

## Impact of Psychiatric Disorders on the Quality of Life of Brazilian HCV-Infected Patients

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The aim of our study was to determine the impact of psychiatric comorbidities on the health-related quality of life of HCV-infected patients. Assessment of clinical, socio-demographic and quality of life data of the patients followed up at a Hepatology unit was performed by using a standard questionnaire and the SF-36 instrument. Psychiatric diagnoses were confirmed by using the Mini International Neuropsychiatric Interview, Brazilian version 5.0.0 (MINI Plus). Evaluation using the MINI plus demonstrated that 46 (51%) patients did not have any psychiatric diagnosis, while 44 (49%) had at least one psychiatric diagnosis. Among patients with a psychiatric comorbidity, 26 (59.1%) had a current mental disorder, out of which 22 (84.6%) had not been previously diagnosed. Patients with psychiatric disorders had lower scores in all dimensions of the SF-36 when compared to those who had no psychiatric diagnosis. Scores of physical functioning and bodily pain domains were lower for those suffering from a current psychiatric disorder when compared to those who had had a psychiatric disorder in the past. Females had lower scores of bodily pain and mental health dimensions when compared to males. Scores for mental health dimension were also lower for patients with advanced fibrosis. The presence of a psychiatric comorbidity was the variable that was most associated with the different scores in the SF-36, compared to other variables such as age, gender, aminotransferase levels, and degree of fibrosis.

**Key-Words:** Mental disorders, quality of life, HCV.

Hepatitis C virus (HCV) infection is a public health problem throughout the world. In Brazil, its prevalence is estimated to be 2.5%-4.0% of the general population [1]. This disease progresses slowly and evolves into chronic infection in 85% of the cases, of which 20 to 30% may develop liver cirrhosis [2].

Different studies have reported impairment in health-related quality of life (HRQOL) in patients with chronic hepatitis C (CHC) infection, when compared to the general population [3-5]. Factors such as presence of clinical comorbidities, including psychiatric ones, stage of liver disease, awareness of diagnosis and neurocognitive alterations, have been associated with this impairment, although there is no consensus as to what is the main determinant of the decrease in HRQOL among these patients [6-12]. The majority of the studies concerning HRQOL of patients with HCV infection have not investigated psychiatric comorbidities nor do they adequately measure the impact of such an association [13]. Some of them merely evaluate depression and anxiety symptoms by using self-rating instruments, or seek out this information in medical files on the patient's chart, which may not accurately reflect the mental state of these patients [5,8,14].

The objective of our study was to determine the impact of psychiatric comorbidities on the HRQOL of HCV-infected patients.

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### Material and Method

#### Participants

Patients were included if they tested positive for anti-HCV antibody by the ELISA III method (Abbott, Chicago, IL), confirmed by qualitative and/or quantitative determination of HCV-RNA by AMPLICOR (Roche, Basel). The exclusion criteria were: current or previous treatment with interferon (IFN) during the previous three months, presence of non-psychiatric comorbidity such as hypertension, diabetes mellitus, hypothyroidism, or other medical conditions with systemic repercussion, current use of propranolol or other drugs associated with an increased risk of psychiatric symptoms, cirrhosis classified as Child Pugh B and C or liver disease decompensation. This study was done in accordance with the Declaration of Helsinki and was approved by the local Institutional Review Board. Written informed consent was obtained from each patient.

#### Procedures

Assessment of clinical and socio-demographic data was performed by using a standard questionnaire; we also included aminotransferase levels from the last measurement recorded on the chart and the degree of fibrosis as measured by hepatic biopsy, according to METAVIR classification [15]. Psychiatric diagnoses were confirmed by using a Brazilian version of the Mini International Neuropsychiatric Interview, 5.0.0 (MINI Plus) [16], consisting of a brief standardized diagnostic interview that encompasses the main axis I disorders of the Diagnostic and Statistical Manual of Mental Disorders (DSM IV- American Psychiatric Association, 1994) and the International Classification of Diseases (ICD-10- World Health Organization-WHO, 1992). Before using MINI Plus, a reliability study with two interviewers (LCQ, SB-N) was performed.

HRQOL was evaluated by using the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36), which is a self-administered as well as a generic instrument, previously validated in Portuguese [17]. The SF-36 is composed of 36 items divided into eight dimensions: physical functioning, physical role, bodily pain, general health, vitality, social functioning, emotional role and mental health. Scores in each dimension vary from zero to 100, representing the worst and the best state of health, respectively.

#### Data Analysis

The data were entered into EPIDATA software version 3.1 and analyzed with the R Package program version 2.3.1. [18,19]. The measurements of epidemiological occurrence and association were calculated, as well as the 95% confidence interval, prevalence and prevalence rate. Analysis of parametric variance was performed in order to investigate the joint contribution of predictor variables in explaining the variability of each dimension. The Student's t-test for independent samples and the Mann-Whitney test were used to compare the groups of the study in relation to each dimension.

#### Results

In this cross-sectional study, 95 consecutive outpatients with CHC from the University Hospital Liver Unit provided written informed consent. Five of these later declined and removed consent. The final study sample consisted of 90 individuals. Their ages ranged from 20 to 64, with a median of 45 years. Of these, 50 (55.5%) were male and 40 (44.4%) were female. The majority of the patients were married (58.9%). Thirty percent of HCV-infection transmission was through blood transfusions; other means of infection included razor blades, dental procedures, vitamin complex injections (14.4%), use of injected drugs (8.9%), and tattooing (2.2%), while 44.4% did not know the means of infection (Table 1).

Aminotransferase levels were altered in 59 (65.5%) of the patients with CHC infection and 30 (33.3%) presented persistently normal rates. Forty-nine (54.5%) patients were submitted to biopsy, nine of them (18.4%) presented fibrosis stage 1; 24 (49%) presented fibrosis stage 2; 12 (24.5%) presented stage 3; and four (8.2%) demonstrated cirrhosis. The majority of the patients (77 - 85.5%), had no prior antiviral treatment, while 13 (14.4%) had been treated more than three months before. Fifty (55.5%) had HCV genotype 1 and 20 (22.2%) had genotypes 2 and 3 (Table 2).

Evaluation using MINI plus demonstrated that 46 (51%) patients did not have any psychiatric diagnosis while 44 (49%) had at least one psychiatric diagnosis. Among those with a psychiatric comorbidity, 16 (36.4%) had two or more psychiatric diagnoses. The frequency found was: 26 (28.9%) with alcohol and other substance abuse or dependence, 17 (18.9%) with mood disorders and 14 (15.6%) with anxiety disorders. Among patients with a psychiatric comorbidity, 26 (59.1%) had a current mental disorder, out of which 22 (84.6%) had not been previously diagnosed.

Patients whose aminotransferase levels were elevated had 53% more psychiatric disorders than those with normal aminotransferase levels; though this difference was not significant ( $p > 0.05$ ). The presence of advanced fibrosis (stage 3 or 4), prior treatment, age  $\geq 40$  years or female gender did not have a significant association with psychiatric disorders. Patients with psychiatric disorders (past and current) had lower scores in all of the eight dimensions of the SF-36, when compared to those who had no psychiatric diagnosis ( $p < 0.05$ , Figure 1). Scores of physical functioning and bodily pain domains were lower for those suffering from a current psychiatric disorder when compared to those who had had a psychiatric disorder in the past ( $p < 0.05$ , Figure 2). Females had lower scores of bodily pain and mental health dimensions when compared to their male counterparts ( $p < 0.05$ ). Scores for mental health dimension were also lower for patients with advanced fibrosis ( $p < 0.05$ ).

#### Discussion

We found that psychiatric comorbidity was the variable that was most associated with the different scores on the SF-36, compared to other variables such as age, gender, aminotransferase levels, and degree of fibrosis.

Additionally, patients with a current psychiatric comorbidity had lower scores in only two dimensions (physical functioning and bodily pain), when compared to those who had experienced psychiatric morbidity in the past. This result is difficult to explain because having a current disorder could be associated with greater loss in all dimensions, since psychiatric symptoms can worsen HRQOL, as reported in other studies [14,20].

Other authors who have also used a standardized diagnostic interview have demonstrated that depression is associated with low SF-36 scores; although in these studies HCV-infected patients undergoing treatment with IFN were not excluded, which could have interfered negatively in the assessment of HRQOL and increased the incidence of psychiatric events [21-24].

Similar to most previously-published studies, the liver aminotransferase levels were not related to SF-36 scores, perhaps because they were not associated with increased rates of psychiatric comorbidity [5,8,9,25-27]. Patients with CHC that presented more advanced fibrosis (stage 3 and 4) did not differ in their SF-36 scores, except in the dimension of mental health, in comparison to those who presented less advanced fibrosis (stage 1 and 2). Most studies have not demonstrated an association between stage of fibrosis and quality of life, except in cases of advanced cirrhosis [3,8,9,14,20,28,29]. In our study, only 54.5% were submitted to a biopsy and only four of them (8.2%) had cirrhosis. Furthermore, the small number of intravenous drug users is consistent with previous reports regarding the route of infection in Brazil [21,30,31]. Therefore, it may not be possible to generalize these results to our population.

**Table 1.** Socio-demographic data and sources of HCV infection in patients treated at the Hepatology Unit, University Hospital, Bahia, Brazil.

Variables	N	%
Gender		
Male	50	55.5%
Female	40	44.4%
Age		
<40	20	22.2%
≥40	70	77.8%
Marital status		
Married	53	58.9%
Separated/Widow(er)	14	15.5%
Single	23	25.5%
Sources of infection		
Transfusion/surgery	27	30.0%
Injected Drug Use	8	8.9%
Tattoo	2	2.2%
Others (razor blades, dental procedures, vitamin complex injections)	13	14.4%
Unknown	40	44.4%

**Table 2.** Characteristics of chronic hepatitis C in patients treated at the Hepatology Unit, University Hospital, Bahia, Brazil.

Variables	N	%
Aminotransferase		
Normal rate	30	33.3%
Elevated rate	59	65.5%
Had no result	1	1.1%
Biopsy W/Fibrosis		
Stage 1 or 2	33	36.7%
Stage 3 or 4	16	17.8%
Did not do biopsy	41	45.5%
Genotype		
1	50	55.5%
2 or 3	20	22.2%
Genotype unknown	20	22.2%
Prior treatment		
Yes	13	14.4%
No	77	85.5%

In conclusion, our data suggest that a psychiatric comorbidity is an important factor influencing quality of life among HCV-infected patients. Further investigations with larger sample sizes are necessary to provide better information to confirm our findings.

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#### References

1. Hepatitis C-global prevalence (update). *Wkly Epidemiol Rec* **2000**;75:18-9.
2. Seeff L.B., Hoofnagle J.H. National Institutes of Health Consensus Development Conference Panel Statement: Management of Hepatitis C: 2002. *Hepatology* **2002**;36(suppl 1):S1-S2.
3. Foster G.R., Goldin R.D., Thomas H.C. Chronic hepatitis C virus infection causes a significant reduction in quality of life in the absence of cirrhosis. *Hepatology* **1998**;27:209-12.
4. Bonkovsky H.L., Woolley J.M., the Consensus Interferon Study Group. Reduction of health-related quality of life in HCV and improvement with interferon therapy. *Hepatology* **1999**;29:264-70.

**Table 3.** Association between psychiatric disorders and clinical-demographic characteristics of chronic hepatitis C patients, Bahia, Brazil.

	Psychiatric disorders	PR	95% CI
Aminotransferase			
Elevated rates	55.9%	1.53	[0.91-2.57]
Normal rates	36.7%		
Fibrosis			
Stage 3 or 4	62.5%	1.15	[0.70-1.87]
Stage 1 or 2	54.5%		
Prior Treatment			
Yes	61.5%	1.32	[0.81-2.15]
No	46.8%		
Gender			
Female	47.5%	0.95	[0.62-1.43]
Male	50.0%		
Age			
≥ 40 years	51.4%	1.29	[0.72-2.30]
< 40 years	40.0%		

PR= prevalence rate. CI= confidence interval.

- Fontana R.J., Moyer C.A., Sonnad S. et al. Comorbidities and quality of life in patients with interferon refractory chronic hepatitis C. *Am J Gastroenterol* **2001**;96:170-8.
- Rodger A.J., Jolley D., Thompson S.C. et al. The Impact of Diagnosis of Hepatitis C Virus on Quality of Life. *Hepatology* **1999**;30:1299-301.
- Dalgard O., Egeland A., Skaug K. et al. Health-related of life in active injecting drug users with and without chronic hepatitis C virus infection. *Hepatology* **2004**;39:74-80.
- Hussain K.B., Fontana R.J., Moyer C.A. et al. Comorbid illness is an important determinant of health-related quality of life in patients with chronic hepatitis C. *Am J Gastroenterol* **2001**;26:2737-44.
- Younossi Z.M., Boparai N., Price L.L. et al. Health-related quality of life in chronic liver disease: the impact of type and severity of disease. *Am J Gastroenterol* **2001**;96:2199-200.
- Cordoba J., Flavia M., Jacas C. et al. Quality of life and cognitive function in hepatitis C at different stages of liver disease. *J Hepatol* **2003**;39:231-8.
- Lim J.K., Cronkite R., Goldstein M.K., Cheung R.C. The impact of chronic hepatitis and comorbid psychiatric illnesses on health-related quality of life. *J Clin Gastroenterol* **2006**;40:528-34.
- Forton D.M., Taylor-Robinson S.D., Thomas H.C. Cerebral dysfunction in chronic hepatitis C infection. *J Viral Hepat* **2003**;10:66-81.
- Batista-Neves S.C., Quarantini L.C., Galvão-Almeida A. et al. High frequency of unrecognized mental disorders in HCV-infected patients. *Gen Hosp Psychiatry* **2008**;30:80-2.
- Gallegos-Orozco J.F., Fuentes A.P., Argueta J.G. et al. Health related quality of life and depression in patients with chronic hepatitis C. *Arch Med Res* **2003**;34:124-9.
- Bedossa P., Poynard T. An algorithm for the grading of activity in chronic hepatitis C. The METAVIR Cooperative Study Group. *Hepatology* **1996**;24:289-93.
- Amorim P. Mini International Neuropsychiatric Interview (MINI): validação de entrevista breve para diagnóstico de transtornos mentais. *Rev Bras de Psiquiatr* **2000**;22:106-15.
- Ciconelli R.M., Ferraz M.B., Santos W.S. et al. Tradução para a língua portuguesa e validação do questionário genérico de avaliação de qualidade de vida "Medical Outcome Study 36-Item Short Form Health Survey (SF-36)". *Rev Bras Reumatol* **1999**;39:143-50.
- Lauritsen J.M., Bruus M. EpiData (version 3). A comprehensive tool for validated entry and documentation of data. The EpiData Association, Odense Denmark, **2003-2004**.
- R Development Core Team (2006). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. ISBN 3-900051-07-0, URL <http://www.R-project.org>. **2006**.
- Rowan P.J., Al-Jurdi R., Tavakoli Tabasi S., et al. Physical and psychosocial contributors to quality of life in veterans with hepatitis C not on antiviral therapy. *J Clin Gastroenterol* **2005**;39:731-6.
- Quarantini L.C., Miranda-Scippa A., Schinoni M.I., et al. Effect of amantadine on depressive symptoms in chronic hepatitis C patients treated with pegylated interferon: a randomized, controlled pilot study. *Clin Neuropharmacol* **2006**;29:138-43.
- Quarantini L.C., Miranda-Scippa A., Sampaio A.S., et al. Acute dystonia after injection of pegylated interferon alpha-2b. *Mov Disorders* **2007**;22:747-8.
- Quarantini L.C., Cruz S.C., Batista-Neves S.C., et al. Psychosis during Peginterferon- $\alpha$ 2a and ribavirin therapy: case report. *Braz J Infect Dis* **2006**;10:406-7.
- Lotrich F.E., Rabinovitz M., Gironda P., Pollock B.G. Depression following pegylated interferon-alpha: Characteristics and vulnerability. *J Psychosom Res* **2007**;63(2):131-5.
- Miller R.E., Hiller J.E., Shaw D.R. Quality of life in HCV-infection: lack of association with ALT levels. *Aust N Z J Public Health* **2001**;25:355-61.
- Schwarzinger M., Dewedar S., Rekecewicz C., et al. Chronic hepatitis C virus infection: does it really impact health-related quality of life? A study in rural Egypt. *Hepatology* **2004**;40:1434-41.
- Von Wagner M., Lee J.-H., Kronenberger B., et al. Impaired health-related quality of life in patients with chronic hepatitis C and persistently normal aminotransferase levels. *J Viral Hepat* **2006**;13:828-834.
- Teixeira M.C.D., Ribeiro M.F.G.S., Gayotto L.C.C., et al. Worse quality of life in volunteer blood donors with hepatitis C. *Transfusion* **2006**;46:278-83.
- Marchesini G., Bianchi G., Amodio P., et al. Factors Associated With Poor Health-Related Quality of Life of Patients With Cirrhosis. *Gastroenterology* **2001**;120:170-8.
- Parana R., Lyra L., Trepo C. Intravenous vitamin complexes used in sporting activities and transmission of HCV in Brazil. *Am J Gastroenterol* **1999**;94:857-8.
- Quarantini L.C., Bressan R.A., Galvão-de Almeida A., et al. Incidence of psychiatric side effects during pegylated interferon alpha retreatment in nonresponder hepatitis C virus-infected patients. *Liver International* **2007**;27:1098-102.