

*Research Article***Neuropsychiatric Profiles in HCV-related Chronic Liver Diseases**

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Abstract

Background: Hepatitis C virus (HCV) infection is one of the main causes of chronic liver disease worldwide. HCV infection is considered a systemic disease because of involvement of other organs and tissues concomitantly with liver disease. Among the extrahepatic manifestations, neuropsychiatric disorders have been reported in up to 50% of chronic HCV infected patients. **The aim of this study is to** evaluate the common neuropsychiatric disorders in patients with chronic liver diseases (CLD), and their effects on patients' quality of life. **Materials and methods:** The study included 80 participants (60 patients with chronic liver diseases and 20 healthy controls matched for age, sex, and educational level), patients with liver cirrhosis were classified according to Child Pugh classification into: Child A, B, and C, **All individuals were subjected to:** Thorough medical history, physical examination, liver function tests, hepatitis markers, abdominal ultrasonography, and neuropsychiatric assessment using: (Unified Parkinson's Disease Rating Scale (UPDRS), Chronic liver disease Questionnaire. **Results:** The data showed that patients with CLD had significant, Cirrhotic patients had extrapyramidal signs, bradykinesia, rigidity and resting tremors increasing in frequency with increased severity of liver disease by Child Pugh classification ($P \sim 0.001$). Rigidity and difficulty in dressing using (UPDRS) were the most frequent signs. The data showed that patients with CLD had significant impairments of quality of life. Chronic liver disease patients had lower quality of life scores compared with normal persons that were highly statistically significance as regard all six domains of the HRQOL questionnaire ($P \sim 0.001$), and increasing with increased severity of liver disease. **Conclusion:** Patients with HCV infection had neuropsychiatric problems. These problems decrease quality of life on those patients.

Keywords: Hepatitis C virus (HCV), chronic liver disease (CLD), Health related quality of life

Introduction

Hepatitis C virus (HCV) infection is a serious global health problem that affects 180 million people worldwide. Hepatitis C virus causes acute and chronic hepatitis which can eventually lead to permanent liver damage and hepatocellular carcinoma¹. HCV infection is considered a systemic disease. Among the extrahepatic manifestations, neuropsychiatric disorders have been reported in up to 50% of chronic HCV infected patients². Patients with cirrhosis frequently showed mild extrapyramidal signs secondary to alterations of basal ganglia circuitry³. HRQOL is becoming a key component in the estimation of the disease impact and

outcome, evaluation of any therapeutic intervention⁴.

Subjects and methods

The study included 60 patients with chronic HCV related chronic liver disease, in addition to 20 healthy persons matched for age, sex and educational level. The patients with chronic liver disease were randomly selected from the outpatient clinic and the in-patient of the Tropical Medicine department, Minia University Hospital. The controls were randomly selected from outpatient clinic and relatives of the patients admitted to our department. The studied groups included (Patients with chronic hepatitis $n = 20$;

patients with liver cirrhosis n = 40; control group included 20 apparently healthy persons). Patients with liver cirrhosis were classified according to Child Poughclassification into: Child A, Child B, Child C. Both patients and control groups were subjected to the following: clinical assessment and laboratory investigations in the form of (complete Liver function tests, complete blood count, serological investigations, abdominal ultrasonography). Neuro-psychiatric assessment using: 1- Unified Parkinson's Disease Rating Scale (for detection presence of extra pyramidal signs), 2-Chronic liver disease Questionnaire (for assessment of HRQOL).

All analyses were performed with version 16 of Statistical Package of Social Science (SPSS). Qualitative data were expressed as proportions, while quantitative data were expressed as mean \pm standard deviation (SD). Qualitative data were analyzed by Chi square (χ^2) test. Statistical significance was defined as p values less than 0.05.

Results

The present study included sixty patient in addition to twenty apparently healthy

volunteers who served as a control group. All results summarized in tables (1-9). Comparison between the studied groups regarding frequency of extra pyramidal signs are shown in tables (1, 2): There was statistically significant absence of extrapyramidal signs in patients with Chronic hepatitis and control group, but there was extrapyramidal signs were detected in cirrhotic patients (P~ 0.001). The cirrhotic patients (child B and C) showed high significant frequency of extrapyramidal signs than those with child A. The difficulty in dressing and rigidity were the most frequent extrapyramidal manifestations in cirrhotic patients (10%). Comparison between the studied groups regarding HRQOL, according to chronic liver disease questionnaire are shown in tables (3-9): The worst scores of the questionnaire was found in liver cirrhosis Child (A, B, C patients) and CHC patients in comparison to control group with highly statistically significant (P~0.001). This impairment was greater with increased severity of liver disease except worry was found in chronic hepatitis patients than other studied groups.

Table (1): comparison between the studied groups regarding frequency of extra pyramidal signs

Extra pyramidal	Controls	Chronic hepatitis	Child A	Child B , C	P
	N=20	N=20	N=20	N=20	
Absent	20(100%)	20(100%)	18(90%)	11(55%)	0.001*
Present			2(10%)	9(45%)	

Table (2): Frequency of extrapyramidal manifestations in cirrhotic patients

Extra pyramidal signs	Child A	Child B , C	P
No	18(90%)	11(55%)	0.2
Dressing	-	2(10%)	
Hygiene	-	1(5%)	
Freeze with walking	-	1(5%)	
Tremor at rest	1(5%)	1(5%)	
Rigidity	1(5%)	2(10%)	
Arising the chair	-	1(5%)	
Brady kinesia	-	1(5%)	

Table (3): comparison between the studied groups regarding HRQOL, according to chronic liver disease questionnaire

HRQOL Score	Controls	Chronic hepatitis	Child A	Child B , C	P
Range	7	5-6	3-6	1-4	0.001*
Mean±SD	7±0	5.3±0.4	4.3±0.8	2.2±0.8	

Table (4): comparison between the studied groups regarding different DOMAINS of chronic liver disease questionnaire

AS	Controls	Chronic hepatitis	Child A	Child B , C	P
Range	7	5-6	3-6	1-4	0.001
Mean±SD	7±0	5.2±0.85	4.35±0.98	2.45±1.05	

Table (5): comparison between the studied groups regarding different DOMAINS of chronic liver disease questionnaire

FA	Controls	Chronic hepatitis	Child A	Child B , C	P
Range	7	4-6	2-6	1-4	0.001
Mean±SD	7±0	5.1±0.74	4.3±1.1	2.1±1.15	

Table (6): comparison between the studied groups regarding different DOMAINS of chronic liver disease questionnaire

SS	Controls	Chronic hepatitis	Child A	Child B , C	P
Range	7	4-7	2-6	1-5	0.001
Mean±SD	7±0	5.3±0.74	4.35±1.22	2.1±1.03	

Table (7): comparison between the studied groups regarding different DOMAINS of chronic liver disease questionnaire

AC	Controls	Chronic hepatitis	Child A	Child B , C	P
Range	7	4-7	3-6	1-5	0.001
Mean±SD	7±0	5.45±0.68	4.5±0.82	2.3±1.08	

Table (8): comparison between the studied groups regarding different DOMAINS of chronic liver disease questionnaire

EF	Controls	Chronic hepatitis	Child A	Child B , C	P
Range	7	5-7	3-6	1-4	0.001
Mean±SD	7±0	5.6±0.68	4.3±0.8	2.3±0.86	

Table (9): comparison between the studied groups regarding different DOMAINS of chronic liver disease questionnaire

WO	Controls	Chronic hepatitis	Child A	Child B , C	P
Range	7	1-4	4-7	3-6	0.001
Mean±SD	7±0	2.3±0.92	5.3±0.65	4.3±0.8	

Discussion

Neuropsychiatric disorders had been reported in up to 50% of chronic HCV infected patients, and range from peripheral neuropathy to cognitive impairment². In the study by Burkhard et al., (2003)⁵ revealed the now classical, symmetrical hyperintensities on T1-weighted imaging in globuspallidus and, additionally, in substantianigra. The authors went on to suggest that this previously unreported finding of signal hyperintensities in substantianigra was characteristic of cirrhotic patients who manifested Parkinsonian symptoms. The present study assessed presence of extra pyramidal signs in patients with chronic liver diseases. The data showed that cirrhotic patients had mild extrapyramidal signs as bradykinesia, rigidity and resting tremors. Jover et al., (2003)⁶ who had found extrapyramidal signs in 47.8% of cirrhotic patients. Spahr, et al., (2000)⁷ also had similar results, who reported that advanced cirrhotic patients had mild extrapyramidal signs secondary to alterations of basal ganglia circuitry. Basal ganglia impairment is mainly related to manganese deposition in this cerebral structure. Butterworth (2013)⁸, reported that cirrhotic patients with extrapyramidal signs have a greater cognitive impairment than patients without this neurological problem. Health related quality of life is becoming a key component in the estimation of the disease impact and outcome, and evaluation of any therapeutic intervention⁴. patients with chronic liver disease had significant abnormalities of HRQOL as measured by the chronic liver disease questionnaire. Chronic liver disease patients had the worst scores of the questionnaire was found in as regard all six domains of the questionnaire.in patients with liver cirrhosis Child (A, B, C

patients) and CHC in comparison to control group (P~0.001). This impairment was greater with increased severity of liver disease. Similar results were reported by Arguedas et al., (2003)⁹, Van der Plas et al., (2003)¹⁰, Sherman et al., (2004)¹¹, Teixeira et al., (2005)¹², and Sumskiene et al., (2006)¹³ who concluded that HRQOL in chronic liver patients depended on disease stage and decompensated patients showed a significantly worse disease-specific and generic HRQOL than non-cirrhotic patients. This was in agreement with Miller et al., (2012)¹⁴ who demonstrated reduced HRQOL during the treatment and improved HRQOL post-treatment. Similarly, Modabbernia et al., (2013)¹⁵ found that patients with cirrhosis had lower HRQOL scores than CHC patients. These results came in contrast the study of Iwasaki et al., (2002)¹⁶ that examined the potential symptoms in 60 patients with chronic HCV in comparison with normal controls, they found no characteristic subjective symptoms in patients with HCV compared to healthy controls. In another study (Schwarzinger et al., 2004)¹⁷, who reported that no statistically significant differences were shown between individuals who turned out to be infected and individuals who were negative. The changes in quality of life observed cannot be related exclusively to knowledge of the diagnosis, which does not appear to be the only probable explanation for such changes. Although the mechanisms remain unclear, the presence of the virus itself must be taken into account (Forton et al., 2003)¹⁸.

Conclusions

Patients with HCV infection had neuropsychiatric problems. These problems decrease quality of life on those patients. The majority of HCV-positive patients

display alterations of concentration, attention, executive function, and memory when they are evaluated by suitable neuropsychological tests. Assessment of HRQOL is essential as a non-traditional diagnostic workup in patients with chronic liver diseases.

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