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Original Research Article

TO EVALUATE THE CLINICAL AND ELECTROPHYSIOLOGICAL PATTERN OF PERIPHERAL NEUROPATHY IN HEPATITIS B AND HEPATITIS C

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ABSTRACT

Background: Hepatitis is the diffuse inflammation of liver resulting due to Hepatitis A,B,C,D and E out of which hepatitis B virus (HBV) and the hepatitis C virus (HCV) are the main culprits for serious liver illness like cirrhosis, hepatocellular carcinoma (HCC) and end-stage liver disease. Peripheral neuropathy is one of the common neurological conditions seen with HBV and HCV and may involve central nervous system and peripheral nervous system. Peripheral neuropathy is linked to chronic liver illness, and that the severity of the condition is correlated with an increased risk of peripheral neuropathy (PN). The viral particles may have direct neurotoxic effect on brain cells and indirect effect on the immune system. As per study by Yoihenba K in Manipur, 72% patients were found to have peripheral neuropathy, with sensory involvement being the most prevalent form of the condition and mainly involving lower limbs. For the purpose of determining the prevalence of peripheral neuropathy in patients infected with hepatitis C and hepatitis B, as well as evaluating the clinical and electrophysiological pattern of peripheral neuropathy in patients infected with HCV and HBV, a cross-sectional research was carried out.

Materials and Methods: This was a cross sectional study conducted in the Department of Medicine, Regional Institute of Medical Sciences, Imphal for from March 2023 to March 2025. All patients ≥18 years diagnosed with Hepatitis B and Hepatitis C infection who attended Medicine /Gastroenterology/ Neurology OPD and those admitted in medicine ward were recruited in the study. Routine blood investigations, viral markers, ultrasonography of whole abdomen and nerve conduction velocity study were done for every patient. SPSS (IBM) version 21 was used for statistical analysis. A P-value < 0.05 was considered as statistically significant.

Results: Among 113 study subjects enrolled in the study, hepatitis C infection was present in 51 patients and hepatitis B infection in 62 patients. Male predominance was seen (65.5%, 74), mostly belonging to the age range of 41 to 50 years old (35,31%) with the mean age ± SD of45 ±14.18 years. On clinical examination, 16.8 % (19) of the patients had neuropathic symptoms. Hepatitis B patients had 9.7% (6) sensory and 4.8%(3) motor impairment. While hepatitis C patients had 25.5% (13) sensory and 9.8% (5) motor impairment. On the other hand, peripheral neuropathy was seen in 21.2% (24)

patients in Nerve Conduction Study (NCS) with 16.1% (10) in hepatitis (Hep) B and 27.5% (14) in Hep C patients. Peripheral neuropathy was mostly of normal pattern in Hepatitis B (52,83.8%) and hepatitis C (37,72.6%) patients followed by sensory axonal in Hep B (6,9.7%) and Hep C (13,25.5%) and sensory motor axonal in Hep B (4,6.5%) and Hep C (1,1.9%). Peripheral neuropathy had significant correlation with age but not with gender.

Conclusion: The present study concluded that both Central nervous system and peripheral nervous system could be involved in Hep B and C infection. Their involvement is often underestimated by clinical examinations alone. Clinically, 16.8% patients were having PN, which increased to 21.2% after NCV. Sensory impairment was more than motor involvement in both Hep B and C infection.The likelihood of peripheral neuropathy being experienced by those who were of a more advanced age was higher. Therefore, it is vital to do regular screenings for neurological abnormalities especially PN in patients with chronic hepatitis B and hepatitis C.

Keywords: Hepatitis B, hepatitis C, peripheral neuropathy, pattern, nerve conduction study, motor, sensory, sensory axonal, sensory motor axonal.

INTRODUCTION

The most common clinical condition in the field of hepatology is Hepatitis, an inflammatory disease of the liver caused by viruses. Hepatitis A virus, B virus, C virus, D virus, E virus and hepatitis G virus are the viruses that are responsible for hepatitis.[1] Both the hepatitis B virus (HBV) and the hepatitis C virus (HCV) are among the most prevalent causes of serious liver illness, also contributing to Hepatocellular carcinoma (HCC) and end-stage liver disease. Peripheral neuropathy is one of the common neurological conditions seen in clinical settings of Hepatitis B and C.[2] In the majority of Asian and African areas, the combined prevalence of HBV and HCV infection was>50%. Globally, Hepatitis B was present in 42% and hepatitis C was seen in 21 percent of the patients with liver cirrhosis.[3]

In viral hepatitis, there can be variety of neurological abnormalities involving brain, spinal cord and the peripheral nervous system. Both the direct neurotoxic impact of viral particles on brain cells and the indirect effect created by the influence of viruses on the immune system.[4,5] Peripheral neuropathy, which is one of the extrahepatic manifestations of chronic viral hepatitis can manifest in the form of numbness, burning, pins and needles sensations, crawling skin, and itching, etc. Hands and feet are commonly affected though it may involve other areas of body.[1]Mononeuritis multiplex and pure sensory axonopathy are the clinical manifestations of involvement of central nervous system. Painful asymmetric paresthesia is the most prevalent symptom of a distal sensory or sensory-motor polyneuropathy, which is the most common kind of polyneuropathy though multiple mononeuropathy can rarely occur.[6] In most cases, neuropathies that are developed as a consequence of HCV are associated with mixed cryoglobulinemia.[1] Polyneuropathy are common in those tested positive for cryoglobulin and either mononeuropathy or multiple neuropathy are usually seen in patients tested negative for cryoglobulin.[7]

The state of Manipur has a relatively high number of persons who inject drugs than any other state in the country and is susceptible to drug trafficking, contributing to the transmission of HBV and HCV infections.[1]Direct or indirect repercussions of HCV infection have been postulated as possible contributors to the pathogenesis of nerve damage. Inflammatory vascular lesions and axonal degeneration have been identified in sural nerve biopsy operations carried out on HCV patients with and without mixed cryoglobulinaemia and the role of ischemia process rather than a direct role of the virus were also postulated.[8]In order to better understand the features of peripheral neuropathy in people who have hepatitis B and hepatitis C infection, this study was conducted to determine the extent of peripheral neuropathy and study the various spectrum of peripheral neuropathy.

MATERIALS AND METHODS

This was a Hospital based cross sectional study conducted in the Department of Medicine, Regional Institute of Medical Sciences, Imphal for a period of 2 years from March 2023 to March 2025. Patients aged 18 years and above attending Medicine OPD, Gastroenterology OPD or Neurology OPD and who were admitted under medicine ward were enrolled.

Inclusion Criteria: Patients aged 18 years and above diagnosed with Hepatitis B and Hepatitis C infection and those giving consent for the study were included.

Exclusion Criteria: HIV co-infected patients, patients with diabetes, chronic renal disease chronic alcoholic liver disease and those not willing to participate were excluded.

Sample size: In a study conducted by Cacoub Pet al,[6] on extrahepatic manifestation, associated with Hepatitis C virus infection, proportion of peripheral neuropathy on Hep C patients was found to be 9% and a study conducted by Garg Pet al,[9]on

proportion of peripheral neuropathy was reported to be 11.1% in HBV patients. Sample size, N =1.962PQ/L2

For Hepatitis C, P = Taking proportion of the patients having peripheral neuropathy among Hepatitis C as 9%. Data taken from a study conducted by Cacoub Pet al,[6] Precision (L) = 8% , Alpha = 1.96. Therefore, N = 51

For Hepatitis B, P = Taking proportion of the patients having peripheral neuropathy among Hepatitis B as 11.1%. Data taken from a study conducted by Garg Pet al,[9]Precision (L) = 8% , Alpha = 1.96. Therefore, N = 62. Thus total sample for the study was 51+62 = 113.

Study variables: Socio-demographic characteristics like age, sex, religion, symptoms, HBsAg, Anti HCV Antibody, etc. were the independent variables. Outcome variables were peripheral neuropathy, nerve conduction study, etc.

Study tools:

Hepatitis C serology was performed with Flaviscreen method,

Hepatitis B serology conducted by Viruschek rapid test,

HIV I & II serology done by Retrogine HIV kit

PCR test for HBV DNA and HCV RNA

Ultrasound Whole Abdomen- Sono Ace X S

Nerve conduction study machine was EMG/EP Measuring System Model. Manufacturer – Natus Neurology Incorporate.Model number – C200922123 (USA)

Operational definition:

Nerve conduction study

Amplitude: The measured difference between the negative and positive peaks or the height of the negative peak relative to the baseline

Distal Latency: The time taken for an impulse in moving from the stimulation location to the recording electrode, expressed in milliseconds.

Conduction velocity can be computed by taking the distance in millimeters (d) between the stimulation site and the recording site, then subtracting the distal latency from the proximal latency.Distal latency means time taken by distal stimulus to reach recording site.

Proximal latency means the time taken by proximal stimulus to reach recording site.

Motor conduction velocity =d/(proximal latency – distal latency)

Signs of peripheral neuropathy

A distal loss of pin, temperature, and vibratory awareness, in addition to a loss of proprioception, are all symptoms that are associated with sensory disruption. In majority of the patients, the first symptoms are only present in the feet and toes. A Romberg sign that is positive is usually seen as a result of a loss of proprioceptive function in the lower extremities.

One of the indications of motor dysfunction is distal weakness, where distal muscles will be atrophic. It is common for the muscle tone to be flaccid and decreased.

Muscle stretch reflexes cease to function and the majority of people who suffer from peripheral neuropathy do not exhibit ankle jerks, which is one of the first symptoms of the condition.

Peripheral neuropathy on Nerve conduction study: Defined as Prolonged Distal Latency, reduced Conduction Velocity, reduction of Amplitude. Prolonged Distal Latency and reduced Conduction Velocity is seen in Demyelination type and reduction of Amplitude is seen in Axonal type.[9] Interpretations for NCV for motor and sensory impairment for upper and lower limbs were given in table 1-4.

Table 1: Nerve conduction velocity intepretation for motor impairment for upper limbs

UPPER LIMBS			
NERVE	**AMPLITUDE**	**LATENCY**	**CONDUCTION VELOCITY**
MEDIAN	>4 mV	<4.0ms	>50
ULNAR	>6 mV	<3.5ms	>50

Table 2: Nerve conduction velocity for motor impairment for lower limbs

LOWER LIMBS			
NERVE	**AMPLITUDE**	**LATENCY**	**CONDUCTION VELOCITY**
TIBIAL	>4 mV	<6.0ms	>40
PERONEAL	>3 mV	<6.0ms	>40

Table 3: Nerve conduction velocity intepretation for sensory impairment for upper limbs

UPPER LIMBS			
NERVE	**AMPLITUDE**	**LATENCY**	**CONDUCTION VELOCITY**
MEDIAN	>20 mV	<3.5ms	>50
ULNAR	>20 mV	<3.2ms	>50

Table 4: Nerve conduction velocity for sensory impairment for lower limbs

LOWERLIMBS			
NERVE	**AMPLITUDE**	**LATENCY**	**CONDUCTION VELOCITY**
SURAL	>6 mV	<4.4ms	>40

Study procedure: A well design proforma was used which included socio-demographic information, the comprehensive clinical history of the patients, the general physical examination, the typical hematological and radiological examinations, and any other pertinent information was included. Nerve conduction study was done for every patient.

Statistical analysis: For statistical analysis, SPSS (IBM) version 21 was used. Mean, standard deviation and percentages were used for summarizations of data. For association between age group and peripheral neuropathy, Chi-square test and Fisher's exact test were used. Independent-t test was employed to test the association of mean age with peripheral neuropathy. P-value < 0.05 was taken as statistically significant.

Approval of research ethics board: Ethical approval for this study was obtained from the Research Ethics Board, Regional Institute of Medical Sciences, Imphal [No.A/206/REB-Comm(SP)/RIMS/2015/1008/39/2023].

RESULTS

A total of 113 individuals participated in the research, including 45% (51) patients with hepatitis C infection and 62(55%) patients with hepatitis B infection. The baseline characteristics of the study subjects were given in table 5. Majority of the study subjects were males 65.5% (74) and rest 35.5% (39) were females. Most of the patients belonged to the age range of 41 to 50 years old (35, 31%) and the mean age + SD was 45 +14.18 years. The most common symptom of the patients were nausea (61, 54%) followed by easy tiredness (60, 53.1%), myalgia (57, 50.4%), vomiting (48, 42.5%), fever (45,39.8%) and anorexia (36,31.9%). Neuropathic symptoms were seen in 16.8 percent (19) of the patients during the clinical assessment. Sensory and motor PN was shown in table 6.Sensory impairment was seen in 9.7% (6) of hepatitis B and 25.5% (13) of hepatitis C. A discernible impairment of motor function was seen in 4.8% (3) of hepatitis B and 9.8% (5) of hepatitis C patients. In Nerve Conduction Study (NCS), peripheral neuropathy was seen in 21.2% (24) of the participants. Peripheral neuropathy was observed in 16.1% (10) of hepatitis B and 27.5% (14) of Hep C patients. Majority of the patients have normal pattern of peripheral neuropathy in Hepatitis B(52,83.8%) and hepatitis C (37,72.6%) patients followed by sensory axonal in Hep B (6,9.7%) and Hep C (13,25.5%) and sensory motor axonal in Hep B (4,6.5%) and Hep C (1,1.9%), as shown in table 7. The correlation of peripheral neuropathy with age is significant while it was not statistically significant for gender (as given in tables 8 & 9).

Table 5: Baseline characteristics of the study subjects (N = 113)

Characteristics	Study subjects (n, %)
Age (in years)	
18-30	17(15%)
31-40	28(24.8%)
41-50	35(31%)
51-60	14(12.4%)
>60	19(16.8%)
Gender	
Male	74(65.5%)
Female	39(35.5%)
Religion	
Hinduism	81(71.7%)
Christian	18(15.9%)
Muslim	14(12.4%)
Signs & Symptoms	
Anorexia	36(31.9%)
Nausea	61(54%)
Vomiting	48(42.5%)
Fever	45(39.8%)
Myalgia	57(50.4%)
Easy fatique	60(53.1%)
Peripheral neuropathy	
Clinical	19(16.8%)
NCV	24(21.2%)
Type of infection	
Hepatitis B	62(55%)
Hepatitis C	51(45%)
Peripheral neuropathy	
Hepatitis B	10(16.1%)
Hepatitis C	14(27.5%)

Table 6: Types of peripheral neuropathy in Hepatitis patients (N=113)

Sl.no.	Neuropathy	Hepatitis B(N =62) (n , %)	Hepatitis C(N =51) (n , %)
1.	Sensory impairment	6(9.7%)	13(25.5%)
2.	Motor impairment	3(4.8%)	5(9.8%)

Table 7: Pattern of peripheral neuropathy in Hepatitis B and C patients (N=113)

Sl.no.	Neuropathy	Hepatitis B(N =62) (n , %)	Hepatitis C(N =51) (n , %)
1.	Sensory axonal	6 (9.7%)	13 (25.5%)
2.	Sensory motor axonal	4(6.5%)	1(1.9%)
3.	Normal study	52(83.8%)	37(72.6%)

Table 8: Association between mean age and peripheral neuropathy (N=113)

Sl.no.	NCS Peripheral neuropathy	Age in years,		P value
		Mean	Standard deviation	
1.	Yes	62.13	10.16	< 0.001
2.	No	40.38	11.30	

Table 9: Association between peripheral neuropathy and gender (N=113)

Sl.no.	Gender	Peripheral neuropathy, n(%)		P value
		Yes	No	
1.	Male	16 (21.6)	58 (78.4)	0.547
2.	Female	8 (20.5)	31 (79.5)	

DISCUSSION

Viral hepatitis C causes a chronic persistent infection in the majority of people, that is accompanied by complex immune responses. This infection may induce neurological disorder either by direct infection of brain cells or via immune-mediated processes, such as the amplification of autoimmune reactions. Consequently, neurologists are increasingly faced with the task of identifying or predicting various neurological issues that may emerge due to or as a consequence of treatment for hepatitis virus infection.[1] In this study, a total of 113 patients were included in the study with 51 Hepatitis C infection patients and 62 hepatitis B infection patient. Majority of the patients were male (74, 65.5%) followed by females (39, 35.5%) in this study, which was consistent with the studies done by Yoihenba K et al,[1] (83.9% males), Mapoure NY et al,[10] (51.2% males) and Abbas SY et al,[11] (61% males). In this study, both hepatitis B patients and hepatitis C patients had male population more than the female patients.

In the current study, the age group of 41 – 50 years has the maximum patients (35,31%) followed by 31-40 years (28,24.8%) in both hepatitis B patients and hepatitis C patients, Whereas only 16.8% of the study population were above 60 years of age in this study. In this study, the mean age of the patients was found to be 45 ± 14.18 years, which,was similar to the study conducted by Yoihenba K et al,[1] (mean age of 42.5 ± 7.39 years) in hepatitis C patients and Santoro L et al[8] (mean age of 52.3+13.7) years.

In the present study, majority of the patients were Hindu (81, 71.7%) followed by Christian (18, 15.9%) and Muslim (12.4%, 14). This may be due to the fact that majority of the population in the catchment area of this hospital is Hindu. In the present study, the most common symptoms at the time of presentation were nausea (61, 54%) and easy fatigue (60, 53.1%) followed by myalgia (57, 50.4%) and vomiting (48, 42.5%). Fever (45, 39.8%) and anorexia (36, 31.9%) were also present in this study, which were much higher than the study done by Garg P et al,[9] (30 % patients had myalgia 14 % had fatigability , 22% had nausea and 18 % had vomiting).

On clinical examination, peripheral neuropathy was evident in (19, 16.8%) of the total patients in this study, which was more than the studies done by Cacoub P et al,[6] (9%) and Santoro L et al,[8] (10.6%). While Mapoure NY et al,[10] reported a higher incidence of 50.4% peripheral neuropathy with the main form being sensory neuropathy (96.6%).

In the current study, Nerve Conduction Study (NCS) was done in all the patients and peripheral neuropathy was present in 21.2%(24) of the total patients, 16.1%(10) in hepatitis B patients and 27.5%(14) in hepatitis C, which was comparable to the study done by Polukchi TV et al,[12] (Hep B - 17% and Hep C - 22.6%) and Cuciureanu T et al,[13](HCV -27.3%). Yoihenba K et al,[1] reported a higher prevalence of 74.2% peripheral neuropathy among their study population.

In the present study, among 62 patients of hepatitis B, sensory impairment was seen in 9.7% (6) and motor impairment in 4.8% (3) patients. While among 51 hepatitis C patients, 25.5% (13) patients had sensory impairment and 9.8% (5) patients had encountered motor impairment. Majority of the sensory impairment was paraesthesia and most common motor impairment was hypoactive ankle jerk reflex in this study. Comparable findings were reported by Kharbanda PS et al,[14] (clinical peripheral neuropathy in 21% out of which 12% had sensory impairment and 6.1% had motor weakness, ankle jerk was absent or impaired in 15.1% patients) and Garg P et al [9] (clinical signs of sensory peripheral neuropathy in 5% in HBV and 23.1% in HCV patients and 2.7% HBV patients and 7.6% HCV patients had motor impairment). Khalek MA et al,[15] did electrophysiological examination in all of their study population and unveiled 18 subclinical PN and found a total of 67.5% of their patient with peripheral neuropathy on NCV. Thus majority of the

studies reported a varying prevalence of peripheral neuropathy ranging from 9% to 74%. These variations in results from different studies may be due to differences in patient selection or variation in the criteria used for the definition of neuropathy. Although in this study no relation was observed between peripheral neuropathy and gender. Age on the other hand was found to be significantly associated with peripheral neuropathy in this study. The mean age of patients with peripheral neuropathy was substantially higher than that of individuals without peripheral neuropathy. It was shown that the severity of chronic liver disease grade is connected with an increased prevalence of peripheral neuropathy. Additionally, the advanced age group and male gender were found to be associated with higher neuropathy.[16]

In this study, on NCV test, sensory axonal neuropathy was seen in 9.7%(6) and sensory motor axonal in 6.5%(4) of the hepatitis B infected patients. But sensory axonal neuropathy was seen in 25.5% (13) and sensory motor axonal in 1.9%(1) of the hepatitis C infected patients. Yoihenba K et al,[1] studied hepatitis C infected patients and reported, sensory axonal neuropathy to be present in 35.5% of the patients and sensory motor axonal neuropathy in 32.3% of their patients which is higher than this study finding. Clinical evaluations alone have a tendency to underestimate the involvement of PNS in the general population of HCV patients. According to England JD et al,[17] polyneuropathy is characterized by the presence of various symptoms, signsand abnormal electro diagnostic investigations. On the other hand, symptoms alone have a rather low diagnostic accuracy when it comes to predicting the existence of polyneuropathy.

CONCLUSION

In the present study, infection with hepatitis B virus and hepatitis C virus was shown to be substantially more prevalent among men and mostly presenting during the middle years of their lives with main symptoms of nausea, fatigue, and myalgia. The NCV test has increased the diagnostic accuracy of peripheral neuropathy to 21.2% from 16.8% of the patients diagnosed on the basis of clinical assessment. On NCV, Pure Sensory Axonal and Sensory Motor Axonal type of peripheral neuropathy were predominant forms of neuropathy seen, more in advanced age. Therefore, it is vital to do routine screenings for peripheral neuropathy in patients who have chronic hepatitis B and C.

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