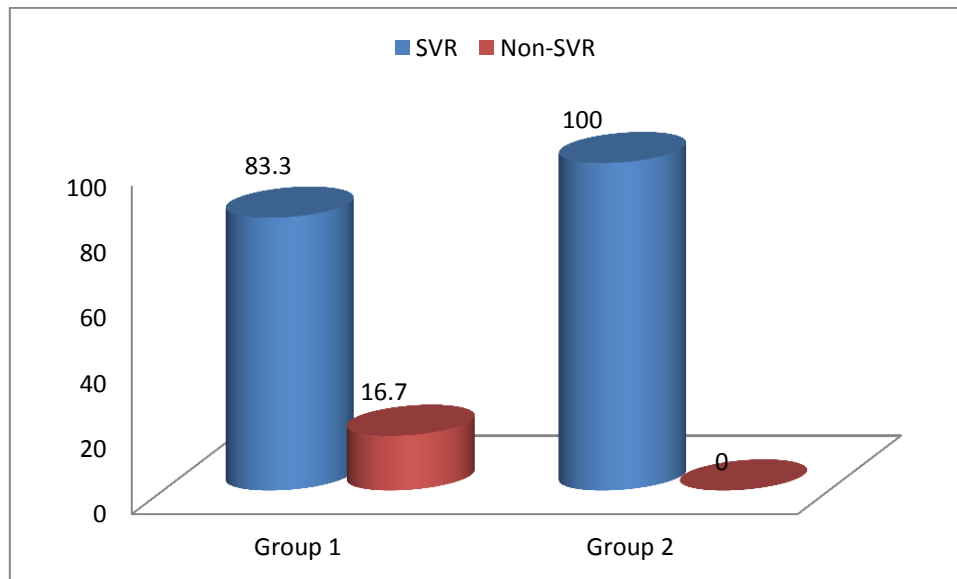


Figure 1. Combined bar chart showing SVR in the studied groups.

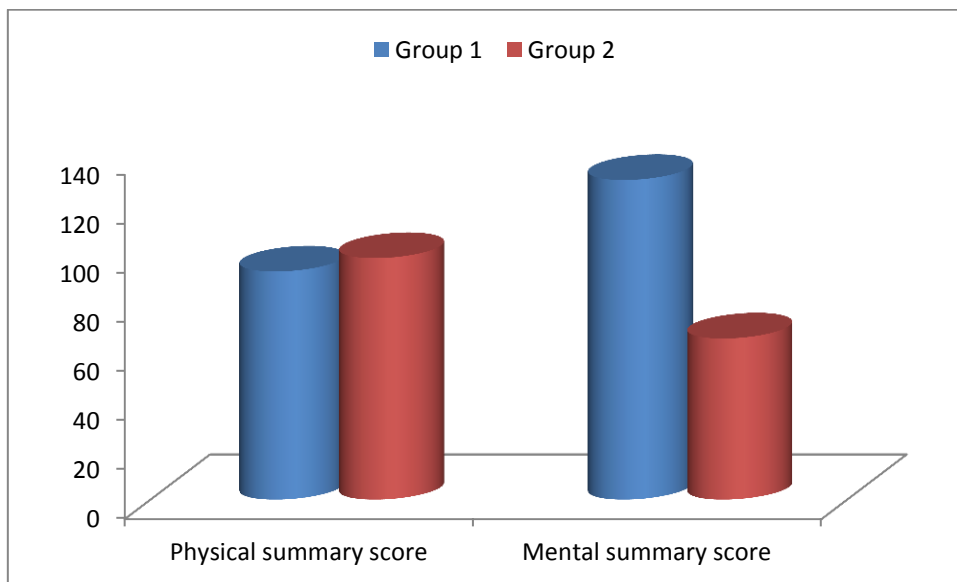


Figure 2. Combined bar chart showing percent change in physical and mental summary scores between two groups.

DISCUSSION

Our study discussed treatment of 100 HCV infected patients with Sofosbuvir plus daclatasvir with or without weight based ribavirin.

Patients were divided into 2 groups. Group 1 included 35 HCV positive patients who treated with sofosbuvir 400 mg orally once daily and daclatasvir 60 mg orally once daily for 12 weeks and Group 2 included 65 HCV positive Patients who treated with Sofosbuvir , daclatasvir and weight based ribavirin for 12 weeks.

Regarding HRQoL domains of studied patients, a highly significant difference has been reported between it before and after therapy ($p \leq 0.001$), the patients reported significant improvement in all HRQoL domains after therapy, also there were significant improvement within each group. This matched with the study done by Younossi et al., 2016 which show treatment with the novel generation of DAAs maximizes PRO scores during treatment and also after reaching SVR [6].

There is significant improvement in physical summary score and in mental summary score

within each group, this match with Zobair et al., 2016 who showed no residual decrease in PRO rates when compared with standard levels were observed in the group taking IFN-free RBV-containing regimens. In that group, many PROs started to determine enhancements rather than decrements from the standard reference points and enhancements in the IFN-free RBV-free group became even more prominent[6]. Also Zobair et al., 2014 found that attaining SVR-12 with SOF and RBV is associated with an enhancement in HRQL[11].

Our study showed that there was significant difference regarding percent change in physical and mental summary scores where the group2 receiving DAC/SOF/RBV had higher percent change in physical score while those receiving DAC/SOF therapy reported higher improvement. This in agreement with Younossi et al., 2016 who showed the use of an IFN-free RBV containing regimen is unconventionally accompanying with mild PRO Impairment and the use of IFN-free and RBV-free regimen with SOF/LDV was associated with enhancement rather than deteriorating of PRO rates, all these effects were observed at a similar magnitude in both cirrhotic and non-cirrhotic patients despite substantial baseline impairment of PROs in patients with cirrhosis[6].

As regarding sustained virological response ,There is significant difference between two groups ($p < 0.05$),as SVR-12 in patient received DAC/SOF was 83.3 % and in patient received DAC/SOF/RBV was 100% (Total 93%) and this result was different from that done by Abdel-Aziz et al.,2017 showed SVR-12 for HCV genotype 4 treated with DAC/SOF was 93.3% and SVR-12 in naïve, SVR-24 in experienced patient treated with DAC/SOF/RBV was 87.5% (Total 91%)[12]. Also this result was different from that done by Zobair et al.,2016 which show patients with HCV genotype 1 who were treated with LDV/SOF+RBV the SVR-12 was 98% and who were treated with LDV/SOF the SVR-12 was 100%[13].

On the other hand the result match with Sulkowski et al.,2013 which studied daclatasvir and sofosbuvir with and without RBV in treatment naïve patients with

genotypes [1 – 3] patients for 12 or 24 weeks. Patients with Genotype 2 or 3 achieved SVR 24 at rates of (86 - 100%) while Genotype 1 patients in the 12 week groups have attained SVR 12 at rates of 95 - 100%[14]. In our study Patients received DAC/SOF+RBV achieved SVR 12 at rates of (93 - 100%).

The present study showed statistically significant differences in platelet count ($p < 0.001$) before and after treatment with improvement in platelet count after treatment ,this agree with previous study done by Abdel-Aziz et al.,2017[12].

There was significant decline in AST and ALT level ($P < 0.001$ for both) after end of the antiviral treatment which agree with previous study by Ahmed et al .,2018 who study the safety and efficacy of Sofosbuvir and Daclatasvir for treatment of chronic hepatitis C infections as treatment responders compared to pretreatment showed significant improvement in transaminases values after 12weeks of treatment with SOF/DAC showing their role in Improving necro inflammation in patients with chronic hepatitis C infection [15].

CONCLUSION

In conclusion , Sofosbuvir and Daclatasvir with or without ribavirin are effective in treatment of chronic HCV infections with nominal adverse events and better improvement in HRQoL. Early screening for chronic HCV infection and early management will improve general community health.

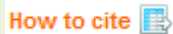
Conflict of Interest: Nothing to declare.

Financial Disclosures: Nothing to declare.

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