Research Article

Factors affecting Health-related quality of life in chronic hepatitis C patients receiving interferon treatment, Minia Governorate, Egypt

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Abstract
Background: hepatitis C is a serious public health problem that threatens the quality of life of patients with the disease. This study explores the course of and factors associated with Health-related quality of life (HRQOL) in chronic hepatitis C patients given interferon treatment. **Aim of the study:** To determine factors associated with reduced HRQOL in chronic hepatitis C patients receiving interferon treatment. **Subjects and methods:** This prospective hospital based study included 120 chronic hepatitis C patients of them 63 patients attending the Interferon Unit in Samalot city and 57 attending the Health Insurance Hospital in El-Minia city from January 2013 to January 2015. The study was conducted to determine factors associated with reduced HRQOL in chronic hepatitis C patients receiving interferon treatment (pretreatment and during treatment) using "SF-36V2 questionnaire". **Results**: At baseline, the most important socio-demographic and clinical factors affecting physical component score (PCS) was sex, while the least factors were age and residence, while mental component score influenced by marital state. During treatment, physical component score (PCS) influenced by occupation and fibrosis stage followed by hemoglobin level (HB) and thyroid stimulating hormone (TSH). As regard mental component score, the most important factors were PCR and occupation. **Conclusion**: Main determinants of physical component score (PCS) of HRQOL during interferon treatment were occupation and fibrosis stage followed by hemoglobin level (HB) and thyroid stimulating hormone (TSH). As regard mental component score, influenced by PCR and occupation.

Key words: Hepatitis C, factors, Health-related quality of life, therapy, Minia.

Introduction
Chronic Hepatitis C (CHC) is an infectious disease caused by the hepatitis C virus (HCV)[1]. World Health Organization (WHO) figures show that around 200 million people globally are infected with HCV, which is particularly concentrated in the blood. Around 170 million people are chronic carriers of the virus, which can lead to cirrhosis, liver failure, and hepatocellular carcinoma [2].

Egypt has the largest burden of HCV infection in the world, with a 10% prevalence of chronic HCV infection among persons aged 15–59 years [3]. HCV transmission is ongoing in Egypt and incidence rates have been estimated at 2.4 per 1,000 person-years (165,000 new infections annually) [4], HCV transmission in Egypt is associated primarily with inadequate infection control during medical and dental care procedures[5, 6].

Health-related quality of life (HRQOL), which reflects what patients are concerned with and what they experience, has been widely researched in patients with CHC.

Pegylated interferon and ribavirin have significant side effect profiles that reduce quality of life. Examples of common side effects which negatively affect quality of life include fatigue, flu-like illness, anxiety, depression, irritability, insomnia, mood swings, and loss of concentration, anemia, rash, pruritus, joint pains, muscle aches and fever [7].

Patients chronically infected with hepatitis C virus (HCV) have a decreased health related quality of life (HRQL) compared to the general population [8, 9]. The impact of the disorder is comparable with other stressful life events and chronic diseases, like diabetes [10]. In part, the reduction in HRQL is due to the mental components of HRQOL. With regard to these mental components, patients aware of their diagnosis have a more reduced HRQOL than those who are unaware [11]. Furthermore, many HCV patients have a previous or ongoing addiction and/or psychiatric problems, reflected in lower HRQOL. In addition, patients with hepatitis C are stigmatized in society and the majority of the population of hepatitis C patients has a lower social economic status compared to the general population.[12.] The reduction of HRQL is probably also due to physical and psychiatric symptoms as a direct consequence of this chronic infection and its sequelae (such as cirrhosis). The chronic inflammation is believed to signal the brain and to give rise to neurovegetative symptoms (e.g. malaise and fatigue) and to amongst others depression and concentration difficulties [13]. Possibly, also the brain itself is infected by HCV[14].

Health-related quality of life (HRQOL), which reflects what patients are concerned with and what they experience, has been widely researched in patients with CHC in the West. Indeed, the factors affecting HRQOL and the adverse effects of antiviral treatment have been documented for Western populations. However, to our knowledge, such studies have not been done for HRQOL in Egyptian patients with CHC.

Subjects and methods:

This prospective hospital based study included 120 chronic hepatitis C patients of them 63 patients attending the Interferon Unit in Samalot city and 57 attending the Health Insurance Hospital in El-Minia city from January 2013 to January 2015. The study was conducted to assess the HRQOL and its relation to socio-demographic and clinical characteristics in HCV-infected patients (at the beginning, after 3 months, and at the end of receiving the interferon treatment using "SF-36V2 questionnaire".

Criteria of inclusion:

- All patients who were clinically and laboratory assessed at the study site and found to be good candidates for receiving treatment (i.e. antiviral therapy in form of ribavirin and interferon) at health insurance hospital and the interferon unit in one day surgery hospital in Samalot district.
- Age above 18 years.

Criteria of exclusion:

- CHC patients not receiving treatment.
-CHC patients who were already on interferon treatment during the emanation of the study.

Assessment tool:

All the participants in the study were interviewed to collect the following data:

1- Socio-demographic data: name, age, sex, residence, marital status, educational level and occupation

2- Quality of life: was assessed by using "SF-36V2 questionnaire" [15].

Which measures health related quality of life (HRQOL). The previously validated Arabic version of the SF-36 questionnaire was used. The SF36 questionnaire measures eight multi-item variables (physical functioning, physical role limitations, bodily pain, general health, vitality, social functioning, emotional role limitations, and mental health).

After the questionnaire being completed, and the resulting scores were transformed onto a scale of 0 (worst possible score) to 100 (best possible score), as recommended by the questionnaire's originators.

We calculated physical component summary (PCS) and mental component summary (MCS) online using US norm-based methods—in which the mean is 50 (SD, 10) in the 1998 general US population.

The questionnaire was administrated in the form of interview schedule .The average time required to complete the questionnaire was 20 minutes .This was done in El Minia health insurance hospital and the interferon

unit of the one-day surgery hospital in Samalot city.

Statistical analysis:

Data entry and analysis were all done with IBM compatible computer using software called Statistical Package for Social Science (SPSS) for windows version 18. Graphics were done using Excel.

Quantitative data were presented by mean and standard deviation, while qualitative data were presented by frequency distribution. Correlation, Chi Square, linear regression, one way-ANOVA and t test were done.

The probability of less than 0.05 used as a cut off point for all significant tests.

Results

This study included 120 chronic hepatitis C patients, of them 63 patients attending the Interferon Unit in Samalot city and 57 attending the Health Insurance Hospital in El-Minia city from January 2013 to January 2015. The age of the subjects attending the Interferon Unit ranged between 22-69 years (mean age was 45.13±10.53), while the age of the subjects attending the Health Insurance Hospital ranged between 30-65 years (the mean age was 46.54±8.45).

Table (1): Socio-demographic characteristics of the studied chronic hepatitis C patients attending the Interferon Unit in Samalot city and the Health Insurance Hospital in El-Minia city from January 2013 to January 2015.

Socio-demographic & clinical characteristics		N (120)	Percent (100%)
Sex	Male	104	86.7%
	Female	16	13.3%
Residence	Urban	31	25.8%
	Rural	89	74.2%
Marital status	Married	116	96.7%
	Not married	4	3.3%
Educational level	Illiterate	11	9.2%
	Read &write	6	5.0%
	Below university	63	52.5%
	University & above	40	33.3%
Occupation	Non worker	10	8.3%
	Farmer	5	4.2%
	Employee	90	75.0%
	Free worker	15	12.5%
Age groups	22-37	27	22.5%
	38-53	60	50%
	54-69	33	27.5%
Type of interferon			
Pegylated interferon alpha-2a (Pegasys)		27	22.5%
Pegylated interferon alpha-2b (pegintron)		36	30.0%
Pegylated interferon alpha-2a (Reiferon Retard)		57	47.5%
Other comorbidities	Yes	32	26.6%
	No	88	73.4%
PCR	Low viremia	73	60.8%
	High viremia	47	39.2%
Fibrosis stage	F1	52	43.3%
	F2	39	32.5%
	F3	29	24.2%
Activity grade	A1	33	27.5%
	A2	59	49.2%
	A3	28	23.3%

Table (1) showed the socio-demographic and clinical characteristics of the studied patients, there were 104 (86.7%) males and 16 (13.3%) females and this difference was not significant. It also shows that 26.6% of them have other comorbidities. 47.5% of the study subjects under Reiferon retard drug, and about 40 % of the patients have high viraemia, 43.3% of patients' fibrosis stage was F1 and 49.2% of patients' activity grade was A2.The age of patients with hepatitis C ranged between 22-69 years, the majority of them lied in the age group between 38-53 years.

Table (2): Multiple regression analysis of socio-demographic and clinical factors affecting the physical component summary (PCS) pretreatment among chronic hepatitis C patients attending the Interferon Unit in Samalot city and the Health Insurance Hospital in El-Minia city from January 2013 to January 2015.

Socio-demographic /clinical factors	Beta	p
Sex	-0.385	0.001
Activity grade	-0.126	0.4
Occupation	0.106	0.3
Education	0.087	0.4
Marital state	-0.066	0.4
Hemoglobin level	-0.060	0. 5
PCR	0.043	0.6
Other comorbidities	0.042	0 .6
Fibrosis stage	0.037	0.8
Age	-0.034	0.7
Residence	0.020	0.8

Dependent variable is physical component score

R^2= 0.2 F= 2.29 p= 0.01

Table (2) showed that the most important socio-demographic and clinical factors affecting physical component score among the studied chronic hepatitis C patients was sex, while the least factors were age and residence.

Table (3): Multiple regression analysis of socio-demographic and clinical factors affecting the mental component summary (MCS) pretreatment among chronic hepatitis C patients attending the Interferon Unit, Minia from Jan. 2013-Jan. 2015.

Socio-demographic /clinical factors	Beta	p
Marital state	-0.202	0.03
Other comorbidities	0.159	0.1
Occupation	-0.141	0.1
Sex	-0.067	0.5
Age	0.063	0.5
PCR	0.058	0.6
Residence	0.048	0. 6
Education	0.035	0 .7
Activity grade	0.028	0.8
Fibrosis stage	0.017	0.9
Hemoglobin level	-0.016	0.8

Dependent variable is mental component score

R^2= 0.1 F= 0.91 p= 0.5

Table (3) showed that the most important socio-demographic and clinical factors affecting mental component score was marital state.

Table (4): Multiple regression analysis of socio-demographic and clinical factors affecting the physical component summary (PCS) during treatment among chronic hepatitis C patients attending the Interferon Unit in Samalot city and the Health Insurance Hospital in El-Minia city from January 2013 to January 2015.

Socio-demographic /clinical factors	Beta	P
Occupation	0.304	0.0001
Fibrosis stage	-0.239	0.04
Thyroid stimulating hormone(TSH)	-0.217	0.003
Hemoglobin level	0.157	0.03
Activity grade	0.131	0.2
Marital state	0.130	0. 07
Type of interferon	-0.060	0.4
Sex	0.055	0 .4
Education	-0.044	0.6
Other comorbidities	-0.040	0.5
Age	0.028	0.7
Residence	0.005	0.9
Polymerase chain reaction (PCR)	-0.004	0.9

Dependent variable is physical component score

R^2= 0.2 F= 3.688 p= 0.002

Table (4) showed that the most important socio-demographic and clinical factors affecting physical component score during treatment among the studied chronic hepatitis C patients were occupation and fibrosis stage, while the least factors were PCR and residence.

Table (5): Multiple regression analysis of socio-demographic and clinical factors affecting the mental component summary (MCS) during treatment among the studied chronic hepatitis C patients attending the Interferon Unit in Samalot city and the Health Insurance Hospital in El-Minia city from January 2013 to January 2015.

Socio-demographic /clinical factors	Beta	P
Polymerase chain reaction (PCR)	-0.227	0.003
Occupation	-0.200	0.02
Sex	-0.129	0.1
Age	0.077	0.3
Type of interferon	0.067	0.3
Other comorbidities	0.067	0. 3
Activity grade	0.063	0.6
Residence	-0.031	0 .6
Education	0.029	0.7
Hemoglobin level	-0.024	0.7
Marital state	-0.019	0.8
Thyroid stimulating hormone(TSH)	0.007	0.9
Fibrosis stage	0.008	0.9

Dependent variable is mental component score

R^2= 0.1 F= 1.62 p= 0.08

Table (5) showed that the most important socio-demographic and clinical factors affecting mental component score during treatment among the studied chronic hepatitis C patients were PCR and occupation, while the least factors were TSH and fibrosis stage.

Discussion

This prospective consecutive hospital based study was carried out in Minia city from January 2013 to January 2015 and included 120 chronic hepatitis C patients (63 patients attending Samalot interferon unit and 57 attending the Health Insurance Hospital) to assess the HRQOL and its relation to socio-demographic and clinical characteristics of HCV-infected patients receiving the interferon treatment; at the beginning, after 3 months, and at the end of treatment. Patients attending the Interferon Unit were slightly younger than subjects attending the Health Insurance Hospital (mean age was 45.13 ± 10.53 Vs 46.54±8.45). The age of patients with hepatitis C ranged between 22-69 years, the majority of them lied in the age group between 38-53 years as shown in table (1). This is in agreement with Mohamoud et al., 2013[16] who found that the prevalence appears to increase dramatically with age with the highest rates observed among populations aged greater than 40 years. Also reported by Cuadros et al., 2014[17] who found that there was a strong association between HCV prevalence in individuals older than 30 years of age (who could have been exposed to parenteral antischistosomal therapy (PAT) and HCV prevalence in individuals 30 years of age or younger (who could not have been exposed to parenteral antischistosomal therapy (PAT). The age-specific prevalence of HCV has been proposed as one of the strongest signatures of the role of the past parenteral antischistosomal therapy (PAT) campaigns in driving HCV infection exposure in Egypt[18, 19].

The study group enrolled 51(81%) males vs. 12(19%) females attending the interferon unit in Samalot city, while 53 (93%) males vs. 4(7.0%) females attending the Health Insurance Hospital as shown in table (2). This sex distribution of HCV in this study is in agreement with Nafeh et al., 2000[20] who found that the prevalence of HCV was higher in males than females due to the fact that males were more susceptible to schistosomiasis than females and this was also reported by Fawzi et al., 2009[21] who found male preponderance in HCV-infected Individuals. Many studies[22-25] have showed that males who had risk of exposure to parenteral antischistosomal therapy and were older than 30 had much higher anti- HCV infection rates than females[18]. However, we are wondering whether this gender preference would simply be a reflection of a difference in risk practices or would females be endowed with some intrinsic characteristics that protect them from contracting HCV infection. Previous literature was not of much help but interestingly, it was noted in a study that female blood donors, compared with male blood donors, had higher prevalence of spontaneous viral clearance as well as biochemical and histological evidence of less advanced liver disease.[26,27] Nevertheless, the lower prevalence of HCV among females could also be secondary to associated factors such as younger age that may denote less exposure. On the other hand, there were studies that did not Support this gender difference[28,29] and even slightly higher prevalence of HCV infection in females has been claimed.[30]

Patients attending the interferon unit in Samalot city were (81%) rural vs (19%) urban, while patients attending health insurance hospital were (66.7%) rural vs (33.3%) urban as shown in table (2) and this was in agreement with Shalaby et al., 2010 [31]who studied prevalence, knowledge, attitude and practice among barbers and clients in Gharbia governorate and found that there was high prevalence of HCV in rural areas and this was ascribed to the endmicity of shistosomiasis in rural areas and the use of glass syringes for parenteral treatment in the past decades. Multiple studies were conducted among village residents in high HCV prevalence areas and reported the prevalence in rural areas averaged about 20%, higher than the national average[4, 16, 32-34.]

In multivariable regression analyses of socio-demographic and clinical factors affecting the physical component summary (PCS) and mental component summary (MCS) before treatment among the studied chronic hepatitis C patients, this study found that female sex was negative predictor of physical QOL score (PCS) as shown in table (4), This is in agreement with Schwarzinger et al., (2004)[35] who studied Chronic Hepatitis C Virus Infection in Rural Egypt and showed that female sex was negative predictor of physical scores. Also in previous studies with HCV patients showed lower scores of HRQOL in female individuals[36,37] but this didn't match with Fábregas et al., (2013)[38] who studied Health related quality of life among patients with chronic hepatitis C and found that Gender did not interfere significantly in any HRQOL domain, or overall HRQOL. Men and women differed in the course of HRQOL with an increase on scores for men on several dimensions and women experiencing a decrease. These differences between men and women were also significant in a multivariate analysis. In the general population, men report a higher HRQOL[39,40,41], a finding possibly of relevance for our findings. Studies show anemia in women plays an important role in HRQOL be one of the explanations for the observed difference [42].

Our study found that the least factors affecting PCS were age and residence as shown in table (4) and this is matched with Fábregas et al., (2013)[38] who found that age also did not influence significantly HRQOL and also found by Kallman et al., (2007)[43] who studied Fatigue and health-related quality of life (HRQOL) in chronic hepatitis C virus infection but this result didn't match with some studies showing negative impact of age on HRQOL[37,44]. Age interference in HRQOL of HCV patients is controversial, with some studies showing negative impact of age, while others no significant influence.

As regard mental component score (MCS) marital status was a positive predictor of mental QOL as shown in table (5), this is in agreement with Fábregas et al., (2013)[38] who found that: Being married was associated with better HRQOL, also shown in previous studies with HCV patients[45-47]. This study also found that fibrosis stage one of the least factors affecting HRQOL and this is matched with Silva et al., (2015)[48] who found that depression rather than liver impairment reduces quality of life in patients with hepatitis C and the same was found by Hsu et al., (2009)[47] who studied the effect of cirrhosis on quality of life in hepatitis C virus-infected patients.

In multivariable regression analyses of socio-demographic and clinical factors affecting physical component score(PCS) during treatment among the studied chronic hepatitis c patients, this study found that occupation and fibrosis stage followed by TSH and HB level were the most important factors as shown in table (6). This is in agreement with Bezemer et al., (2012)[37] who found that occupation was positive predictor for HRQOL. As regard anemia as a negative predictor for physical component score (PCS) of HRQOL this is in agreement with Pockros et al., (2004)[42] who found that Anemia and decreased health-related quality of life (HRQOL) are common in patients receiving combination therapy of interferon alfa (IFN) and ribavirin (RBV) for CHC patients. In a randomized, prospective study evaluating the effectiveness of epoetin alfa in maintaining RBV dose, alleviating anemia, and improving HRQOL in anemic (Hb $\leq$ 12 g/dL) HCV-infected patients receiving combination therapy but as regard fibrosis stage, our results did not matched with Bezemer et al., (2012)[37] who found that the presence or absence of cirrhosis and grade of fibrosis did not play a role in the course of HRQOL.

This study found that thyroid-stimulating hormone (TSH) was a negative predictor for physical component score (PCS) of HRQOL as shown in table (6).This can be explained by the fact that the interferon (IFN-α) therapy for HCV may induce thyroid changes or dysfunction in 2.5% to 20% of treated patients. Moreover, up to 40% of patients become thyroid antibody positive during this treatment[49,50]. Almost all side effects of IFN-α treatment are due to its effects on the

immune system, and data suggest that in addition to its immune-modulatory mechanism, IFN-α precipitates thyroiditis by direct thyrotoxicity[50]. IFN-induced autoimmune thyroid disease is associated with elevated autoantibodies and may manifest with or without clinical disease[51]. Ribavirin could possibly stimulate the immune system alone or synergistically with IFN-α to cause thyroid disease via an autoimmune mechanism[52]. The relative risk of developing thyroid autoimmunity among HCV carriers treated with IFN-α and RIB was 5.8 times higher than the risk for developing hypothyroidism or hyperthyroidism[53]. Autoimmune thyroiditis has been shown to be associated with poor HRQOL in some studies[54]. Furthermore, the same study showed that poor HRQOL was not limited to subjects with overtly symptomatic thyroid disease, either hypo- or hyperthyroidism, but was also present in asymptomatic diseases, such as euthyroid goiter or thyroiditis.

In multivariable regression analyses of socio-demographic and clinical factors affecting mental component summary (MCS) during treatment among the studied chronic hepatitis c patients, this study found that PCR and occupation were the most important factors as shown in table (7) and this is matched with Bezemer et al., (2012) [37] who found that responders had a higher score compared to the non-responders who were aware of their previous non-response to therapy. This underlines the mental aspects of the impact on HRQOL in this disease.

Conflict of interest: None

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