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Quality of Life of Patients with Chronic Hepatitis C in Colombia

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Abstract

Introduction: Data on quality of life in patients with hepatitis C are scarce in our country. To date, no study has determined the burden of chronic hepatitis C in the population of Colombia. **Objectives:** The objective of this study was to determine the quality of life in patients with chronic hepatitis C and to identify its determinants using the SF36V2 survey. **Methodology:** This cross-sectional analytical study was conducted between June 1,2015 and August 31, 2015. A trained interviewer used the Spanish version of the SF-36 V2 survey (Quality Metric Inc.). Then multivariate linear regression identified factors related to Health Related Quality of Life (HRQL). The Charlson Comorbidity Index was used to estimate the weights of comorbidities found in the sample. **Results:** Forty-one patients were available for analysis. The mean age was 57 years (SD 12.6). Fifty percent of the subjects had advanced cirrhosis and/or fibrosis. The physical component summary (PCS) and mental component summary (MCS) were 48.2 and 45.6, respectively. Univariate linear regression analysis identified sex, age, Charlson Comorbidity Index and presence of liver cirrhosis as the main determinants of quality of life. The Charlson Comorbidity Index 10-year survival probability was the only independent predictor of SFD6. **Conclusion:** Age, sex and hepatic cirrhosis were identified as determinants of HRQoL. The Charlson index was the only independent predictor of SFD6. The implementation of multidisciplinary programs is necessary for comprehensive treatment of infected patients.

Keywords

Hepatitis C, Colombia, quality of life, hepatic cirrhosis, Latin America, hepatitis.

INTRODUCTION

Approximately 6.8 to 8.9 million people are infected with hepatitis C virus (HCV) in Latin America, and less than 1% of these people receive antiviral treatment. (1) The prevalence of HCV in Colombia is unknown, but Pan American Health Organization (PAHO) has reported that between 0.7% and 0.9% of donors present antibodies to HCV. (2, 3) Nosocomial transmission is the most frequent source of infections, and prior to 1994 blood transfusions had been identified before as the main risk factor for contracting the virus in Colombia and other Latin American countries. (4, 5)

Approximately 250,000 to 350,000 people are chronically infected with HCV in this country. Annually 2,150 to 2,400 of these people die due to liver cirrhosis and liver cancer, and the disease caused between 84.8 and 106.1 lost years of healthy life for every 100,000 people during 2014 as measured by the Disability-Adjusted Life Year (DALY) metric. (6)

However, the impact of HCV infections is not limited to the occurrence of cirrhosis and hepatocellular cancer. In fact, it detracts from health-related quality of life (HRQL) regardless of the stage of liver disease. (7)

Although several studies conducted in Brazil and the United States have extensively studied HRQL, sociocultural

differences between those populations and that of Colombia prohibit extrapolation of those results locally. (8-12)

Until this study, no studies had been carried out in Colombia to determine the burden of the disease in this population. This has made it impossible to know its real impact on the environment and has also made it difficult to interpret cost-effectiveness studies that facilitated decision-making in clinics before the advent of new antivirals in this country.

The aim of this study is to describe the HRQL in a population of patients infected with HCV in Colombia and to identify its determinants.

METHODOLOGY

This is an analytical cross-sectional study that was conducted from June 1, 2015 to August 31, 2015. All patients diagnosed with chronic hepatitis C by enzyme-linked immunosorbent assay (ELISA) whose diagnoses were confirmed by viral load measurement were initially included. A trained interviewer used the Spanish version of the SF-36 V2 survey to interview each patient, and updated epidemiological, clinical and analytical information was collected on the date of patient inclusion in the study. Patients with hepatic encephalopathy or with physical or mental limitations that prevented completion of the SF-36 V2 interview were excluded. Patients with ascites were not excluded so that the sample was representative of patients at all stages of the disease. Qualitimetric Inc. granted permission for the use of the SF-36 V2 survey and certified researchers in the International Quality of Life Assessment Project Approach (IQOLA). (13) They prepared a Spanish version of the survey that was reviewed by Colombian linguists and researchers who confirmed that this translation is acceptable in Colombia. All patients signed informed consent forms prior to inclusion in the study. The protocol was approved by the ethics committee of the Santa Lucia Cardiovascular Center in the city of Cartagena.

Transient Elastography

We used a fibroscan (Ecosense) series 502 for transient elastography to estimate hepatic rigidity. This apparatus emits a vibrating wave that passes through the hepatic parenchyma. The rate at which this wave travels through the organ is used to estimate the degree of fibrosis which is expressed in kilopascals (kPa). The higher the velocity is, the higher the level of fibrosis is. All patients fasted for at least 8 hours prior to the procedure. The procedure was performed with patients in supine position with the right arm at maximum abduction. Determinations were made on the average axillary line. The median value of 10 measurements was used as the indication of liver rigidity. Results that did not meet the manufacturer's quality criteria were not taken into account for the analysis. An interquartile range of less than 30% and a percentage of validity (number of valid measurements/total measurements) of over 60% were considered indispensable for evaluating the reliability of the result. The cutoff point used for the diagnosis of cirrhosis was 14.5 kPa.

SF-36 V2

As follows, the SF-36 V2 consists of a 36-item questionnaire that evaluates eight areas of HRQL and also generates two indicators that summarize the physical and mental components of the scale:

- Physical Functioning (PF) evaluates limitations on physical activities due to the disease.
- Physical Role Functioning (PRF) evaluates the impact of physical health on work and other activities of daily life.
- Bodily Pain (BP) assesses a patient's limitations due to pain.
- General Health (GH) assesses how the subject sees their personal health and the risk of worsening.
- Vitality (VT) assesses the degree of fatigue or energy of an individual.
- Social Functioning (SF) estimates how much physical or emotional problems interfere with normal social activities.
- Emotional Role (ER) determines the impact of emotional problems on work and activities of daily life.
- Mental Health (MH) evaluates general mood including depression and happiness.
- SPC: summarizes the physical components of SF-36 V2: PF, PRF, BP and SG.
- SMC: summarizes the mental components of SF-36 V2: VT, SF, ER and SM.

Each of the scales of the SF-36 V2 has a range of 0 to 100 where 100 is the best possible score. Differences of more than three points in either the SPC or the SMC are considered relevant.

The SF-6D is an SF-36 health index (utility) developed in the United Kingdom. It weights various aspects of the survey and facilitates economic health assessments. Values are between 0 and 1 which represent the worst and the ideal state of health, respectively. Differences of 0.03 points are considered to be clinically significant.

The Charlson Comorbidity Index

The Charlson comorbidity index predicts mortality for a patient on the basis of twenty-two conditions. Each condition is assigned a score of 1, 2, 3 or 6 depending on the risk

of death associated with this condition. Then the probability of that patient's survival is calculated. Chronic hepatitis is considered to be a mild liver disease while liver cirrhosis is considered to be a severe liver disease.

Statistical Analysis

Numerical variables were expressed as the mean ± standard deviation (SD) and categorical variables were expressed as percentages. Student's T test and the chi-squared test were used for comparison between groups as appropriate. Univariate and multivariate linear regression analyses were used to identify determinants of quality of life. The dependent variables were the SF-6D index, the SMC and the SPC. To facilitate analysis of the Charlson index, we considered a continuous variable that expressed the probability of survival over the next 10 years. The relationship was considered statistically significant with a value of $p < 0.05$.

RESULTS

The final sample included 41 patients with similar numbers of men and women. The mean age was 57 years (SD: 12.6). The most frequent genotype was 1b and approximately 50% of subjects had advanced cirrhosis and/or fibrosis (F3-F4). The average probability of survival at 10 years according to the Charlson index was 53% (SD: 36). Twenty patients had received antiviral treatment, and ten of these had achieved sustained virological responses. The baseline characteristics of the sample can be seen in Table 1.

The SPC and the SMC were 48.2 and 45.6, respectively. These values are lower than those reported for populations without chronic diseases and are similar to those described in patients with diabetes and anemia. The subscales with the lowest scores were VT, SG, BP, SM and FP (Table 2).

Factors Associated with HRQL

The initial bivariate analysis found that BP, ER, SM, SMC and SF-6D scales were significantly lower for women. Similarly, liver cirrhosis was negatively associated with 8 of the 10 scales and subscales of SF-36 V2 and SF-6D. Although subjects who did not achieve sustained virological response (n = 31) after treatment had lower scores on all scales, this had statistical significance only on the VT and PF scales (Table 3). Similarly, all scales and SF-6D decreased as the degree of hepatic fibrosis estimated by transient elastography increased, with PF, PRF, SG, VT, ER and SPC having the closest association (Table 4). However, this relationship disappeared when patients with cirrhosis were excluded.

Table 1. Baseline clinical and demographic characteristics

n	41
Men	22 (53.7)
Age	57 (12.6)
Health Care Regimen	
Pre-paid medicine	9 (22)
Contributory	27 (66)
Subsidized	5 (12)
Diabetes	5 (9.3)
Hypertension	16 (30)
Dyslipidemia	6 (11)
Obesity	3 (5.6)
Genotype	
1a	1 (2.4)
1b	13 (32)
2	2 (5)
4	1 (2.4)
Unknown	21 (51)
Fibroscan	13.6 (14.4)
Antiviral treatment	20 (49)
SVR	10 (50)
Fibrosis	
Unknown	3 (7)
F0	13 (32)
F1	2 (5)
F2	2 (5)
F3	5 (12.2)
Cirrhosis	16 (39)
Child-Pugh-Turcotte	
A	11 (68)
B	5 (32)
INR	1.18 (0.27)
Albumin	3.8 (0.6)
Bilirubin	0.96 (0.6)
Creatinine	0.9 (0.26)
Varicose	9 (56.3)
Ascites	3 (18.8)
Encephalopathy	2 (12.5)

INR: international normalized ratio; SVR: systemic vascular resistance.

Univariate linear regression analysis identified sex, age, Charlson index and liver cirrhosis as the main determinants of SF-6D (Table 5). The Charlson index also showed a positive linear association with the SMC and SPC. Age

Table 2. Scales and subscales of the SF-36 V2 survey

	Mean	Median	P25	P75
PF	72 (23.3)	75	55	90
PRF	66.4 (33.3)	75	37.5	100
BP	65.1 (26.5)	62	41	92
SG	62.9 (19.8)	65	52	77
VT	58.5 (22.6)	62.5	43.7	71.8
SF	71.3 (28.9)	75	50	100
ER	68 (27.3)	66.6	50	91.6
SM	66 (21.5)	70	50	85
SPC	48.2 (9.1)	49.4	40.3	55
SMC	45.6 (11.1)	46.6	36.3	55.4
SF-6D	0.70 (0.15)	0.7	0.57	0.84

and transient elastography values presented negative linear associations with SPC, and male patients had higher scores on the SPC than did women patients (Table 6 and 7).

The Charlson index, expressed as the 10-year survival probability, was the only independent predictor of the utility index in this study (Table 8).

DISCUSSION

This study provides the first data on quality of life and health benefits in patients with chronic hepatitis C in Colombia. This information may be useful for implementation of comprehensive HCV treatment programs and for cost-effectiveness studies for newly available antivirals in this country.

The mean SMC and SPC in subjects without chronic diseases in the United States are 52.2 and 54.3, respectively. In this study their averages were 48.2 and 45.6 respectively. These values are similar to those found in other chronic diseases such as diabetes and depression. (14)

The subscales that assessed the VT, SG, BP, SM and the impact of physical health on work or activities of daily living were the most strongly affected areas in this cohort of patients.

A recent review of the most important published studies that have identified issues affecting the quality of life of populations with chronic hepatitis C in the United Kingdom, the United States and Australia indicated that fatigue and weakness are the most frequent physical symptoms and also were the main cause of decreased physical and sports activity. (15, 16, 17) Others frequent reasons for concern included guilt over being considered an economic burden on the family, previous addictive behaviors, the social stigma of infection, and the possibility of being a source of contagion. (16, 18, 19) These studies also indicated that anxiety, fear, rage and depression are common among those who are infected. (16, 17, 19, 20) Some negative behavior traits were also noted. The most common were keeping the illness secret from family and friends, aggressive attitudes, uncertainty about life expectancy, general health and financial status, unpleasant social attitudes and irrational behavior with a partner. (19, 20)

Several of these studies also reported a decline in social and work activity due to fatigue or emotional stress asso-

Table 3. Relationships between sex, cirrhosis and sustained virological response using several scales and subscales of SF-36 V2

	Female vs. Male	95% CI	p	No cirrhosis vs. cirrhosis	95% CI	p	No SVR vs. SVR	95% CI	p
PF	-6.8	(-21.6)-8.0	0.35	16.6	1.7-31.5	0.03	-23.5	(-47.1)-0.15	0.05
PRF	-17.8	(-38.4)-2.8	0.08	23.9	2.4-45.3	0.03	-13.5	(-46.7)-19.4	0.39
BP	-19	(-35.1)-(-3.4)	0.01	8.8	(-8.8)-26.6	0.31	-6.5	(-29.5)-16.4	0.55
SG	-4.5	(-17.2)-8.13	0.47	20.3	8.2-32.4	0.002	-4.5	(-21.6)-12.4	0.57
VT	-11.6	(-25.6)-2.3	0.1	19	5.0-33.0	0.009	-19.3	(-38.8)-0.14	0.05
SF	-12.7	(-30.9)-5.3	0.16	19.6	0.88-38.3	0.04	-22.5	(-52.9)-7.9	0.13
ER	-17.3	(-33.9)-(-0.7)	0.04	24.7	7.8 -41.7	0.005	-0.2	(-29.5)-29.1	0.98
SM	-19.2	(-31.5)-(-6.8)	0.003	20.5	7.6 -33.4	0.003	-7.3	(-28.6)-13.9	0.47
SPC	-2.8	(-8.6)-2.8	0.32	5.1	(-0.94)-11.15	0.09	-6.2	(-15.5)-(-3.0)	0.17
SMC	-8.5	(-15.1)-(-1.9)	0.01	10.9	4.2-17.6	0.002	-3.5	(-14.9)-7.9	0.52
SF-6D	-0.1	(-0.20)-(-0.013)	0.02	0.11	0.017-0.21	0.02	-0.09	(-0.23)-0.04	0.18

Table 4. Relationship between transient elastography and scales and subscales of SF-36 V2.

	Fibroscan	p
PF	-0.5	0.004
PRF	-0.38	0.03
BP	-0.28	0.11
SG	-0.34	0.05
VT	-0.4	0.02
SF	-0.32	0.07
ER	-0.44	0.01
SM	-0.24	0.17
SPC	-0.4	0.02
SMC	-0.33	0.06
SF-6D	-0.32	0.07

Table 5. Univariate linear regression. The dependent variable is SF-6D.

	b	95% CI	p
Sex	0.34	0.01-0.20	0.02
Cirrhosis	-0.36	(-0.21)-(-0.17)	0.02
SVR	-0.04	(-0.14)-0.11	0.79
Charlson Index	0.56	0.001-0.004	<0.0001
Age	(-0.38)	(-0.008)-(-0.001)	0.015
Fibroscan	-0.32	(-0.008)-0.00	0.07

Table 6. Univariate linear regression. SPC (summary of physical component) is the dependent variable.

	b	95% CI	p
Sex	0.15	(-2.8)-8.6	0.32
Cirrhosis	0.25	(-11.1)-0.94	0.09
SVR	0.028	(-6.9)-8.0	0.87
Survival	0.47	0.04-0.19	0.003
Age	-0.39	(-0.47)-(-0.07)	0.01
Fibroscan	-0.4	(-0.5)-(-0.03)	0.02

Table 7. Univariate linear regression. The dependent variable is SMC (summary of mental component)

	b	95% CI	p
Sex	0.38	1.9-15.1	0.01
Cirrhosis	-0.01	(-3.1)-2.9	0.95
SVR	-0.11	(-10.5)-5.7	0.55
Survival	0.55	0.08-0.25	<0.001
Age	-0.24	(-0.46)-0.06	0.13
Fibroscan	-0.33	(-0.49)-0.017	0.06

Table 8. Multivariate linear regression. The dependent variable is SF-6D

	b	95% CI	p
Sex	0.14	(-0.05)-0.15	0.37
Cirrhosis	0.2	(-0.08)-0.21	0.38
Charlson Index	0.69	0.000-0.006	0.02
Age	0.04	(-0.05)-0.006	0.84

ciated with infection. Similarly, decreased sexual activity due to the fear of transmitting the infection and/or loss of libido was found. (16, 21)

Since this study's approach was predominantly quantitative using a validated scale for measurement of HRQL and generation of utility indexes, qualitative information about specific emotions and patients' concerns was not collected. However, the subscales (VT, SG, PRF, SM and BP) with lower scores in this study can be associated intuitively with concerns of patients reported in other countries such as fatigue, anxiety, tiredness, anger, fear and guilt. In any case, it is important to develop qualitative research that allows us to deepen our understanding of the concerns, physical symptoms, specific psychological and social reactions of our patients to help implementation of comprehensive care programs that will allow us to effectively reduce the burden of this disease.

Women had significant decreases in HRQL. The SF-6D, SPC and SMC decreased significantly among women patients with differences of -0.10 points ($p = 0.02$), -8.5 ($p = 0.01$) and -2.8 ($p = 0$, 32), respectively. A recent study of the quality of life in 44 patients with cirrhosis in Colombia, (5) fifteen of whom had viral etiologies, also identified being a woman as a determinant of quality of life. These studies, together with others performed in North America, (8) point to gender as one of the main determinants of quality of life in patients with chronic liver disease. This circumstance must be taken into account in the design of health care guides and national policies for the control and treatment of the disease.

Increasing age was associated with decreases in SF-6D ($p = 0.015$) which is predictable given that complications of hepatitis C and other prevalent chronic diseases increase as the population ages. Other studies in Latin America have had similar findings. (9)

Subjects who achieved SVR after treatment had increases in all SF-36 V2 and SF-6D scales and subscales. However, no significant association was found with SMC, the SPC or the SF-6D in the multivariate analysis. It is probable that the number of subjects who achieved SVR was too small to show the kind of positive association between control of viral replication and HRQL that has usually been observed when infections are controlled. (22, 23)

On the other hand, the association of cirrhosis with lower values in 8 of the 10 different scales and subscales of the SF-36 V2 and the utility index was statistically significant. This relationship seems to be independent of the presence of complications of the disease, considering that the majority of patients with cirrhosis in this sample were in the compensated phase of the disease and only three had ascites and only two had encephalopathy.

The linear relationship observed between transient elastography and several subscales of SF-36V2 suggests that quality of life decreases as the degree of liver fibrosis increases in infected patients, but this relationship disappeared completely when patients with cirrhosis were excluded. This again indicates that the onset of cirrhosis is the turning point at which a more aggressive stage of the disease with significant impairment of HRQL begins.

The Charlson index allows calculation of patient survival based on 22 conditions and is an indicator of the weight of comorbidities within a given population. The 10-year life expectancy of the patients calculated by the Charlson index was 53%. Although this is low, it is not surprising because HCV infected patients were considered to have mild and moderate or severe liver disease if they had established cirrhosis. This fact together with the impossibility of introducing the impact of the sustained virological response within the index calculations clearly had a negative influence on the predicted life expectancy of the sample.

A study involving 4,781 HCV patients in the United States identified factors associated with the onset of depression and the deterioration of patients' physical health. (8) As in our study, being female and comorbidities estimated through the Charlson index were associated with poorer physical and mental states of patients. Other factors such as stress and work situations also had negative effects on HRQL. Unfortunately, these could not be analyzed in our study because of the lack of tools for quantifying stress in our environment and because of the small sample size.

The Charlson index was the only independent predictor of SF-6D, SPC and SMC in a multivariate linear regression model. This suggests that patient welfare determinants do not depend exclusively on liver disease but also on appropriate treatment of associated comorbidities through the implementation of comprehensive and multidisciplinary programs for HCV patient care.

The size of the sample, undoubtedly the most important limitation of the study, makes it difficult to generalize study results. Even though the difficulty of diagnosing this infection in our country has prevented recruitment of larger samples, it may be possible for a joint effort of government agencies, scientific societies, patient associations, service providers, and institutions with hepatology and infectious diseases programs involved in the care of this population to obtain larger samples and more robust results in research in this and other areas to the disease relevant.

The high proportion of patients in this sample who were in the F3-F4 stage suggests a possible selection bias similar to that observed in highly complex institutions to which patients with more severe conditions are referred. It is important to note that this sample was obtained from the outpatient gastroenterology and hepatology clinic of a primary care center where most of the patients with hepatitis C from four of the largest health care companies (EPS) in the city of Cartagena are referred. Although it is feasible that a systematic pattern of referral to our institution has caused a selection bias, the possibility that a large proportion of HCV patients in the general population may be in advanced stages should also be considered. This possibility exists because of the absence of effective screening programs, the silent nature of the disease, and barriers to accessing treatment that have allowed the disease to progress to these phases. In fact, taking into account that the highest peak of viral exposure in our country was more than 20 years ago through transfusion of blood products before 1994, and keeping in mind the natural history of infection, we could speculate that the number of patients with cirrhosis secondary to hepatitis C in Colombia will increase over the next few years.

In spite of these limitations, these data are the first reported on HRQL in patients infected with hepatitis C in Colombia and provide relevant information about a disease that is still not well known in this country.

CONCLUSION

Age, sex, and liver cirrhosis were identified as the determinants of HRQL. The Charlson index was the only independent predictor of SF-6D. Implementation of multidisciplinary programs are necessary for comprehensive treatment of infected patients.

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Declaration of conflict of interest

The authors declare that they have no conflicts of interest with respect to the presentation of results of this study.

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