The Egyptian Journal of Hospital Medicine (January 2023) Vol. 90, Page 2006-2013

Cognitive Impairment, Extrapyramidal Manifestations, and their impact on Quality of Life in Patients with HCV-Related Chronic Liver Diseases

Salwa M. Rabie*[1], Enas M. Hassan[1], Hana K. Fathelbab[2], Wael M. Abd El Ghani[2], Shimaa Hassanen[2], Nermin A. Hamdy[1], Rasha N. Saleh[1]

Departments of [1]Neurology and Psychiatry and

[2]Tropical Medicine and Gastroenterology, Faculty of Medicine, Minia University, Egypt

***Corresponding author:** Salwa M. Rabie, **Mobile:** (+20) 01142741126, **E-Mail:** znaty2018@yahoo.com

ABSTRACT

Background: Hepatitis C virus (HCV) infection is one of the main causes of chronic liver disease worldwide. It has been shown that up to 50% of patients with chronic HCV infection experience neuropsychiatric issues.

Objective: This study aimed to evaluate the cognitive impairment, extrapyramidal signs and their effects on patients' quality of life.

Patients and Methods: The study included 60 untreated patients (20 chronic hepatitis, 40 patients with liver cirrhosis) and 20 healthy controls matched for age, sex, and educational level. Cirrhotic patients were graded according to the Child-Pugh classification. Patients underwent a thorough clinical and neurological evaluation, liver function tests, hepatitis markers, abdominal ultrasonography, psychometric tests and auditory p300 evoked potentials. Unified Parkinson's Disease Rating Scale (UPDRS) and chronic liver disease questionnaire (CLDQ) were used.

Results: Patients had significant cognitive impairment that became greater with increased severity of liver disease. The extrapyramidal manifestations were absent in chronic hepatitis while present in cirrhotics and their frequencies were increased with cirrhotic severity (P~0.001). P300 latency was delayed in patients with and without extrapyramidal signs. Quality of life measured by CLDQ was significantly lower in all patients than controls (P~ 0.001), and became worse with increased severity of liver disease except worry increased in chronic hepatitis.

Conclusion: Patients with HCV infection had cognitive impairment, which increased with chronic liver disease (CLD) severity. Extrapyramidal signs were absent in chronic hepatitis patients, while, present in cirrhotics and increased with increasing severity of cirrhosis. Cognitive impairment was not attributed to the extrapyramidal affection. The CLD and cognitive impairment had negative impact on the quality of life.

Keywords: HCV, CLD, Cognitive impairment, Health related quality of life (HLQOL).

INTRODUCTION

A severe global health issue that affects 200 million individuals globally is the hepatitis C virus (HCV) infection. Hepatocellular carcinoma and irreversible liver damage are potential outcomes of both acute and chronic hepatitis. Up to 50% of people with chronic HCV infection have been observed to have neuropsychiatric problems. Even before hepatic cirrhosis manifests, hepatitis C virus (HCV) patients report cognitive decline, which they have referred to as "brain fog" [(1)]. Growing data suggests that chronic hepatitis C virus infection affects cognitive function, with viremic people specifically showing worse focus and working memory speed [(2)].

Two forms of dysfunctions in hepatic patients without acute hepatic encephalopathy and without evident neurological damage can be identified. These cognitive impairments, also known as mild hepatic encephalopathy (mHE), are typically accompanied by attentional problems and atypical extrapyramidal motor behavior [(3-4)]. Both abnormalities might be caused by basal ganglia lesions that result in subcortical cognitive impairment, which could also account for the motor and cognitive changes seen in cirrhotic patients [(5-6)].

When it comes to spotting early alterations in cirrhotic patients' brain function, event-related potentials (ERPs) appear to be a more sensitive instrument than psychometric assessments. The potential biases of fatigue, latent depression, or poor self-rating in psychometric testing are eliminated by ERPs, an objective and objectively independent assessment of brain information processing. P300 amplitude displays the synchronisation and activation of the cortical regions in charge of carrying out the task, whereas P300 delay illustrates the processing time required to classify the stimuli [(7)].

This study aimed to evaluate the cognitive impairment, extrapyramidal signs and their effects on patients' quality of life.

PATIENTS AND METHODS

This study included 60 untreated patients with chronic HCV related liver disease without overt hepatic encephalopathy (20 with chronic hepatitis and 40 with liver cirrhosis) and 20 age- and sex- matched apparently healthy persons as a control. Patients were registered for follow-up in the outpatient department, no intervention or blood samples or extra-ordinary investigations were requested.

From the inpatient and outpatient clinics of the Tropical Medicine department at Minia University Hospital, patients with chronic liver disease were chosen. The relatives of the patients were used to randomly choose the controls.

Exclusion criteria: Patients with hepatocellular carcinoma or other malignancies, chronic medical diseases, psychiatric or neurological diseases or patients

Received: 16/08/2022
Accepted: 19/10/2022

with chronic HCV having cognitive dysfunction aberrant results from the brief mental state assessment. Patients with liver cirrhosis were classified according to Child Pugh classification into: Child A, Child B, Child C. Both patients and control groups were subjected to the following: clinical and neurological assessment and laboratory investigations including (complete Liver function tests, complete blood count, abdominal ultrasonography, serological investigations (HCV-AB, HCV PCR and genotype for HCV virus).

In addition, neuropsychiatric assessment was done using:

1- The Psychometric Hepatic Encephalopathy Score (PHES), which comprises of five tests: the line-tracing test, the serial dotting test, the digit symbol test, and the number connection test (or trails test) A and B (LTT). An attention and processing speed test is the DST. Other methods for measuring processing speed include serial dotting and line tracing. These assessments are all compared to controls with similar age and educational backgrounds. Therefore, better performance is shown by higher DST scores rather than by lower scores on the other exams. The DST result was within the control performance's mean ± standard deviation and received a score of 0 for a normal score. Results were graded as -1, -2, and -3, respectively, for SDs between -1 and -2, -2 and -3, and greater than -3. However, the outcomes (NCT-A/B, SDT, and LTT) that fell within the control performance's mean ± SD were given a score of 0 for normal. Results with a standard deviation (SD) between +1 and +2 SD, between +2 and +3 SD, and worse than +3S D received -1, -2, and -3 points, respectively. The sum of the results from the five tests, which varied from +5 to -15, was used to determine the PHES final score [(8)].

2- On a Nihon Kohden Neuropack MEB-9204, auditory evoked potentials (peak of p300 latency) were measured using an oddball paradigm task. Three distinct locations were used to capture the electrophysiological activity: Fz (forehead midline), Cz (coronal midline), and Pz (parietal midline). Artifacts were automatically rejected at ±50 V, and impedances were kept between 5 and 10 kΩ. Only once the patients showed that they fully understood the task, the exam was started. Different components of the ERPs are elicited by the passive and active tasks. The highest positive-going peak resulting from a response to the deviant (unusual) stimuli within a particular latency window of 250-450 msec was identified as the P300 component. Peak latency was calculated from the moment the stimulus began, and peak amplitude was calculated in relation to the pre-stimulus baseline (100 ms).

3- The motor component of the UPDRS (Unified Parkinson's Disease Rating Scale) (for detection of presence of extra pyramidal signs). It has a scale of 0 (Normal) to 4. (The worst). The following motor symptoms were evaluated using it: bradykinesia, dressing, tremor at rest, stiffness, rising from a chair, and tremor [(9)].

4- To evaluate HRQOL (health-related quality of life), the Chronic Liver Disease Questionnaire (CLDQ) was employed. Each item is graded on a scale of 1 to 7, with 1 being all the time and 7 being never. It assesses six subscales. By calculating the average of all subscale values, a summary score is created, with a higher score indicating greater HRQOL [(10)].

Ethical consent:

The study was authorised by Minia University's Ethical Institutional Review Board. All study participants provided written informed consents after being informed of our research's goals. The Declaration of Helsinki for human beings, which is the international medical association's code of ethics, was followed during the conduct of this study.

Statistical analysis

Statistical Package of Social Science version 25 was used for all analyses (SPSS). Quantitative data were represented as mean ± standard deviation, whereas qualitative data were expressed as proportions. Data that were regularly distributed were compared between two groups using an unpaired Student's t-test. ANOVA test was utilised to compare the results among the 4 groups. The Chi Square test was used to assess the qualitative data. The threshold for statistical significance was set at $p \leq 0.05$.

RESULTS

I-demographic data of different groups.

II- comparison of psychometric testes, Unified Parkinson's Disease Rating Scale and p300 evoked potentials between studied groups.

III- comparison between the different groups in chronic liver disease questionnaire parameters including health-related quality of life.

The mean age of the control group was 42.3 ± 9.7 years (range 25-60) and 13 were males (65%). The distribution of subjects according to age and sex was as follows: chronic hepatitis 25-62 years (42.6 ± 10.4), 11 males and 9 females (45%), Child A: 28-64 years (47.8 ± 10.9), 13 males and 7 females (35%) and Child B & C: 28-66 years (49.5 ± 10.8), 11 males and 9 females (45%). In this study, the percentage of PHES impairment was significantly higher in chronic hepatitis and cirrhotic patients than control group ($P < 0.02$) (table 1). This impairment was significantly worse in cirrhotic Child B & C group than Child A and chronic hepatitis groups.

Table (1): Distribution of PHES assessment between chronic liver disease patients and control groups

PHES	Controls	Chronic hepatitis	Child A	Child B & C	P
	N=20	N=20	N=20	N=20	
Normal	20 (100%)	14 (70%)	12 (60%)	10 (50%)	0.02*
-1	-	5 (25%)	7 (35%)	7 (35%)	
-2	-	1 (5%)	1 (5%)	3 (15%)	

PHES=psychometric hepatic encephalopathy scores

The digit symbol test showed higher frequency of impairment than other tests (table 2).

Table (2): Comparison of different psychometric tests between patients with chronic liver disease and control groups

Domains		Controls	Chronic hepatitis	Child A	Child B & C	P
		N=20	N=20	N=20	N=20	
NCT	Normal -1 -2	20(100%) - -	14(70%) 5(25%) 1(5%)	12(60%) 7(35%) 1(5%)	10(50%) 7(35%) 3(15%)	0.003*
DST	Normal -1 -2	20(100%) - -	11(55%) 8(40%) 1(5%)	10(50%) 9(45%) 1(5%)	8(40%) 9(45%) 3(15%)	0.009*
LTT	Normal -1 -2	20(100%) - -	16(80%) 3(15%) 1(5%)	13(65%) 6(30%) 1(5%)	12(60%) 5(25%) 3(15%)	0.001*
SDT	Normal -1 -2	20(100%) - -	15(75%) 4(20%) 1(5%)	13(65%) 6(30%) 1(5%)	10(50%) 7(35%) 3(15%)	0.001*

NCT=number connection test, DST=digit symbol test, LTT= line tracing test, SDT=serial dot test,

Table (3) showed that, abnormal P300 evoked response (delayed peak latency) occurred more frequently among both chronic hepatitis and cirrhotic groups than controls (p~0.02). Moreover, the P300 peak latency between Child B & C and Child A as well as chronic hepatitis patients was delayed significantly (p~0.01), but was not between chronic hepatitis and Child A patients. The most prolonged peak latency was in the cirrhotic B & C group (329.1 ± 65.1) [p~0.001]. As regards the amplitude of the p300 evoked response was insignificant between patients and controls.

Table (3): Distribution and comparison of p300 evoked potential latency between the studied groups.

a-

P300 latency (msec)	Controls	Chronic hepatitis	Child A	Child B&C	P value
	N=20	N=20	N=20	N=20	
Normal	20(100%)	12(60%)	10(50%)	8(40%)	0.02*
Abnormal	-	8(40%)	10(50%)	12(60%)	
Range(ms)	190-297	188-454	189-365	211-432	0.001*
Mean ± SD	251.2±32.6	278.1±65.1	279.8±52.2	329.3±67.8	

b-

P300 latency	P
Chronic hepatitis versus child A	0.7
Chronic hepatitis versus child B,C	0.01
Child A versus Child B,C	0.01

Table (4 a & b) showed that all patients with abnormal psychometric tests had prolonged P300 evoked potential latency, while patients with normal psychometric tests showed delayed p300 evoked latency (12.5% in chronic hepatitis and 30.8% in Child B & C) with statistical significance [P~ 0.001& P~ 0.003] respectively.

Table (4): Comparison between P300 evoked potential latency and psychometric tests among patients with hepatitis.

(a)

Tests		Chronic hepatitis	Child A	Child B&C
		N=20	N=20	N=20
P300 latency	Normal Abnormal	12(60%) 8(40%)	10(50%) 10(50%)	8(45%) 12(55%)
Psychometric tests	Normal -1 -2	14(70%) 5(25%) 1(5%)	12(60%) 7(35%) 1(5%)	10(50%) 7(35%) 3(15%)

(b)

Groups	Psychometry	P300		P
		Normal	Abnormal	
Chronic HCV	Average (16) Deficient (4)	14(87.5%) 0	2(12.5%) 4(100%)	0.001*
Child A	Average (18) Deficient (2)	12(66.7%) 0	6(33.3%) 2(100%)	0.06
Child B,C	Average (13) Deficient(7)	9(69.2%) 0	4(30.8%) 7(100%)	0.003*

On the other hand, the extrapyramidal signs were absent in patients with chronic hepatitis. Their frequencies were significantly higher in cirrhotic Child B & C (45%) than in Child A patients (10%) with p value (P~ 0.001) (Table 5). The difficulty in dressing, rigidity and bradykinesia were the most frequent extrapyramidal manifestations in cirrhotic child B & C group (10%) while in child A patients tremors at rest and rigidity were the main extrapyramidal manifestations (5%).

Table (5): Distribution of extra pyramidal signs among the studied groups

Extra pyramidal	Controls	Chroinc hepatitis	Child A	Child B , C	P value
	N=20	N=20	N=20	N=20	
Absent Present	20(100%) 0	20(100%) 0	18(90%) 2(10%)	11(55%) 9(45%	0.001*

Table (6) showed that, all cirrhotic patients with extrapyramidal manifestations had abnormal (delayed latency) of p300 evoked response. This difference was particularly significant in Child B & C patients (P< 0.004). However, about half of Child A group without extrapyramidal manifestations had prolonged p300 peak latency (44.4%). Similarly, those in group Child B & C.

Table (6): The relation between P300 and extra pyramidal signs among the cirrhotic patients

Groups	Extra pyramidal	P300 peak latency		P
		Normal	Abnormal	
Child A	Present (2) Absent (18)	- 10 (55.5%)	2(100%) 8(44.4%)	0.4
Child B, C	Present (9) Absent (11)	- 8 (72.7%)	9 (100%) 3 (27.3%)	0.004*

The HRQO (measured by chronic liver disease questionnaire of patients) with Child (A, B & C groups) and chronic hepatitis C showed significantly worse scores than control group (P~0.001). All subscales' scores (abdominal symptoms, fatigue, systemic symptoms, activity and emotional function) were worse with increased severity of liver disease (in child B & C cirrhotic patients) except worry, which was worse in chronic hepatitis patients (Table 7). There was significant negative correlation between P300 peak latency and HRQOL scores in chronic hepatitis, child A and child B, C (r -0.51, p~ 0.01; r -0.49, p~ 0.02 and r-0.52 p~ 0.01respectively).

Table (7): Frequency of chronic liver disease questionnaire scores and comparison of its different domains of between the studied groups

CLDQ AS range Mean±SD	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	
AS range	7	5-6	3-6	1-4	
Mean+SD	7±0	5.2±0.85	4.35±0.98	2.45±1.05	
FA range	7	4-6	2-6	1-4	
Mean±SD	7±0	5.1±0.74	4.3±1.1	2.1±1.15	
SS range	7	4-7	2-6	1-5	
Mean±SD	7±0	5.3±0.74	4.35±1.22	2.1±1.03	
Ac range	7	4-7	3-6	1-5	
Mean±SD	7±0	5.45±0.68	4.5±0.82	2.3±1.08	
EF range	7	5-7	3-6	1-4	
Mean±SD	7±0	5.6±0.68	4.3±0.8	2.3±0.86	
WO range	7	1-4	4-7	3-6	
Mean±SD	7±0	2.3±0.92	5.3±0.65	4.3±0.8	

CLDQ=chronic liver disease questionnaire, AS= abdominal symptoms, FA=fatigue, SS=systemic symptoms, AC=activity, EF=emotional function, WO=worry.

DISCUSSION

Numerous studies have documented a range of cognitive abnormalities in chronic HCV-infected patients, including slow working memory and focus, difficulty sustaining attention, and slowed psychomotor speed [(11)]. According to **Karmer *et al.*** [(12)] findings, although it was thought to primarily affect patients with decompensated cirrhosis, cognitive deterioration has long been associated with chronic liver disease. However, there is mounting evidence that many HCV patients experience fundamental cognitive abnormalities before cirrhosis develops that are independent to markers of liver disease, viral load, or genotype [(13)].

In this study, patients with chronic liver disease (CLD) had significant cognitive impairment (both those with chronic hepatitis and cirrhosis) than control group as evaluated with psychometric tests (P< 0.02). Cognitive impairment was evident in chronic liver disease, even without cirrhosis suggesting the presence of virus-related brain dysfunction. This impairment was greater with increased severity of liver disease measured by Child Pugh classification. The digit symbol test, which was used to assess the attention and processing speed had high frequency of impairment than other tests. Similar to this result, According to **Hilsabeck *et al.*** [(14)] analysis of 80 patients, HCV patients significantly struggle with focus, education, psychomotor swiftness, and mental adaptability. They also discovered that the severity of the impairment increased with the fibrosis stage. Furthermore, **Abu Faddan *et al.*** [(15)] found that tests of concentration and information processing speed revealed greater cognitive impairment in HCV-infected patients than in healthy volunteers. In a case-control study including kids with hepatitis C, this happened. In a different research, **Hamdy *et al.*** [(16)] discovered that the majority of patients had minor cognitive functions of the dominant hemisphere that were most frequently hampered by cognitive impairment (attention, name, memory, fluency, abstraction, and orientation). A different research had found that HCV patients exhibited cognitive deficits relative to healthy members of the general community, and that this impairment was worsened by greater severity of liver disease as defined by the Child Pugh classification [(17)].

Although there was a correlation between cognitive dysfunction and the degree of hepatic fibrosis in **Cherner *et al.*** [(18)] study non-cirrhotic subjects had levels of cognitive impairment comparable to those of cirrhotic participants' outperformed non-cirrhotic subjects in numerous categories, suggesting that chronic liver illness, even without cirrhosis, is associated with cognitive disadvantages. Contrary to the current study, **Cordoba *et al.*** [(19)] showed no association between HCV infection and cognition in patients, and the participants in their study were drawn from blood donors (accidentally discovered). In line with this, **Soogoor *et al.*** [(20)] discovered no cognitive impairment in their HCV patients (very young subjects). Furthermore, **Abrantes *et al.*** [(21)] did not discover a link between HCV infection and cognitive impairment, although the interpretation of their findings may have been impacted by the study's small sample size. When people are being tested for HCV, cognitive impairments are frequently ignored unless they are obvious or limit functionality, which lowers the quality of life associated with one's health [(22)].

Abnormal P300 evoked response peak latency was significantly delayed in both patients with chronic hepatitis and cirrhotic groups than controls (p~0.02). This impairment was more frequent with increased severity of liver disease by Child Pugh classification (B & C group). Furthermore, the peak P300 latency was significantly prolonged in the cirrhotic B & C patients (p~0.001). However, the amplitude of the p300 evoked response was insignificant between patients and controls. These results are in partial agreement with **Desoky *et al.*** [23] who found a significantly reduced P300 amplitude (P=0.011) and prolonged latencies (P=0.035) in patients with chronic hepatitis C and B compared with healthy controls with no significant difference between both groups of patients. In addition, **Cieko-Michalska *et al.*** [6] found that the latency of the P300 component of ERPs is patients with cirrhosis who do not have encephalopathy live noticeably longer than controls, and that the p300 amplitudes showed equal but insignificant differences between control and patients (means 7.72 and 7.75, respectively), concluding that delayed latency of p300 is observed and suggests MHE in patients with liver cirrhosis without manifestation.

Furthermore, **Kramer *et al.*** [24] observed that 100 patients who underwent analysis revealed that HCV +ve patients had aberrant P300 latencies (25 of whom had cirrhosis). On the other hand, some researchers [25]. Claimed that p300 was ineffective in identifying alterations in brain function in cirrhotic patients without obvious encephalopathy. The difference in the delay of P300 peak latency between patients with Child B & C and cirrhotic Child A as well as chronic hepatitis was significant (p~0.01), however the difference between chronic hepatitis and Child A was insignificant, indicating more deterioration in severe cirrhotic patients.

In our study, all patients with abnormal psychometric tests had prolonged P300 evoked potential latency while patients with normal psychometric tests showed delayed p300 evoked latency (12.5% in chronic hepatitis and 30.8% in Child B & C) with statistical significance [P~ 0.001& P~ 0.003respectively]. This revealed the sensitivity of the p300 latency in detecting early changes in cognitive function in the presence of normal psychometric tests. According to **Cieko-Michalska *et al.*[6],** the auditory peak p300 outperformed every neuropsychological screening test used to identify mHE. Consequently, it has been reported that event-related potentials appear to be a more sensitive tool than psychometric tests for identifying early abnormalities in the brain function of cirrhotic patients. In the visual ERPs investigation, **Jones *et al.*** [26] had also discovered that the P300 latency lengthening in cirrhotic patients without overt HE, even in the absence of abnormalities on a typical psychometric test, may appear.

In our study, extrapyramidal indications were significant, but their therapeutic use in cirrhotic patients has not yet been shown. In the present study, the extrapyramidal signs were not present in patients with chronic hepatitis but present in cirrhotic patients. These extrapyramidal manifestations were present more frequently in Child B & C (45%) than Child A patients (10%). The difficulty in dressing, rigidity, bradykinesia and tremors were the most frequent extrapyramidal manifestations. In accordance, clinical extrapyramidal symptoms were observed in 57 patients (59.4%) of the 98 viral liver cirrhotic patients in **Ashour *et al.*** [4] study, and akinetic rigid syndrome (ARS) was the most common diagnosis (87.7%). The most common symptoms were bradykinesia and axial characteristics (89.5% and 70.2%, respectively). 38.6% of patients experienced postural tremors, as opposed to 3.5% of patients who had rest tremors. Anomalies in the population's posture and gait were found in 38.6% and 36.8% of people, respectively. Parkinson's-like symptoms have been linked to advanced liver cirrhosis. According to **Jover *et al.*** [5]**,** extrapyramidal symptoms were present in 47.8% of cirrhotic patients.

Burkhard *et al.* [27] discovered that cirrhotic patients with advanced disease had a greater incidence of extrapyramidal symptoms such as akinesia, stiffness, stooped posture, postural tremor, and, in rare cases, focal dystonia. According to **Spahr *et al.*** [28], up to 80% of patients with liver cirrhosis show significant extrapyramidal symptoms, which are typically related with the severity of liver disease even in the absence of evident hepatic encephalopathy. Extrapyramidal symptoms in cirrhotic people are thought to be caused by impaired basal ganglia connections [29]. In this study, all cirrhotic patients with extrapyramidal manifestations had abnormal (delayed latency) of P300 evoked response with significant difference in favor of Child B & C group (P< 0.004). The same was true for those with absent extrapyramidal manifestations also, indicating that, the cognitive impairment was not attributed to the extrapyramidal affection. According to **Butterworth** [30], extrapyramidal symptoms such hypokinesia, dystonia, and stiffness that increase swiftly and may not be reliant on the degree of cognitive loss are what distinguish Parkinsonism in cirrhosis.

Health related quality of life was becoming a key component in the estimation of the disease impact and outcome. The present study showed that both chronic hepatitis and cirrhotic patients (Child A & B & C groups) had worse scores of the CLD questionnaire in comparison with control group (P~0.001). This impairment was greater with increased severity of liver disease in all domains of the questionnaire except for worry, which was increased in chronic hepatitis group. This might be explained by persistent fear of patients with chronic hepatitis about their fate of illness, its progress and its complications, feel stigmatized, and feel guilty about the possibility to infect their spouses or their kids [31]. According to our findings, **Atiq *et al.*** [32] discovered that patients with advanced liver disease experience a larger decline in utilities reflecting quality of life than patients with early or no cirrhosis (CLDQ). Additionally, **Modabbernia *et al.*** [33] discovered that

patients with cirrhosis had poorer HRQOL ratings than those with chronic hepatitis C. They came to the conclusion that the disease stage affected HRQOL in chronic liver patients and that decompensated patients had considerably lower illness-specific and overall HRQOL than non-cirrhotic patients.

Schwarzinger *et al.* [34], on the other hand, found that among persons with chronic HCV infection who were uninformed of their HCV status in the extended period prior to clinical symptoms, HRQOL was not significantly decreased. Higher mortality rates and HCV infection risk factors (intravenous drug use is rare in rural Egypt, and the attributable fraction of HCV infections related to past injections, including parenteral antischistosomal therapy), the viral genotype 4, and the socio-demographic variables that were observed in rural Egypt could all be contributing factors. For example, 60% of the population was illiterate, and 89% lived their entire lives in the village. **Iwasaki *et al.* [35]** came to the same conclusion in another study that patients with chronic hepatitis C who did not have any serious problems did not exhibit any different subjective physical symptoms from healthy controls. Although worry could not be measured since the question was about "thoughts about liver transplant," which is neither available in their culture nor well known, **Atiq *et al.* [32]** found that anxiety was not significantly correlated with advanced liver disease.

In the current study, there was also a significant negative association between HRQOL ratings and P300 peak latency in patients with chronic hepatitis and cirrhosis, proving that cognitive impairment negatively affects quality of life. According to **Jover *et al.* [5]**, who showed that motor and cognitive impairment had a negative impact on cirrhotic patients' quality of life, this is in line with their findings.

Limitation of the study: Brain fMRI (functional magnetic resonance imaging) is better to be performed and correlated with the p300 auditory evoked potential.

CONCLUSIONS

Patients with HCV infection had impairment of concentration, attention, processes speed and update representation. These impairments were increased with CLD severity. Chronic hepatitis patients had no extrapyramidal signs while these signs (difficulty of dressing, bradykinesia, rigidity and tremors) were more frequent with increasing cirrhosis severity. Cognitive impairment was not attributed to the extrapyramidal affection. The CLD and its severity as well as cognitive impairment had negative impact on the quality of life. The auditory p300 evoked potentials represent a promising tool for the objective diagnosis of cognitive impairment in HCV patients.

Competing interests: Authors declared no competing interests.

Funding: Authors did not receive any funds.

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