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HEALTH RELATED QUALITY OF LIFE IN PATIENTS WITH CHRONIC HEPATITIS C NAIVE TO TREATMENT.

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ABSTRACT

Background: Hepatitis C is a major cause of liver disease world-wide. It has been associated with decreased health related-quality of life (HRQL) and psychiatric symptoms. **Aim:** To assess HRQL and depression in a group of cirrhotic and non-cirrhotic chronic hepatitis C patients without previous interferon therapy. **Methods:** Consecutive patients attending a Liver Clinic at a referral center were enrolled. HRQL was measured using the SF-36 questionnaire and depression was assessed with the Zung self-rating depression scale. Patients responded prior to any medical consultation by the liver specialist. **Results:** Of 157 patients enrolled, 112 were female (71%) and 45 were male (29%). Thirty-seven patients (23.5%) were less than 45 years old. Ninety-seven patients (61.8%) had cirrhosis. HRQL was significantly decreased in chronic hepatitis C patients compared to historical normal controls in all eight domains of the SF-36. In hepatitis C cirrhotic patients HRQL was significantly lower among Child-Pugh class B and C subjects, mainly in the domains that reflect physical health. Ninety-two patients (58.6%) had depression. One hundred-fourteen patients (72.6%) had a poor illness perception of hepatitis C. These subjects had significantly lower HRQL scores in 7 of the 8 SF-36 domains when compared to patients with a better understanding of chronic hepatitis C. **Conclusion:** Chronic hepatitis C patients attending a tertiary referral center had a significant decrease in HRQL associated with depression (58.6%) and poor illness perception (72.6%). Educational programs and their impact on HRQL need to be addressed in detail, particularly in the pre-treatment scenario.

Key words: chronic hepatitis C; health-related quality of life; depression; SF-36 questionnaire; Zung self-rating depression scale; cirrhosis.

INTRODUCTION

Hepatitis C virus infection is one of the main causes of liver disease world-wide (1). Among the general population in Mexico the estimated prevalence of HCV infection is 0.5% to 1.3% (2,3). The great majority of subjects infected with hepatitis C virus are asymptomatic, however, they will go on to develop chronic hepatitis.

Patients with chronic hepatitis C complain more frequently of severe physical symptoms such as musculoskeletal pain and fatigue when compared to patients with other forms of chronic liver disease (4). Several studies have demonstrated a consistent and significant reduction in their health related quality of life (HRQL) compared to population controls, particularly in the physical health related domains (5-6). The determinants of impaired HRQL in chronic hepatitis C patients have so far not been clearly defined, however it has been demonstrated that HRQL improves when a sustained viral response is obtained (7-9), but even so, HRQL does not reach the level encountered in normal subjects. In addition, increased levels of depression have been reported in these patients as compared with the general population (10-11).

The aim of the present study is to evaluate HRQL and depression in a sample of Mexican chronic hepatitis C patients, naive to treatment, attending a tertiary referral center as well as determining their risk perception and knowledge of the disease.

PATIENTS AND METHODS

This study included 157 adult patients with HCV infection attending their first visit to the Liver Clinic at the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán during a 12-month period. Patients were enrolled if they had not been treated for chronic hepatitis C with interferon-based therapies, had positive hepatitis C antibody in serum and persistently elevated serum alanine transaminase levels. Subjects with other chronic liver diseases, significant co-morbid conditions (e.g. cardiovascular disease, chronic renal disease and cancer), pregnancy or evidence of substance abuse, were excluded from the study. All patients gave written informed consent. The study was approved by the Institutional Ethics Committee.

A validated Spanish translation of the Medical Outcomes Study Short Form 36 Health Survey (SF-36) was used to evaluate HRQL. The SF-36 questionnaire consists of 36 items measuring 8 domains: physical function, role limitations-physical, vitality, general health perception, pain, social function, role limitations-emotional and mental health (12). The SF-36 has been shown to have good reliability and validity in primary care and chronic disease populations, including chronic hepatitis C (13).

Depression was measured using the Spanish version of the Zung self-rating depression scale. This 20-item questionnaire covers affective, psychological and somatic symptoms and is a general gauge of depression and mood. It is scored on a 20 to 80 scale (scores below 50 are considered normal; 50 to 59, mild depression; 60 to 69, moderate depression and scores of 70 or above are considered as severe depression)(14).

Illness perception was evaluated with a self-applied 10-item questionnaire relating to the natural history of hepatitis C. It is graded on a scale of 1 to 10, with the higher score indicating a better knowledge of the disease. Patients with a score of less than 5 were defined as having a poor knowledge and risk perception of hepatitis C.

The questionnaires were applied before any clinical procedure or consultation regarding treatment were made, to ensure that patients responses were not influenced by their clinical evaluations.

Statistical analysis was performed with the SPSS version 10 software for Windows, using Student's T test and ANOVA for comparing groups and considered statistically significant when $P < 0.05$.

RESULTS

Of 157 patients enrolled, 112 were female (71%) and 45 were male (29%). Thirty-seven patients (23.5%) were less than 45 years old. Ninety-seven patients (61.8%) had clinical, biochemical or histological evidence of cirrhosis (54 were Child-Pugh's class A, 25 class B and 18 class C).

Health related quality of life. HRQL was significantly decreased in chronic hepatitis C patients compared to historical normal controls (15) in all eight domains of the SF-36 questionnaire (table 1). In hepatitis C cirrhotic patients HRQL was significantly lower among Child-Pugh class B and C subjects, mainly in the domains that reflect physical health (figure 1).

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Depression. Ninety-two patients (58.6%) had depression (Zung scale score greater than 50); in nine of them (5.7%) depression was considered severe (Zung scale score greater than 69). No differences were observed among patients with chronic hepatitis C and those with cirrhosis in the Zung self-rating depression scale (42.3 ± 11.9 in cirrhotic vs. 43.9 ± 9.8 in non-cirrhotic patients, $P = 0.37$), or in the cirrhotic patients regarding the Child-Pugh class.

Risk perception and disease knowledge. One hundred-fourteen patients (72.6%) had a low risk perception of hepatitis C as a disease, in particular as to the modes of transmission of the virus and on the role limitations imposed by the infection on their physical functions. Patients with a poor risk perception and knowledge of the disease had significantly lower HRQL scores in 7 of the 8 SF-36 domains (table 2).

DISCUSSION

The finding in the present study that patients with chronic hepatitis C not previously treated have a decreased HRQL as compared to normal population adds further evidence to the fact that HCV by itself has a negative impact on the patients well-being. This becomes a challenge for the physician, in particular when deciding on the use of interferon-based therapies.

All the patients in the present study were referred to the Liver Clinic by primary care physicians and were aware of their positive HCV status. Of particular relevance to our findings is the fact that the study was conducted at the time of their first visit to the Clinic and the questionnaires were applied before any clinical

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All the patients in the present study were referred to the Liver Clinic by primary care physicians and were aware of their positive HCV status. Of particular relevance to our findings is the fact that the study was conducted at the time of their first visit to the Clinic and the questionnaires were applied before any clinical intervention. The patients had a significant reduction on their HRQL in the 8 domains of the SF-36 when compared to the general Mexican population (15). These individuals had a subjective perception of poor physical and mental health, leading to limitations in daily activities. None of them had any other concomitant illness or a history of IV drug abuse or alcohol dependence likely to affect HRQL. We did not find any association between HRQL scores and age, gender or educational level.

Almost 75% of the patients in the study had a poor risk perception and knowledge of the disease, which appears to have a direct negative impact on HRQL (table 2). Confirmation of these findings is important because it would imply that the decreased HRQL associated with HCV infection prior to treatment, could be improved through successful educational programs.

The natural history of chronic hepatitis C remains controversial. The general impression has been that it is a relatively indolent disease that is often discovered incidentally as most of the patients are asymptomatic and do not seek early medical care. In the present study, 97 patients (61.8%) already had liver cirrhosis when referred to a tertiary care medical institution. This late referral can either be attributed to lack of symptoms, unwillingness of the patient to seek medical attention or primary care physician undermining pertinence of early treatment. Once more, all these issues could be addressed by coherent and especially designed educational programs.

Although the decrease in HRQL scores in chronic hepatitis C patients was not directly related to liver dysfunction as a group, it is evident that in those patients with advanced cirrhosis (Child's class B or C), the disease was associated with a deterioration in HRQL. These patients had lower scores on the SF-36 questionnaire when compared to chronic hepatitis C patients without cirrhosis. These findings suggest that impairment of HRQL in patients with chronic hepatitis C could be related to factors different from the degree of liver dysfunction, such as the cognitive impairment which has been recently recognized in chronic hepatitis C patients (16).

The decreased quality of life in patients with chronic hepatitis C may be in part due to the high rate of depression documented in the present study, as 58.6% of the patients presented depression according to the Zung self-rating depression scale. Nine of the patients were considered as severely depressed. This is relevant as current treatment of hepatitis C includes the use of interferon which has well described adverse psychological effects such as mood disorders and depressed patients are not generally considered candidates for interferon-based therapies. The frequency of depression in the present study is higher than that encountered in similar settings, as 24% of chronic hepatitis C patients referred to a tertiary care center were depressed and 60% of them were taking antidepressant medication at their first visit (17).

A strong relationship between psychiatric symptoms and HRQL scores has been previously reported in other chronic diseases (18).

The Zung self-rating depression scale was chosen as a mood-assessment instrument because of its ease of administration, scoring and interpretation. The primary limitation of the Zung scale and other self-reported rating scales is the potential for response bias. However, the Zung scale has undergone extensive validation and reliability testing in medical and psychiatric patient populations. It has also been shown to be a sensitive means of detecting emotional distress in patients with varying severity of chronic liver diseases (19-22).

The high frequency of emotional distress found in our study before any significant clinical intervention emphasizes the need of education on the natural history and treatment of chronic hepatitis C to improve patients emotional status. Other authors have found that the duration of knowledge of one's diagnosis with hepatitis C is associated with poorer coping skills and higher incidence of depression (23,24). Measuring illness perception is of obvious importance to better evaluate patients assessment of their functional status and emotional well-being. Our findings suggest that poor comprehension of the disease has a negative impact on health related quality of life. In addition, objective evaluation of patients understanding of hepatitis C as a chronic disease, the impact on their future health, and the risks and benefits of medical intervention may be useful in predicting health services utilization and work disability. Hence, they may be used in the economic assessment of health care interventions.

In summary, chronic hepatitis C patients attending a tertiary referral center had a significant decrease in HRQL associated with depression (58.6%) and poor illness perception (72.6%). These findings suggest that emotional disturbances in chronic hepatitis C patients occur independently of antiviral therapy. The ethiopathogenesis of emotional distress in hepatitis C merits further study, the underlying cause of the perceived disability must be addressed in more detail, the mechanisms remain elusive. Educational programs and their impact on HRQL need to be ascertained in detail, particularly in the pre-treatment scenario.

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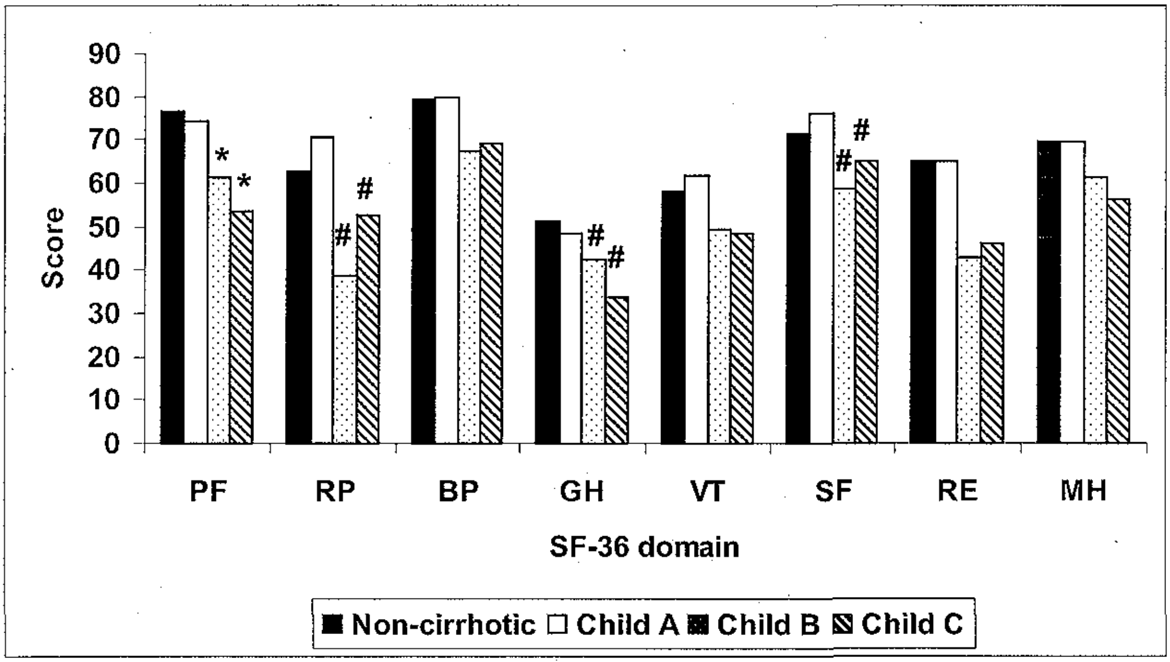
Figure 1. Health related quality of life in chronic hepatitis C cirrhotic patients according to Child-Pugh class.



PF = physical function; RP = role physical; BP = bodily pain; GH = general health; VT = vitality; SF = social function; RE = role emotional; MH = mental health.

* P = 0.001, # P < 0.05, when compared to non-cirrhotic patients.

Table 1. Health-related quality of life in patients with chronic hepatitis C.

SF-36 domain	Chronic hepatitis C patients, mean (SD) (n=157)	General population, mean (SD) (n=170) (ref. 15)	P value	95% confidence interval
PF	70.6 (25.1)	94.6 (8.6)	< 0.001	19.98 to 28.02
RP	60.5 (42.1)	94.5 (15.4)	< 0.001	27.2 to 40.8
BP	76.5 (27.9)	88.6 (15.4)	< 0.001	7.25 to 16.95
GH	46.9 (23.1)	79.9 (15.5)	< 0.001	28.75 to 37.25
VT	56.9 (23.0)	81.8 (11.6)	< 0.001	20.18 to 28.02
SF	70.4 (27.5)	86.9 (15.6)	< 0.001	11.68 to 21.32
RE	57.9 (41.0)	83.4 (25.1)	< 0.001	18.17 to 32.83
MH	66.6 (21.1)	79.6 (13.9)	< 0.001	9.14 to 16.86

PF = physical function; RP = role physical; BP = bodily pain; GH = general health; VT = vitality; SF = social function; RE = role emotional; MH = mental health.

Table 2. Health-related quality of life in patients with chronic hepatitis C according to risk perception and knowledge of the disease.

SF-36 domain	Poor awareness, mean (SD) (n=114)	Satisfactory awareness, mean (SD) (n=43)	P value	95% confidence interval
PF	66.5 (25.1)	81.7 (21.6)	0.001	-23.7 to -6.6
RP	55.0 (43.1)	75.0 (35.8)	0.004	-33.4 to -6.5
BP	73.9 (28.9)	83.0 (24.2)	0.07	-18.8 to 0.8
GH	44.9 (22.5)	52.3 (24.0)	0.08	-15.5 to 0.8
VT	53.8 (22.1)	65.0 (23.8)	0.006	-19.2 to -3.2
SF	67.3 (27.9)	78.5 (24.8)	0.02	-20.7 to -1.5
RE	53.2 (43.6)	70.5 (30.2)	0.006	-29.5 to -5.1
MH	63.8 (22.2)	74.1 (15.9)	0.002	-16.7 to -4.1
PCS	49.9 (17.5)	61.3 (18.6)	0.001	-17.7 to -5.1
MCS	49.9 (17.9)	60.5 (18.2)	0.001	-16.9 to -4.2

PF = physical function; RP = role physical; BP = bodily pain; GH = general health; VT = vitality; SF = social function; RE = role emotional; MH = mental health; PCS = physical component summary; MCS = mental component summary.