science, engineering and health studies

Research Article

Science, Engineering and Health Studies
https://lio1.tci-thaijo.org/index.php/sehs
ISSN (Online): 2630-0087

Assessment of neurological disorders in patients with chronic viral hepatitis: A prospective cohort study

Tatyana Vasiliyevna Polukchi

Department of Infectious Diseases and Dermatovenerology, South Kazakhstan Medical Academy, Shymkent 160001, Republic of Kazakhstan

ABSTRACT

This prospective cohort study aimed to determine the prevalence and factors associated with neurological manifestations in patients with chronic hepatitis. The study involved 233 patients with chronic viral hepatitis from the Shymkent City Infectious Diseases Hospital and the Hepatological Center of the Shymkent Regional Clinical Hospital, conducted between March 2021 and January 2022. To identify neurological disorders, the neurological status of patient was assessed. The prevalence of neurological manifestations in the study population was 49.4%, which 43% of cases involving disorders of the peripheral nervous system. Peripheral neuropathy was common, affecting nearly half of the patients (49.4%). Factors associated with neurological manifestations included age over 50 years disease duration (greater than 5 years) alanine aminotransferase (ALT) level ($p < 0.014$), and aspartate aminotransferase (AST) level above 40 IU/L. Thus, patients with chronic viral hepatitis exhibit a range of neurological manifestations. We recommend routine screening for neurological disorders, particularly among older patient and those with a longer disease duration.

Keywords: viral hepatitis; fibrosis; cirrhosis; neurological disorders; peripheral neuropathy

Corresponding author:
Tatyana Vasiliyevna Polukchi
tatyana_polukchi@mail.ru

Received: *14 March 2024*
Revised: *2 May 2024*
Accepted: *6 May 2024*
Published: *11 December 2024*

Citation:
Polukchi, T. V. (2024). Assessment of neurological disorders in patients with chronic viral hepatitis: A prospective cohort study. Science, Engineering and Health Studies, 18, 24050017.

1. INTRODUCTION

Viral hepatitis is a global public health problem that causes severe damage to individuals, communities, and health systems (Ramamurthy et al., 2017). The prolonged course of viral hepatitis leads to progressive liver damage, eventually resulting in cirrhosis and hepatocellular carcinoma (Basnayake and Easterbrook, 2016). According to the latest data, more than 170 million people worldwide are living with chronic hepatitis C virus (HCV) infection, which causes more than 2.4 million deaths annually (Basnayake and Easterbrook, 2016). Statistically, more than 350 million people are affected by chronic hepatitis B virus (HBV) infection, and over 12 million are co-infected with both hepatitis B and hepatitis D (Stockdale et al., 2020; Polaris Observatory HCV Collaborators, 2022). A recent analysis conducted in the Republic of Kazakhstan revealed a significant increase in new cases of viral hepatitis in the country. In 2020 alone, 23,906 cases of HBV infection, 31,927 cases of hepatitis C, and 2,428 cases of hepatitis D were detected (Jumabayeva et al., 2022). Among the regions with the highest prevalence of viral hepatitis in Kazakhstan are Shymkent city and the Turkestan region. In 2015, the prevalence of hepatitis B was 56.2 cases per 10,000 in Shymkent, while the prevalence of hepatitis D was 18.2 cases per 100,000 in Shymkent and 20.8 cases per 100,000 in the Turkestan region (Jumabayeva et al., 2022).

Chronic viral hepatitis B and C are systemic diseases characterized by a wide range of extrahepatic manifestations, which result from immunological disorders caused by viral

replication in the liver and other tissues, as well as the direct pathological effects of viral particles. In many cases, extrahepatic manifestations may be the only sign of a viral infection, often becoming prominent in the clinical picture and influencing the prognosis of the disease (Sherman and Sherman, 2015; Tassi et al., 2021; Polukchi and Slavko, et al., 2023). Researchers use the term CHASM (Systemic Manifestations Associated with Hepatitis C) to describe a variety of diseases related to hepatitis C, including thyroid disorders, cardiovascular diseases, kidney diseases, eye diseases, skin diseases, diabetes mellitus, and nervous system disorders (Sherman and Sherman, 2015). These extrahepatic manifestations can sometimes precede liver damage, necessitating additional diagnostic and treatment methods, which can significantly alter treatment strategies and disease prognosis (Flores-Chávez et al., 2017; Boglione et al., 2020). Statistically, approximately 3% of the global population is infected with hepatitis C, and among those with chronic infection, at least one extrahepatic manifestation is observed in half of these patients. This has a considerable impact on the prognosis and unfavorable outcome of the disease (Cacoub, 2016). In the chronic course of the disease, not only the central nervous system (CNS) but also the peripheral nervous system (PNS) can be affected, leading to a broad range of clinical disorders, including cerebrovascular phenomena, encephalopathy, myelitis, encephalomyelitis, and cognitive impairment. In addition, the HCV can trigger various forms of peripheral neuropathies, and in combination with mixed cryoglobulinemia, it increases the risk of stroke in infected patients (Wu et al., 2015; Sonavane et al., 2018; Choi et al., 2020). Research has shown that viral hepatitis B is responsible for 1% of all cases of acute inflammatory demyelinating polyneuropathy. Hepatitis viruses also contribute to the development of Guillain-Barre syndrome, a condition characterized by a wide clinical variety of manifestations due to the immune-mediated destruction of the peripheral nervous system (Sonavane et al., 2018; Wei and Duan, 2021).

The mechanism underlying the development of extrahepatic manifestations in the chronic course of viral hepatitis is not yet fully understood and remains complex. However, it has been established that the long-term persistence of viruses directly affects the central nervous system, likely due to their ability to replicate in microglial and endothelial cells, leading to prolonged inflammation in these cells (Iriana et al., 2017; Schwendimann and Minagar, 2017). Patients with chronic hepatitis B may also experience rare muscle diseases (Zangeneh et al., 2022). Recent studies have shown that HIV-infection can contribute to the development of Parkinson's disease, with pathogenetic mechanisms involving excessive release of inflammatory markers (Wu et al., 2015; Wijarnpreecha et al., 2018; Goldstein et al., 2019).

On the one hand, in the long-term course of chronic viral hepatitis, particularly hepatitis C, perivascular T-cell infiltrates and microglial nodules formed around neurons, indicating inflammation of the brain and/or cerebral membranes. On the other hand, neuronal demyelination and cryoglobulin deposition may be associated with nerve ischemia, secondary to occlusion or vasculitis of nerve vessels, leading to fascicular ischemia and axonal degeneration (Adinolfi et al., 2015). Evidence suggests that up to 50% of patients with chronic hepatitis C may experience neurological disorders (Adinolfi et al., 2015). In this context, investigating the development of neurological disorders in patients with chronic viral hepatitis and viral etiology-related cirrhosis, as well as their impact on disability, is of significant interest.

2. MATERIALS AND METHODS

2.1 Study design

A cohort study was conducted at the Department of Infectious Diseases of Shymkent City Hospital and the Regional Hepatological Center of Shymkent from March 2021 to January 2022. A total of 233 patients with a history of chronic viral hepatitis were recruited as participants. Basic information was collected, and demographic, clinical, laboratory, and instrumental data were analyzed after obtaining written informed consent from each patient. Laboratory tests and instrumental investigations were performed according to the required investigations outlined in the Clinical Protocol of the Ministry of Healthcare of the Republic of Kazakhstan. All procedures were provided free of charge to the patients. The inclusion criteria were patients aged 18 years or older with chronic viral hepatitis. Patient under 18 years, as well as those with a history of pregnancy, cancer, obesity, acute viral hepatitis, or who were registered at a neuropsychiatric dispensary, were excluded from the study.

2.2 Study procedure and data collection

The participants exhibited a range of clinical symptoms and changes in laboratory parameters, corresponding to varying degrees of disease activity. The criteria published by the European Association for the Study of the Liver (EASL) were used to confirm the etiology of chronic viral hepatitis (Terrault et al., 2018; European Association for the Study of the Liver, 2018). Indirect ultrasound elastography was used to assess the stage of liver fibrosis, and data interpretation followed the recommendations of EASL-ALEH clinical practice guideline (Terrault et al., 2018; European Association for the Study of the Liver, 2018). Neurological disorders were identified through patient interview and a neurological examination.

2.3 Neurological assessment

A comprehensive neurological examination was conducted, which included assessment of the patient's mental status, cranial nerve function, motor system, muscle strength, gait, posture, coordination of movements, superficial and deep sensation, reflexes, and the autonomic nervous system. Cognitive dysfunction was evaluated using a structured protocol that included the collection of medical history, with various cognitive domains assessed, including attention and concentration, visual-constructive and executive functions, memory, speech, abstract thinking, calculation and orientation. Peripheral neuropathy was assessed through tactile sensitivity on the extremities using a standard microfilament, pain sensitivity using a neurological needle, temperature sensitivity by alternately touching test tubes with water of different temperatures (20°C and 40°C), vibration sensitivity using a 128 Hz tuning fork.

2.4 Operational definitions

Serological markers of hepatitis B (HBsAg, Anti-HBc) and hepatitis C (anti-HCV) were identified in patients. In cases of Hepatitis D virus (HDV)-coinfection, markers for both

hepatitis B and D were detected in the blood serum, including HBsAg, anti-HBc IgM, along with anti-HDV IgM and anti-HDV IgG. The presence of IgG antibodies to the HDV in the blood serum not only indicated the chronicity of the infection but also facilitate the diagnosis of hepatitis of previously unknown etiology. Subsequently, patients underwent virological testing for HBV, HCV, HDV infections to assess viral replication. For this purpose, a polymerase chain reaction (PCR) test (qualitative test) was carried out using automated real-time closed-type systems, with a lower limit of detection of 6-10 IU/mL. This test allowed for the detection of HBV DNA, HDV RNA, and HCV RNA.

During the study, all patients at the Regional Hepatological Center of Shymkent underwent indirect ultrasound elastometry using the FibroScan 502 device (Echosens, Paris, France). This procedure was used to assess the degree of fibrous transformation of the liver and to determine the presence of cirrhosis. The patients were then categorized into 5 groups based on the stages of liver fibrosis (F_0, F_1, F_2, F_3, F_4). Specifically, stage F_0 indicated the absence of liver fibrosis, stage F_1 referred to mild, focal fibrosis, stage F_2 indicated moderate fibrosis, stage F_3 represented severe fibrosis, stage F_4 denoted severe diffuse fibrosis, or liver cirrhosis.

In patients with chronic hepatitis C, the viral load was determined. A viral load greater than $2x10^3$ copies /mL was considered high in chronic viral hepatitis B, while a viral load greater than $2x10^6$ copies/mL was considered high in chronic hepatitis C.

2.5 Statistical analyses

For categorical variables, frequencies and percentages were reported. Continuous variables were presented as mean±standard deviation or median (minimum-maximum). The normality of distribution for continuous variables was assessed using the Kolmogorov-Smirnov test. A p-value of <0.05 was considered statistically significant. Statistical analysis was performed using SPSS version 27.0 software for Windows (IBM Corp; Armonk; NY; 2020).

2.6 Ethical approval and consent to participate

The study was conducted following approval from the Institutional Ethics Committee (IEC) of Kazakh Medical University of Continuing Education (Approval No. 3 dated 17.03.2020, and No. 3, dated 16.03.2021) and Asfendiyarov Kazakh National Medical University (Approval No. 7, dated 30.05.2022). Written informed consent was obtained from all individual participants.

3. RESULTS

The study population consisted of 233 patients, including 111 males and 122 females, with a mean age of 47.14 years (ranges: 18 to 79). These patients were residents of urban (28.3%) and rural (71.6%) areas. The diagnoses were as follows: chronic viral hepatitis B in 44 patients (18.9%), chronic viral hepatitis C in 132 patients (56.7%), and chronic viral hepatitis D in 57 patients (24.4%). The distribution of fibrosis stages was as follows: mild fibrosis in 99 patients (42.9%), moderate fibrosis in 78 patients (33.5%), and severe fibrosis in 56 patients (23.6%).

Clinical and demographic data for patients with chronic viral hepatitis were analyzed across different stages of fibrosis. It was observed that clinical manifestation tended to increase with the stage of fibrosis, although there was variability in the clinical symptoms. The mean age of the total study population with chronic viral hepatitis was 47.1±14.1 years. Specifically, the average age in the stage F_0 group was 40.0±13.5 years, in the stage F_1 group 47.4±13.8 years, in the stage F_2 group 46.1±14.0 years, in the stage F_3 group 48.2±14.3 years, and in the stage F_4 group 52.6±12.9 years. The mean duration of disease for the entire cohort was 5.5±4.6 years. For each stage of fibrosis, the duration of disease was as follows: F_0—5.0±4.1 years, F_1—4.6±2.9 years, F_2—6.3±5.5 years, F_3—5.1±5.5, and F_4—6.6±4.9 years.

The mean fibrosis in all patients was 10.7±7.9 kPa. In stage F_0, the mean was 4.8±0.6 kPa; in stage F_1, 6.6±0.3 kPa; in stage F_2, 8.1±0.7 kPa, in stage F_3, 8.1±0.7 kPa; and in stage F_4, 21.8±9.6 kPa.

The mean ALT level in all patients was 56.1±49.4 U/L. In stage F_0, the mean was 31.3±19.9 U/L; in stage F_1, 54.8±50.5 U/L; in stage F_2, 51.7±38.9 U/L; in stage F_3, 62.7±50.6 U/L; and in stage F_4, 77.1±61.8 U/L. The average AST level in all patients was 49.5±41.3 U/L. In stage F_0, the average was 29.4±17.7 U/L; in stage F_1, 43.4±31.0 U/L; in stage F_2, 46.6±30.1 U/L; in stage F_3, 54.3±44.6 U/L; and in stage F_4, the average was 71.5±57.0 U/L. The clinical and demographic characteristics of patients with chronic viral hepatitis are summarized in Table 1.

Table 2 presents the results of the analysis performed to evaluate neurological manifestations separately for the three types of infection. As shown in the table, the most frequent and severe neurologic disorders in patients with chronic viral hepatitis were associated with chronic hepatitis C ($p<0.015$) and chronic hepatitis D ($p<0.009$).

Further, patients with chronic viral hepatitis were assessed for neurological status through a detailed examination of various areas: cranial nerves, motor function (muscle mass, tone and strength), reflexes (deep tendon and superficial reflexes), sensory function (pain of various localization, superficial and deep sensitivity), coordination and gait, and higher brain functions (cognitive assessment).

We determined the prevalence of neurological manifestations to be 49.4% (115 patients), with peripheral nervous system (PNS) involvement observed in 43% (100 patients). Peripheral neuropathy was frequent, affecting about half of the patients (49.4%, or 115 patients). The prevalence of neurological manifestations in patients with chronic viral hepatitis at various stages of fibrosis is shown in Table 3.

In patients with chronic viral hepatitis, there was a tendency for neurological manifestations to increase with an increase in the stage of fibrosis. However, the neurological symptoms were very variable (Table 4).

Thus, headache complaints were presented by 10.6% of patients at stage F_0, 22.6% of patients at stage F_1, 45% of patients at stage F_2, 71% of cases had headache at stage F_3 and 83.6% at stage F_4. Dizziness was noted in 2.1% of patients at stage F_0, 7.5% patients at stages F_1 and F_2, 18.4% of patients at stage F_3 and 16.3% at stage F_4. 25.5% of patients at the F_0 stage complained of nausea, 24.5% of patients at the F_1 stage, 45% of patients at the F_2 stage, 57.8% of cases had headache at the F_3 stage and 58.1% at the F_4 stage. Pain in the eyeballs was felt by 2.1% of patients at the F_0 stage, 7.5% of patients at the F_1 stage, 20% of patients at the F_2 stage, in 21% of cases it was noted at the F_3 stage and 21.8% at the F_4 stage. Sleep disorder was observed in 17% of patients at stage F_0, 28.3% of patients at stage F_1, 40% of patients at stage F_2, 50% of cases had headache at stage F_3 and 70.1% at stage F_4.

Table 1. Clinical and demographic characteristics of patients with chronic viral hepatitis

Characteristics	Total number (n = 233)	F_0 (n = 47)	F_1 (n = 53)	F_2 (n = 40)	F_3 (n = 38)	F_4 (n = 55)
Age (years) Range (min-max)	18 - 75	19 - 66	25 - 72	25 - 72	26 - 70	20 - 75
Mean±standard deviation	47.1±14.1	40.0±13.5	47.4±13.8	46.1±14.0	48.2±14.3	52.6±12.9
Gender (n, %)						
Male	111 (47.6%)	27 (57.4%)	21 (39.6%)	21 (52.5%)	17 (44.7%)	25 (45.5%)
Female	122 (52.4%)	20 (42.6%)	32 (60.4%)	19 (47.5%)	21 (55.3%)	30 (54.5%)
Duration of disease mean ± standard deviation	5.5±4.6	5.0±4.1	4.6±2.9	6.3±5.5	5.1±5.5	6.6±4.9
Fibrosis (kPa) mean ± standard deviation	10.7±7.9	4.8±0.6	6.6±0.3	8.1±0.7	10.7±0.8	21.8±9.6
ALT level mean ± standard deviation	56.1±49.4	31.3±19.9	54.8±50.5	51.7±38.9	62.7±50.6	77.1±61.8
AST level mean ± standard deviation	49.5±41.3	29.4±17.7	43.4±31.0	46.6±30.1	54.3±44.6	71.5±57.0

Table 2. Relationship between different types of viral hepatitis (B, C, D) and specific neurologic manifestations

Parameter	Chronic viral hepatitis B (n = 44)		Chronic viral hepatitis C (n = 132)		Chronic viral hepatitis D (n = 57)	
	Sig. (2-tailed)	p-value	Sig. (2-tailed)	p-value	Sig. (2-tailed)	p-value
Neurological manifestations (total number)	0.593	0.083	0.862	0.015	0.945	0.009

Table 3. Prevalence and clinical picture of neurological manifestations in patients with chronic viral hepatitis

Variable	F_0 (n = 47)	F_1 (n = 53)	F_2 (n = 40)	F_3 (n = 38)	F_4 (n = 55)
Neurological manifestations					
Present	21.3%	41.5%	62.5%	76.3%	81.8%
Absent	78.7%	58.5%	37.5%	23.7%	18.2%
CNS disorders	14.8%	18.8%	35%	42.1%	45.4%
PNS disorders	17%	22.6%	50%	73.6%	58.2%

Emotional lability was recorded in 10.6% of cases at the F_0 stage, in 9.4% of cases at the F_1 stage, in 10% of cases at the F_2 stage, in 45% of cases at the F_3 stage, in 58.1% at the F_4 stage. When assessing attention, 21% of patients at stage F_0, 24% of patients at stage F_1, 32% of patients at stage F_2, 45% of patients at stage F_3, 51% of patients at stage F_4 made mistakes. Attention disorder was registered in 23% of patients at stage F_0, in 32% of patients at stage F_1, 41% of patients at stage F_2, 45% of patients at stage F_3, in 52% of patients at stage F_4. Hearing loss was detected only at stages F_3 and F_4, it was noted in 5.2% of cases at stage F_3 and 7.2% at stage F_4.

In 34.7% of patients (81 patients), the most frequent complaints were paresthesia, manifested as tingling in 20.1% (47 patients) and burning in 14.6% (47 patients). Thus, paresthesia was diagnosed in 4.2% of patients at the F_0 stage, in 26.4% of patients at the F_1 stage, in 37.5% of patients at the F_2 stage, in 60.5% of patients at the F_3 stage and in 70.1% at the F_4 stage.

The most frequent neurological sign detected during the examination was an abnormal perception of vibration in 32.2% (75 patients), accompanied by a hypoactive Achilles tendon reflex in 19.7% (47 patients). Thus, tendon hyporeflexia was detected in 3.7% of patients at the F_1 stage, 7.5% of patients at the F_2 stage, 45% of patients at the F_3 stage, and 45.5% of patients at the F_4 stage. Pathological signs were detected only at stages F_3 and F_4, it was noted in 2.6% of cases at stage F_3 and 3.6% at stage F_4. Instability in the Romberg pose was observed in 5% of patients - at the F_2 stage, in 5.2% of cases there was a headache at the F_3 stage and 7.3% at the F_4 stage. Tremor was detected in 12.1% of patients (28 patients): in 2.1% of cases at the F_0 stage, in 3.7% of cases at the F_1 stage, in 17.5% of cases at the F_2 stage, in 18.4% of cases at the F_3 stage and in 23.6% at the F_4 stage.

Table 5 presents the results of a pre-specify multiple regression analysis conducted to assess factors associated with neurological manifestations in patients with chronic viral hepatitis. As shown in this table, the presence of neurological manifestations in patients was associated with etiology of chronic viral hepatitis (p<0.000), thus, patients with chronic viral hepatitis C had more severe neurological manifestations and also age more 50 years (p<0.009), duration of the disease (more than 5 years) (p <0.057), ALT level (p<0.014) and AST level (p<0.021) (above 40 IU/l).

Table 4. Frequency of registration of neurological manifestations in patients with chronic viral hepatitis at various stages of fibrosis

Symptoms	F_0 (n = 47)	F_1 (n = 53)	F_2 (n = 40)	F_3 (n = 38)	F_4 (n = 55)
Headache	10.6%	22.6%	45%	71%	83.6%
Dizziness	2.1%	7.5%	7.5%	18.4%	16.3%
Nausea	25.5%	24.5%	45%	57.8%	58.1%
Pain in the eyeballs	2.1%	7.5%	20%	21%	21.8%
Sleep disorder	17.0%	28.3%	40%	50%	70.1%
Emotional lability	10.6%	9.4%	10%	45%	58.1%
Impaired concentration	21%	24%	32%	45%	51%
Memory degradation	23%	32%	41%	45%	52%
Hearing loss	0%	0%	0%	5.2 %	7.2 %
Tendon hyperreflexia	0%	3.7%	7.5%	45%	45.5%
Paresthesia	4.2%	26.4%	37.5%	60.5%	70.1%
Pathological signs	0%	0%	0%	2.6%	3.6%
Instability in the Romberg pose	0%	0%	5%	5.2%	7.3%
Tremor	2.1%	3.7%	17.5%	18.4%	23.6%

Table 5. Predictors of neurological manifestations in patients with chronic viral hepatitis

Parameter	Multiple regression analysis	
	beta	p-value
Age≥50 years	0.546	0.001*
Gender	-0.032	0.820
Duration of the disease ≥ 5 years	0.027	0.057*
Etiology of chronic viral hepatitis	-0.434	0.000
Serum ALT levels	-0.018	0.014*
Serum AST levels	-0.058	0.021*
Viral load	0.237	0.820
Fibrosis	0.234	0.277
Regression statistics	R square adjusted = 0.295	

In our study, neurological disorders were correlated with the age of the patients, as it older patients with chronic viral hepatitis exhibited higher rates of these disorders compared to younger patients. This was likely du because younger patients may be more aware of their condition than the general population. We found that patients with a longer duration of the disease tended to experience more severe neurological disorders, while those in the early stages of the disease often had reversible manifestations. The severity of the patients' condition was also influenced by the activity of the viral disease, as the patients with higher levels of serum transaminases were more likely to develop neurological manifestations.

4. DISCUSSION

In this study, it was found that 49.4% of patients with chronic viral hepatitis had neurological manifestations. The most common neurological disorders at various stages of fibrosis included headache, nausea, sleep disorder, emotional lability, impaired concentration, memory impairment, paresthesia.

Factors associated with neurological manifestations included age more 50 years (p<0.009), disease duration greater than 5 years (p<0.057), ALT level (p<0.014) and AST level (p<0.021), particularly when levels were above 40 IU/L. However, in another study, the main predictors of neurological manifestations in patients with chronic hepatitis were the age≥55years, longer duration of illness and a high viral load (Mapoure et al., 2018). Our findings are consistent with the results of this previous study, although we did not find a link between neurological disorders and viral load.

As far as we know, this study is one of the few to examine the overall prevalence and types of neurological disorders in patients with chronic viral hepatitis. The prevalence of neurological manifestations in our study was 49.4%, indicating that almost half of patients with chronic viral hepatitis experience neurological disorders. This is

consistent with the findings of an existing systematic review (Mathew et al., 2016). In a study conducted by Mapoure et al. (2018), the prevalence rate was slightly higher, at 54.5%.

The study demonstrated that the frequency of peripheral nervous system disorders symptoms in participants was 43% of all examined, which is higher than in the 23% reported in the study by Zanone et al. (2021). The differences may be attributed to the smaller sample size in Zanone et al.'s study which included only 94 patients. In another similar study by Mapoure et al. (2018), which included 121 participants, the prevalence of peripheral neuropathy was 47.9%, which aligns closely with the results of our study. However, according to a different study, which included 69 participants, 47 had peripheral neuropathy; this study specially investigated the relationship between peripheral neuropathy with the duration of cryoglobulinemia (Biasiotta et al., 2014). Several authors have suggested that viral hepatitis is associated with a wide range of immuno-mediated complications, particularly affecting the peripheral nervous system (Ferro et al., 2016). The mechanisms underlying neurological disorders in this infection are likely multifactorial, involving endocrine effects, virus replication in extrahepatic cells, and enhanced immune response with systemic effects (Negro et al., 2015; Grignoli et al., 2015; Polukchi et al., 2023).

This study had several limitations, primarily due to the fact that neurological disorders in patients with chronic viral hepatitis were not compared before and after antiviral therapy.

5. CONCLUSION

The prevalence of neurological manifestations in patients in the study population was 49.4%, with peripheral nervous system disorders observed in 43% of patients. Cognitive impairment was detected in 36% of patients. In patients with chronic viral hepatitis, there was a tendency for neurological manifestations to increase with the stage of fibrosis. The most common neurological disorders at various stages of fibrosis included headache, nausea, sleep disorder, emotional lability, impaired concentration, memory impairment, paresthesia. The main predictors of neurological manifestations in these patients were age (over 50 years), disease duration (more than 5 years), ALT and AST levels. We consider it appropriate to use routine screening for neurological impairment in this patient population, particularly focusing on older individuals and those with a longer duration of the disease. Strengthening social and medical support, especially for patients in the late stages of the disease can help improve their quality of life.

ACKNOWLEDGMENT

I am grateful to Abassova Gaukhar, Head of Neurology Department at Khoja Akhmet Yassawi International Kazakh-Turkish University Turkistan, Kazakhstan, for her support. The author also thanks the patients who agreed to participate in the study.

REFERENCES

Adinolfi, L. E., Nevola, R., Lus, G., Restivo, L., Guerrera, B., Romano, C., Zampino, R., Rinaldi, L., Sellitto, A., Giordano, M., and Marrone, A. (2015). Chronic hepatitis C virus infection and neurological and psychiatric disorders: An overview. *World Journal of Gastroenterology*, 21(8), 2269–2280.

Basnayake, S. K., and Easterbrook, P. J. (2016). Wide variation in estimates of global prevalence and burden of chronic hepatitis B and C infection cited in published literature. *Journal of Viral Hepatitis*, 23(7), 545–559.

Biasiotta, A., Casato, M., La Cesa, S., Colantuono, S., Di Stefano, G., Leone, C., Carlesimo, M., Piroso, S., Cruccu, G., and Truini, A. (2014). Clinical, neurophysiological, and skin biopsy findings in peripheral neuropathy associated with hepatitis C virus-related cryoglobulinemia. *Journal of Neurology*, 261(4), 725–731.

Boglione, L., Lupia, T., Cariti, G., and Di Perri, G. (2020). Efficacy and safety of interferon-free regimens in patients affected by chronic hepatitis C and psychiatric disorders. *Journal of Infection and Chemotherapy*, 26(1), 18–22.

Cacoub, P. (2016). Extrahepatic manifestations of chronic hepatitis C virus infection. *Therapeutic Advances in Infectious Disease*, 3(1), 3–14.

Choi, H.-Y., Mai, T. H., Kim, K.-A., Cho, H., and Ki, M. (2020). Association between viral hepatitis infection and Parkinson's disease: A population-based prospective study. *Journal of Viral Hepatitis*, 27(11), 1171–1178.

European Association for the Study of the Liver. (2018). EASL Recommendations on treatment of hepatitis C 2018. *Journal of Hepatology*, 69(2), 461–511.

Ferro, J. M., Viana, P., and Santos, P. (2016). Management of neurologic manifestations in patients with liver disease. *Current Treatment Options in Neurology*, 18(8), 37.

Flores-Chávez, A., Carrion, J. A., Forns, X., and Ramos-Casals, M. (2017). Extrahepatic manifestations associated with Chronic Hepatitis C Virus Infection. *Revista Española de Sanidad Penitenciaria*, 19(3), 87–97.

Grignoli, R., Goossens, N., and Negro, F. (2015). Extrahepatic manifestations of HCV. *Minerva Gastroenterol Dietol*, 61(1), 31–38.

Goldstein, L., Fogel-Grinvald, H., and Steiner, I. (2019). Hepatitis B and C virus infection as a risk factor for Parkinson's disease in Israel-A nationwide cohort study. *Journal of the Neurological Sciences*, 398, 138–141.

Iriana, S., Curry, M. P., and Afdhal, N. H. (2017). Neurologic manifestations of hepatitis C virus infection. *Clinical Liver Disease*, 21(3), 535–542.

Jumabayeva, A., Nersesov, A., Kulzhanov, M., Nefedova, M., Nuraliyeva, G., Rakhimbekova, G., Tanabayeva, S., and Fakhradiyev, I. (2022). Prevalence of viral hepatitis B, C, and D in Kazakhstan. *Scientific World Journal*, 2022, 9102565.

Mapoure, N. Y., Budzi, M. N., Eloumou, S. A. F. B., Malongue, A., Okalla, C., and Luma, H. N. (2018). Neurological manifestations in chronic hepatitis C patients receiving care in a reference hospital in sub-Saharan Africa: A cross-sectional study. *PLoS One*, 13(3), e0192406.

Mathew, S., Faheem, M., Ibrahim, S. M., Iqbal, W., Rauff, B., Fatima, K., and Qadri, I. (2016). Hepatitis C virus and neurological damage. *World Journal of Hepatology*, 8(12), 545–556.

Negro, F., Forton, D., Craxì, A., Sulkowski, M. S., Feld, J. J., and Manns, M. P. (2015). Extrahepatic morbidity and mortality of chronic hepatitis C. *Gastroenterology*, 149(6), 1345–1360.

Polaris Observatory HCV Collaborators. (2022). Global change in hepatitis C virus prevalence and cascade of care between 2015 and 2020: A modelling study. *Lancet Gastroenterol Hepatol*, 7(5), 396–415.

Polukchi, T. V., Abuova, G. N., and Slavko, Y. A. (2023). The neuropsychiatric aspect of the chronic viral hepatitis. *Prague Medical Report*, 124(2), 94–107.

Polukchi, T. V., and Slavko, Y. A. (2023). Viral hepatitis B and C and neurological impairment. *Ankara Medical Journal*, 23(4), 468–477.

Ramamurthy, M., Sankar, S., Nandagopal, B., Sridharan, G., and Risbud, A. R. (2017). Viral diseases of public health importance in India: Current priorities with special emphasis on prevention. *Journal of Krishna Institute of Medical Sciences University*, 6(4), 1–11.

Schwendimann, R. N., and Minagar, A. (2017). Liver disease and neurology. *Continuum*, 23(3, Neurology of Systemic Disease), 762–777.

Sherman, A. C., and Sherman, K. E. (2015). Extrahepatic manifestations of hepatitis C infection: Navigating CHASM. *Current HIV/AIDS Reports*, 12(3), 353–361.

Sonavane, A. D., Saigal, S., Kathuria, A., Choudhary, N. S., and Saraf, N. (2018). Guillain-Barré syndrome: Rare extra-intestinal manifestation of hepatitis B. *Clinical Journal of Gastroenterology*, 11(4), 312–314.

Stockdale, A. J., Kreuels, B., Henrion, M. Y. R., Giorgi, E., Kyomuhangi, I., de Martel, C., Hutin, Y., and Geretti, A. M. (2020). The global prevalence of hepatitis D virus infection: Systematic review and meta-analysis. *Journal of Hepatology*, 73(3), 523–532.

Tassi, A., Gitto, S., Piras, C., Cursaro, C., Alicandro, T., Margotti, M., Rivi, M., and Andreone, P. (2021). Cognitive, neurological and psychiatric disorders occurring in Hepatitis C Virus infection. *Minerva Medica*, 112(2), 238–245.

Terrault, N. A., Lok, A. S. F., McMahon, B. J., Chang, K.-M., Hwang, J. P., Jonas, M. M., Brown, R. S. Jr., Bzowej, N. H., and Wong, J. B. (2018). Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. *Hepatology*, 67(4), 1560–1599.

Wei, J., and Duan, S. (2021). Severe Guillain-Barré syndrome associated with chronic hepatitis B: A case report and literature review. *Medicine (Baltimore)*, 100(48), e27989.

Wijarnpreecha, K., Chesdachai, S., Jaruvongvanich, V., and Ungprasert, P. (2018). Hepatitis C virus infection and risk of Parkinson's disease: A systematic review and meta-analysis. *European Journal of Gastroenterology & Hepatology*, 30(1), 9–13.

Wu, W. Y.-Y., Kang, K.-H., Chen, S. L.-S., Chiu, S. Y.-H., Yen, A. M.-F., Fann, J. C-Y., Su, C.-W., Liu, H.-C., Lee, C.-Z., Fu, W.-M., Chen, H.-H., and Liou, H.-H. (2015). Hepatitis C virus infection: A risk factor for Parkinson's disease. *Journal of Viral Hepatitis*, 22(10), 784–791.

Zangeneh, M., Mesgarian, M., and Khosravani-Nezhad, Y. (2022). Association of acute hepatitis B and acute myopathy: A case report. *Journal of Medical Case Reports*, 16(1), 143.

Zanone, M. M., Marinucci, C., Ciancio, A., Cocito, D., Zardo, F., Spagone, E., Ferrero, B., Cerruti, C., Charrier, L., Cavallo, F., Saracco, G. M., and Porta, M. (2021). Peripheral neuropathy after viral eradication with direct-acting antivirals in chronic HCV hepatitis: A prospective study. *Liver International*, 41(11), 2611–2621.