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Original Article

Treatment Response of Chronic Hepatitis C Patients and Health-Related Quality of Life

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Abstract

Objective(s): The objectives of present study were to investigate the response of chronic hepatitis C (CHC) patients to pegylated interferon alpha plus ribavirin (PEG-INF/RBV) combination therapy, to identify factors that could predict their response to treatment and to assess their health-related quality of life (HRQOL) before, during and after PEG-INF/RBV combination therapy.

Methods: An intervention study (one group pre-test - post-test design) was used. Data were collected from 300 CHC patients who attended the Hepatology and Interferon Therapy Unit at Gamal Abd El Naser Insurance Hospital using a pre-designed structured interviewing questionnaire and viral hepatitis C quality of life questionnaire. Review of the patients' medical records and their laboratory investigations was also carried out.

Results: The cumulative seronegativity rate of treated patients was 74%. The proportion of CHC patients who survived seronegativity was 0.270 at the 12th week, 0.261 at the 24th week and 0.250 at the 48th week of treatment. Patients' age and viral load significantly affected seronegativity. Significant univariate main effects for age were statistically associated with poor HRQOL in the domains of physical functioning, role limitations due to physical health, emotional problems and pain. Presence of chronic diseases and HC viral load had a significant effect on physical functioning, role limitations due to physical health problems, emotional problems and pain. All domains of the HRQOL short form (SF36) decreased by the end of the 4th week and started to increase at the 24th and 48th weeks of the follow up period.

Conclusion: The proportion of CHC patients who survived seronegativity was 0.250 at the 48th week of treatment. Factors associated with seroconversion were age and hepatitis C virus (HCV) load. CHC patients aged 55 years and above, those with chronic diseases and those with HC viral load of ≥ 900,000 IU/ml were found to be statistically associated with poor HRQOL. All the domains of the SF36 decreased by the end of the 4th week and started to increase at the 24th and 48th weeks of follow up period.

Keywords: hepatitis C, treatment, quality of life.

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INTRODUCTION

Hepatitis C (HC) is an infectious liver disease caused by hepatitis C virus (HCV). The virus can cause both acute and chronic hepatitis infection, ranging in severity from a mild illness lasting a few weeks to a serious lifelong illness. About 15–45% of infected persons spontaneously clear the virus within 6 months of infection without any treatment. The remaining 55–85% of persons will develop chronic hepatitis C (CHC) infection. Of those with CHC infection, the risk of cirrhosis of the liver is 15–30% within 20 years.(1) Once cirrhosis is established, the rate of developing hepatocellular carcinoma is about 1–4% per year.(2) It is estimated that about 3% of the world's population are living with CHC. About 3–4 million people are infected per year, and more than 350,000 people die yearly from HC related diseases.(3,4) During 2010, it was estimated that 16,000 people died from acute infections while 196,000 deaths occurred from liver cancer secondary to the infection.(5) Egypt has the highest prevalence of HC in the world. Overall estimates of the HCV rate in the general population have ranged between 10 and 20% (20-30% HCV antibodies in rural areas). Geographically, HC prevalence has been shown to be higher in Lower Egypt

(Nile Delta) than in Upper Egypt and lower in urban compared to rural areas. HCV infection has become the leading risk factor for hepatocellular carcinoma (HCC) in Egypt (antibodies present in as many as 75–90% of HCC cases).[6]

The current and future burden of disease caused by viral hepatitis in Egypt is significant. It is not an exaggeration to say that viral hepatitis (particularly HCV) is currently and will remain for some time Egypt's most pressing public health issue. Current liver mortality, including liver cirrhosis and cancer, is over 40,000/year and is increasing annually. This represents more than 10% of total mortality.[7] Liver disease is thus the second commonest cause of death in Egypt, after heart disease. Hepatitis C related morbidity and mortality are predicted to at least double in the coming 20 years.[8, 9] Several specificities of the Egyptian epidemic are to be noted. First, nearly all Egyptian HCV infections (upwards of 95%) are genotype 4. While HCV genotype has no impact on the course of the disease, different genotypes do react differently to treatment: genotype 4 has an intermediate resistance to treatment. For this reason, Egyptian patients must undergo longer courses of treatment: 48 weeks instead of the 24 weeks recommended for patients infected with genotypes 2 and 3. Egyptian patients may also be co-infected with Schistosomiasis, a pathogen that also harms the liver and accelerates the course of liver disease.[7] The standard therapy is a combination of peginterferon and ribavirin (PEG-IFN/RBV). Overall, 50–80% of people treated are cured. Those who develop cirrhosis or liver cancer may require a liver transplant. Hepatitis C is the leading reason for liver transplantation, though the virus usually recurs after transplantation.[10] The ultimate goal of HC treatment is to eradicate HCV infection and thereby reduce the risk of progression to HCV related liver complications, including liver failure, hepatocellular carcinoma, and death. The endpoint of HCV treatment is a sustained virologic response (SVR), which correlates strongly with permanent clearance of the virus and effectively cure. There are, however, a number of intermediate viral endpoints measurement of the HCV RNA level at specific time points during the course of HCV treatment that inform the clinician about the patient's responsiveness to treatment and likelihood of SVR. These benchmarks reflect the second phase kinetics of viral elimination, can vary from patient to patient, and correlate strongly with the final treatment outcome.[11]

Responsiveness to HCV therapy depends not only on viral factors but also on host factors. Age, gender, cirrhosis, steatosis, insulin resistance, diabetes, African American ethnicity and body mass index (BMI) are all events associated to poor response to PEG-IFN/RBV treatment. Insulin resistance, obesity and steatosis are also associated with a higher risk of progression of fibrosis.[12] The burden of HCV infection is not limited to the impact of cirrhosis and HCC. HCV infection is associated with reduced health-related quality of life (HRQOL), even in the absence of cirrhosis.[13, 14] The reduction of HRQOL is probably also due to physical and psychiatric symptoms as a direct consequence of this chronic infection and its sequelae.[15] Treatment of chronic HCV with PEG-IFN/RBV further diminishes HRQOL due to its side-effects such as fatigue, myalgia, influenza-like symptoms, and alterations in mood, inability to concentrate, and change in libido, which may negatively affect the patient's vitality, social interaction, and ability to perform work and other activities, and even lead to discontinuation of therapy.[16]

The study was carried out to investigate the response of CHC patients to the scheduled standardized treatment of PEG-IFN/RBV combination therapy, to identify factors that could predict the response of CHC patients to the treatment and to assess the HRQOL of CHC patients before, during and after PEG-IFN/RBV combination therapy.

METHODS

The study was conducted among CHC patients who attended the Hepatology and Interferon Therapy Unit at Gamal Abd El Naser Insurance Hospital (GAIH). The study was essentially an intervention study (one group pre-test- post-test design).

Adult patients (18 years and more) who had not previously been treated with interferon or ribavirin were eligible for the study if they had a positive HCV antibody test or a detectable serum HCV-RNA by polymerase chain reaction (PCR).

The sample size was determined using MedCalc software, Version 11.5.10. Based on a suspected incidence of virology response to treatment of 60% among HC patients,[17] an α level of 0.05, power of 90% and a null hypothesis value of 45%, the minimum number of patients required was 233. Anticipating a maximum of 15% loss in follow up due to side effects of treatment, the sample was increased to 268 patients and 300 patients were included. The patients were consecutively recruited until completion of the required sample size. The patients were interviewed at baseline, 4, 12, 24 and 48 weeks (during the treatment sessions) to assess the treatment response of CHC patients before, during and after the treatment with PEG-IFN/RBV combination therapy.

A pre-designed structured interviewing questionnaire was used to collect socio-demographic data (including age, gender, and residence, marital status, level of education, occupation, and family size) and medical history of chronic diseases as diabetes mellitus and cardiovascular diseases.

Review of the patients' medical records and their laboratory investigations including haemoglobin level, liver enzymes (AST, ALT), bilirubin, HCV RNA level by PCR and thyroid stimulating hormone (TSH) was also carried out. These investigations were routinely conducted for the patients at the hospital. Haemoglobin level, liver

enzymes (AST, ALT) and bilirubin were recorded before administration of the combined therapy and at 4, 12, 24, 48 weeks after therapy. HCV RNA level by PCR and TSH were recorded before administration of the combined therapy, and at 12, 24 and 48 weeks after therapy. The viral HC quality of life questionnaire was used.[18, 19] It included the SF-36 generic form and measures of concepts thought to characterize the experience of living with CHC. The SF-36 has 36 items and consists of 8 multi-items variables (domains): Physical functioning (10 items), social functioning (2 items), role limitation due to emotional problems (3 items), role limitation due to physical health problems (4 items), emotional well- being (5 items), energy and vitality (4 items), pain (2 items), general perception of health (5 items), and another single item which solicits a self-assessment of health change over the past year. Each SF- 36 was scored using norm-based methods that standardize the scores to a mean of 50 and a standard deviation (SD) of 10, yielding score values of 0 to 100, with high scores indicative of better health. Mantel-Haenszel Chi-square (X2MH), test was used to test the relationship between an outcome and the status of an exposure with stratified data to control for the effect of confounders. Multivariate logistic regression analysis was used to assess predictors of seroconversion among CHC cases treated in Alexandria. It was also used to assess the relationship between predictors' seroconversion among HC cases treated and HRQOL. Survival analysis was also used to assess differences between predictor variables affecting cumulative survival of seronegativity among treated CHC patients in Alexandria. General linear model - Multivariate analysis of variance (MANOVA) was used to test the hypothesis of a significant association between a set of interrelated dependent variables and interdependent variables. In the present study, it was used to explore the impact of the socio-demographic, medical, social and psychological aspects of the patient and family related factors on QOL of CHC patients. It was also performed to compare SF-36 scores between groups. Before implementing the study, frequent meetings were held with the patients to explain the aim of the study.

Ethical Considerations

This study protocol was approved by the Institutional Review Board and the Ethics Committee of the High Institute of Public Health, Alexandria University. The study conformed to the International Guidelines for Research Ethics. Before an individual was included in the study, a verbal consent was obtained after explanation of the purposes and benefits of research.

RESULTS

The age of patients ranged from 24 years to 63 years with a mean age of 48.03±7.62 years. About two thirds of the patients (70.7%) were males, 80.7% were married and 63% lived in Alexandria Governorate. Regarding the level of education, 36.3% of the patients had secondary education and 20.3% had basic education. As for the occupation, 46.7% of the patients were professionals, 26.7% were skilled workers, and 16.3% were merchants. The family size of 61% of the patients was ≤ 4 members (Table I).

Table (1): Distribution of CHC patients according to their sociodemographic characteristics (GANIH, Alexandria, 2013)

Sociodemographic data	No.	%
Age (Mean± SD)	**48.03 ± 7.62**	
Gender		
Males	212	70.7
Females	88	29.3
Level of education		
Primary	61	20.3
Preparatory	40	13.3
Secondary	109	36.3
University	90	30.1
Residence (Governorate)		
Alexandria	189	63.0
Behira	84	28.0
Matrouh	27	9.0
Marital status		
Married	242	80.7
Widowed	25	8.3
Single	24	8.0
Divorced	9	3.0
Occupation		
Professionals	140	46.7
Skilled workers	80	26.7
Merchants	49	16.3
Retired	31	10.3
Family size		
≤4 numbers	183	61.0
>4 numbers	117	39.0

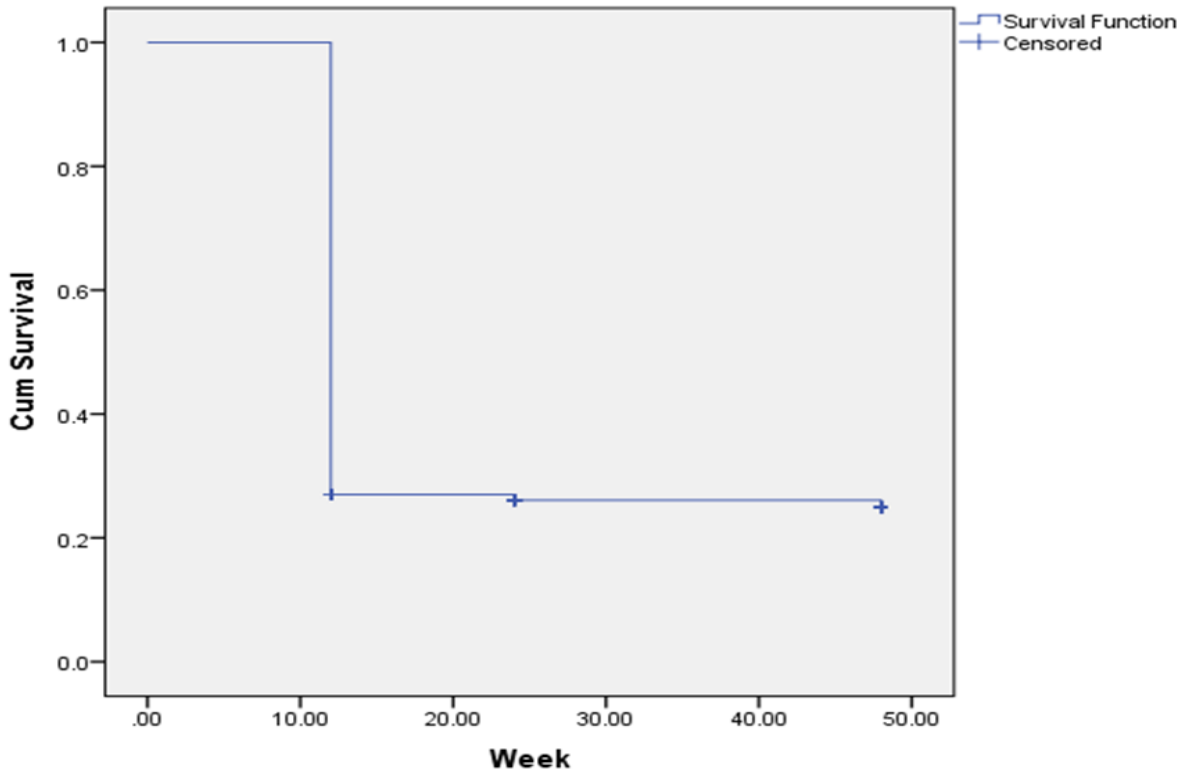

Figure (1): Cumulative proportion of treated CHC patients surviving seronegativity (GANIH, Alexandria, 2013)

Out of the 300 CHC patients treated with PEG-INF/RBV, 222 patients became negative giving a cumulative seronegativity rate of HCV of 74%. Applying the survival analysis to determine the distribution of time to effect for the treatment of HCV, figure 1 shows that the proportion of CHC patients who survived seronegativity was 0.270 at the 12th week, 0.261 at the 24th week and 0.250 at the 48th week of treatment.

Table 2 illustrates the crude odds ratio of seroconversion among CHC patients at the 48th week of treatment, their sociodemographic characteristics and the presence of chronic diseases. Age, sex, patients' occupation, presence of chronic diseases and HC viral load were found to be significantly associated with seronegativity.

Table 3 describes the logistic regression results with the seronegativity of CHC patients at the 48th week of treatment as the dependent variable. Two variables were found to significantly affect the seronegativity. The first was the patient's age and the second was the HC virus load. Patients below 55 years of age had a significant increased seroconversion compared to relevant categories. Patients who become seronegative were 1.3 times more likely to had been less than 55 years of age (OR= 1.26, 95% CI= 1.105-1.449), and were 96 times more likely to have had HC viral load less than 900.000 IU/ml (OR= 96.24, 95% CI=30.650- 302.215). The variables in the model had a 98 % discrimination power for probability of HC negativity among CHC patients.

Studying the effect of the personal characteristics of the CHC patients on HRQOL, one-way MANOVA indicated a significant impact of age ($F = 26.928$, $p = 0.000$), occupation ($F = 1.547$, $p = 0.046$), family size ($F = 2.222$, $p = 0.026$), presence of chronic diseases ($F = 5.306$, $p = 0.000$) and HC viral load ($F = 2.632$, $p = 0.009$) (Table 4). The table also presents Eta square which describes the proportion of total variability attributable to a factor and Wilks' Lambda that measures the percent of variance in the dependent variables that is not explained by differences in the level of the independent variable.

Table (2): Crude odds ratio of seroconversion among CHC patients at 48th week of treatment (GANIH, Alexandria, 2013)

Variable	cOR	95% CI	X^2MH
Age in years (<55 versus 55+ years)	15.505	8.256 - 29.118	88.035, p = 0.000*
Gender (males versus females)	0.538	0.290 - 0.997	3.956, p = 0.049*
Residence (Alexandria and Behira versus Matrouh)	1.773	0.775 - 4.058	1.297, p = 0.255
Level of education (up to secondary versus university)	0.817	0.460 - 1.45	0.297, p = 0.586
Family size (<4 versus 4+)	1.294	0.767 - 2.185	0.689, p = 0.407
Occupation (professionals and skilled workers versus others)	5.20	2.96 - 9.13	36.150, p = 0.000*
Marital status (ever married versus single)	0.383	0.111- 1.321	1.761, p = 0.184
HC viral load (< 900,000 IU/ml versus ≥ 900,000 IU/ml)	210.0	76.038 - 579.976	211.226, p = 0.0000*

cOR, crude odds ratio; CI, confidence interval *Significant (p< 0.05)

Table (3): Logistic regression analysis of the factors affecting seroconversion among CHC patients (GANIH, Alexandria, 2013)

Variable	Coefficient B	S.E.	P. value	Odds Ratio	95% C.I	
					Lower	Upper
Age in years	0.236	0.069	0.001*	1.266	1.105	1.449
Gender	0.144	0.643	0.822	1.155	0.328	4.072
Occupation	0.659	0.647	0.309	0.517	0.145	1.840
Presence of chronic diseases	0.309	0.403	0.443	1.362	0.618	3.002
HC viral load	4.567	0.584	0.000*	96.244	30.650	302.215
Constant	20.293	3.898	0.000*			

Classification accuracy of the model was 93.6%. *Significant (p< 0.05) CI, Confidence interval; SE, standard error

Table (4): MANOVA general F-test, factors affecting HRQL of CHC patients at baseline (GANIH, Alexandria, 2013)

Variable	Wilks' Lambda	F	P. value	Partial Eta Squared	Observed Power
Age in years	0.564	26.928	0.000*	0.010	0.175
Gender	0.990	0.370	0.936	0.436	1.000
Level of education	0.977	0.809	0.595	0.023	0.375
Residence	0.979	0.739	0.657	0.021	0.342
Marital Status	0.975	0.880	0.534	0.025	0.408
Occupation	0.878	1.547	0.046*	0.042	0.965
Family size	0.940	2.222	0.026*	0.060	0.863
Presence of chronic diseases	0.753	5.306	0.000*	0.132	1.000
HC viral load	0.930	2.632	0.009*	0.070	0.923

*Significant (p< 0.05)

Given the significance of the overall test, the univariate main effects were examined. Significant univariate main effects for age were statistically associated with poor HRQOL in the domains of physical functioning, role limitations due to physical health, role limitations due to emotional problems and pain (F=175.716, p= 0.000 and F= 22.049, p= 0.000, F=21.922, p= 0.000, F=123.958, p= 0.000, respectively). Notably, occupation had a significant impact on physical functioning (F= 4.639, p= 0.003). Presence of chronic diseases had a significant effect on physical functioning, role limitations due to physical health problems, role limitations due to emotional problems and pain (F= 23.422, p= 0.000, F= 27.936, p= 0.000, F= 29.911, p= 0.000 and F= 19.863, p= 0.000, respectively). The same picture was observed for the HC viral load. Note that the F does not extend to the univariate tests and the confidence level was divided by the number of tests to be performed (0.05/5= 0.01) (Table 4).

Table (5): MANOVA univariate general F-test for the factors affecting HRQL of CHC patients at baseline (GANIH, Alexandria, 2013)

Source	Dependent Variable	F	P. value	Partial Eta Squared	Observed Power
Age	Physical functioning	175.716	0.000*	0.381	1.000
	Role limitations due to physical health	22.049	0.000*	0.072	0.997
	Role limitations due to emotional	21.922	0.000*	0.071	0.997
	Pain	123.958	0.000*	0.302	1.000
	Emotional well-being	1.969	0.162	0.007	0.288
	Energy/fatigue	0.725	0.395	0.003	0.136
	Social functioning	1.653	0.200	0.006	0.249
	General health	1.335	0.249	0.005	0.210
Occupation	Physical functioning	4.639	0.003*	0.046	0.890
	Role limitations due to physical health	1.343	0.261	0.014	0.356
	Role limitations due to emotional	1.320	0.268	0.014	0.351
	Pain	0.342	0.795	0.004	0.116
	Emotional well-being	0.720	0.541	0.007	0.203
	Energy/fatigue	0.994	0.396	0.010	0.270
	Social functioning	1.289	0.278	0.013	0.343
	General health	1.576	0.195	0.016	0.413
Family size	Physical functioning	0.014	0.907	0.000	0.052
	Role limitations due to physical health	4.616	0.033	0.016	0.572
	Role limitations due to emotional	4.658	0.032	0.016	0.576
	Pain	0.974	0.324	0.003	0.166
	Emotional well-being	0.405	0.525	0.001	0.097
	Energy/fatigue	0.068	0.794	0.000	0.058
	Social functioning	4.969	0.027	0.017	0.603
	General health	2.860	0.092	0.010	0.392
Presence of chronic diseases	Physical functioning	23.422	0.000*	0.141	1.000
	Role limitations due to physical health	27.936	0.000*	0.163	1.000
	Role limitations due to emotional	29.911	0.000*	0.173	1.000
	Pain	19.863	0.000*	0.122	1.000
	Emotional well-being	0.524	0.593	0.004	0.136
	Energy/fatigue	0.220	0.802	0.002	0.084
	Social functioning	4.622	0.011	0.031	0.778
	General health	0.159	0.853	0.001	0.074
HC Viral Load	Physical functioning	12.486	0.000*	0.042	0.941
	Role limitations due to physical health	17.172	0.000*	0.057	0.985
	Role limitations due to emotional	17.732	0.000*	0.058	0.987
	Pain	8.503	0.004*	0.029	0.828
	Emotional well-being	0.778	0.378	0.003	0.142
	Energy/fatigue	0.383	0.537	0.001	0.095
	Social functioning	1.815	0.179	0.006	0.269
	General health	0.992	0.320	0.003	0.168

*Significant ($p< 0.01$)

Chronic HC patients of 55 years and above, those with chronic diseases and those with a HC viral load of ≥900,000 IU/ml were significantly associated with poor HRQOL in the domains of physical functioning, role limitations due to physical health problems, role limitations due to emotional problems and pain in comparison with other age groups as revealed by the Post hoc test results. Retired CHC patients had the worst HRQOL on physical functioning only. As for the HRQL in the follow up period of treatment, all the domains of the SF36 decreased by end of the 4th week and started to increase at the 24th and 48th weeks of follow up period ($p< 0.000$).

Table (6): Means for the SF-36 subscales for CHC patients at baseline, 4th, 12th, 24th and 48th weeks of treatment (GANIH, Alexandria, 2013)

HRQOL Domains	Baseline	4th week	12th week	24th week	48th week	F	P	Mean score for the 5 periods
Physical functioning								
Mean	81.1556	74.7333	62.9222	67.8442	72.0765	33.744	0.000*	71.7993
SD	19.95158	19.40310	19.40248	23.08028	20.79063			21.44367
Role limitation due to physical health problems						14.956	0.000*	
Mean	75.4583	70.2917	63.8333	67.8442	76.9467			70.6866
SD	24.56346	23.95863	21.62149	23.08028	23.70735			23.85715
Role limitation due to emotional problems								
Mean								
SD	75.1111	70.9459	63.5556	67.8442	75.4781	13.279	0.000*	70.4390
	24.70537	24.28810	21.45633	23.08028	22.85116			23.72466
Pain								
Mean	38.1818	44.2727	70.0556	68.1159	69.2250	193.949	0.000*	57.3549
SD	21.42031	23.78029	15.27333	15.20609	16.28516			23.45154
Mental health								
Mean	71.1333	68.0825	61.8222	63.1522	63.6339	77.566	0.000*	65.6801
SD	8.36576	8.56840	6.61166	7.73862	6.16054			8.37516
Vitality						169.414	0.000*	
Mean	74.6667	69.9833	62.5556	64.0550	63.7637			67.1805
SD	6.86677	7.90479	6.22765	6.54511	6.03368			8.23090
Social functioning								
Mean	60.0333	54.5151	62.7000	62.3913	63.8115	45.887	0.000*	60.5426
SD	8.67466	13.58600	7.78323	7.34147	7.01419			9.87518
General health								
Mean	62.3067	64.7492	68.9600	74.7826	75.2295	160.344	0.000*	68.8767
SD	10.52784	7.66938	6.27026	6.46528	6.01751			9.20835
Sleep								
Mean	61.4444	59.7861	57.9259	60.2657	62.9326	8.775	0.000*	60.4039
SD	12.97503	11.07256	10.59458	8.12092	8.18742			10.55620
HCHDS								
Mean	58.7037	52.5105	48.3611	56.1695	62.8529	46.843	0.000*	55.5617
SD	14.05298	11.56404	12.25799	13.31387	15.68827			14.31219
HCLS								
Mean	39.5539	45.4378	76.5304	68.4058	62.7234	273.457	0.000*	58.8361
SD	14.27517	17.85070	13.07674	14.61307	15.98184			20.71120
Sex limitations								
Mean	47.8237	51.5625	77.0523	69.8810	56.6159	79.775	0.000*	61.0088
SD	26.85518	24.01983	15.62404	16.04632	21.29183			24.01412
Satisfaction								
Mean	54.4444	62.2594	76.1333	69.7826	61.2568	65.804	0.000*	64.9448
SD	22.97031	17.03267	13.48344	14.57662	18.47069			19.27702
Physical health								
Mean	64.2539	48.1651	66.4428	69.6467	73.3694	420.412	0.000*	63.9429
SD	6.58122	3.69421	8.07687	11.05263	9.03840			11.78577
Mental emotional health								
Mean	70.2674	65.8479	62.6583	64.3607	66.6718	56.033	0.000*	65.9602
SD	6.95773	6.29473	5.91649	6.93587	6.73697			7.05942
Viral HC Quality of life questionnaire								
Mean	50.6056	53.9551	66.7470	64.5616	61.2547	146.731	0.000*	59.3255
SD	10.67626	9.57555	6.47778	6.58308	6.98211			10.37404

*Significant ($p < 0.05$)

DISCUSSION

Chronic HC is a blood-borne infection. Most patients will have subclinical infection at the onset, but patients who develop acute hepatitis can spontaneously clear the virus upon immune activation. Up to 80% of CHC patients will progress to chronic infection. CHC is unlikely to clear spontaneously.[13] The goal of treatment of CHC is to prevent complications of HC infection; this is principally sought by eradication of the infection. Accordingly, treatment is aimed to achieve a virological response. Pegylated interferon in combination with ribavirin is the standard treatment for CHC virus infected patients. A combination of weekly subcutaneous injections of pegylated interferon and oral ribavirin represents the

standard of care according to The American Association for the Study of Liver Diseases practice guideline.[20]

Regarding the distribution of time to effect for combined PEG-INF/RBV treatment of HCV, the present study showed that most CHC patients who were able to complete the first 12 weeks of therapy achieved early virologic response (EVR) and had a high probability of end of therapy (ETR). This finding coincided with those reported by Yu et al (2009)[21] in China, Huang et al (2010)[22] in Korea and Ponziani et al (2012)[23] in Italy. Moreover, Peignoux et al (2009) in France found that patients who failed to achieve EVR would not clear the virus even if an additional 9 months of therapy was received.[24]

According to the current logistic regression analysis results, two variables were found to be significant predictors of treatment response among CHC patients who received combined PEG-INF/RBV therapy namely; age (below 55 years) and HC viral load of less than 900.000 IU/ml. Similar findings were reported from several studies.[24-30]

In addition to age and viral load, other factors were reported in other studies including higher serum ALT, absence of cirrhosis, body weight and neutrophils 2,300 cells/L or greater.[31-33]

On the other hand, several studies found that HCV genotype was the only significant predictor for treatment response.[34-37] The study conducted by Yu et al (2008) in Taiwan showed that HCV genotype and rapid virologic response (RVR) were the strongest independent factors associated with a virologic response, followed by treatment duration and low baseline viral load.[21]

Quality of life is a significant factor when making decisions about HC treatment. Patients want to know if they are going to get back a better QOL in exchange for a temporarily reduced one caused by the side effects of the HCV medications.[15]

Regarding HRQOL among CHC patients who received combined PEG-INF/RBV treatment, the present study showed that CHC patients of 55 years and above were found to be statistically associated with poor HRQOL in the domains of physical functioning, role limitations due to physical health problems, role limitations due to emotional problems and pain in comparison with other age groups as revealed by the Post hoc test results. Age was statistically associated with poor HRQOL in both the physical and mental domains. Similar findings were reported by other studies in Greece[38], France[15] and Egypt[39, 40].

As regards HRQOL of CHC patients in the follow up period of PEG-INF/RBV therapy, the present study showed that all the domains of the SF-36 decreased by the end of the 4th week and started to increase at the 24th and 48th weeks of follow up period. Similar findings were reported from Pakistan and Taiwan.[41, 42]

Moreover, Mathew et al (2006),[43] and Foster et al (2009)[44] reported that without treatment, CHC patients will be unlikely to see any improvement in HRQOL. The HRQOL scores of patients with HCV infection refractory to prior treatment at baseline were low compared to the general population.

Furthermore, the study conducted in Greece (2010) showed that the course of patients' HRQOL in the middle of treatment values in all SF-36 scales was below those of baseline and they returned to pre-treatment levels at the end of therapy. During treatment, values of HRQOL were worsened possibly due to combined PEG-INF/RBV treatment and in the long-term treatment resulted in improvement of HRQOL.[38]

Transient deterioration of HRQOL of patients submitted to treatment is mainly due to the induction of depression and other side effects of treatment with combined PEG-INF/RBV, but HRQOL frequently improves in all domains after completion of antiviral treatment. Early improvement in the HRQOL of patients who become HCV-RNA negative suggests that the virus itself plays a biological role.[43-45] On the other hand, Chang et al reported that CHC patients who received combined PEG-INF/RBV therapy had poor HRQOL during the treatment period. Treatment duration correlated negatively with the general health domain of HQLQ.[46] IFN and RBV are both associated with well-documented side effects that compromise HRQOL. However, HRQOL can return to or exceed pre-treatment levels in patients who respond well to therapy.[16] Similarly, Pojoga et al (Romania, 2013) reported that CHC patients had a markedly reduced HRQOL both before and after the treatment. The antiviral therapy did not influence the level of the HRQOL.[47] Sovaldi is an antiviral medicine that contains the active substance sofosbuvir. It is used to treat chronic (long-term) HC in adults. It has been marketed since 2013. Compared to previous treatments, sofosbuvir-based regimens provide a higher cure rate, fewer side effects, and a 2—4 fold reduced duration of therapy.[48] Sofosbuvir allows most patients to be treated successfully without the use of peginterferon, an injectable drug with severe side effects that is a key component of older drug combinations for the treatment of HCV.[49, 50]Sofosbuvir – commercial name Sovaldi – was approved in the United States in December 2013 and entered Egypt on 16 October 2014. Sovaldi based oral therapy offers high cure rates for HCV infection with excellent tolerability. The number of patients expected to be treated with Sovaldi is about 160,000 starting in June 2015.[51]

In Egypt, the basic reproductive rate (Ro) of the spread of HCV without treatment was 3.54, suggesting a self-sustained spread. Furthermore, the present national treatment program only decreased Ro from 3.54 to 3.03. Individuals with high rates of medical injections seem to be responsible for the spread of HCV in Egypt; the Ro of the spread of HCV without treatment would be 0.64 if everybody followed the average behavior. The effect of treatment on HCV transmission is greatly enhanced if treatment is provided a mean of 2.5 years after chronic

infection and with drug regimens with more than 80% efficacy. With these treatment parameters, preventive and curative interventions targeting individuals with high rates of medical injections might decrease Ro below 1 for treatment coverage lower than 5%.[51]

The rapid pace of HCV drug development has led to the optimistic prediction that eradication of HCV is feasible. This would be the first chronic viral infection that can be eradicated in the absence of a prophylactic vaccine. Although HCV eradication is potentially feasible, that time is not imminent; there remain many barriers that need to be overcome. Such barriers include the development of simplified and highly effective drug regimens, improving the rates of detection of infection, and the availability of resources (including financial and medical expertise).[51]

CONCLUSION & RECOMMENDATIONS

The proportion of CHC patients who survived seronegative was 0.250 at the 48th week of treatment. Factors associated with seroconversion were age (below 55 years) and HC virus load (< 900,000 IU/ml). CHC patients of 55 years and above, with chronic diseases and those with a HC viral load of ≥ 900,000 IU/ml were found to be statistically associated with poor HRQOL in the domains of physical functioning, role limitations due to physical health problems, role limitations due to emotional problems and pain in comparison with other age groups.
Retired CHC patients had the worst HRQOL on physical functioning only. All the domains of the SF36 decreased by end of the 4th week and started to increase at the 24th and the 48th weeks of follow up period. The same picture was observed in the selected viral HC quality of life questionnaire score, physical health and mental health components.

Identifying the predictors of response to PEG-INF/RBV therapy and tailoring treatment regimens for individual patients based on their risk profile factors may be one approach for achieving maximum antiviral response. These findings will be a baseline for Sovaldi treatment and need to be supported by large, prospective clinical studies that are designed to evaluate the virologic response rates of Sovaldi.

Development of epidemiological models to understand the transmission dynamics of HCV in Egypt, new infections and possibility of eradication of the disease should be carried out. Although HCV eradication is potentially feasible, there remain many barriers that need to be overcome in Egypt. Such barriers include the development of simplified and highly effective drug regimens, the needs assessment for HCV treatment, improving the rates of detection of infection, and the availability of financial resources.

Evaluation of the HRQOL of CHC patients especially those at risk for poor treatment response; older age, those with chronic diseases and those with high HC virus load is important. The questionnaire should be applied through treatment sessions to assess the treatment response and its relation with the quality of life.

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