



## Original Article

## Frequency of Peripheral Neuropathy in Chronic Hepatitis C Patients Presenting at Liaquat University Hospital, Hyderabad

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## ABSTRACT

Hepatitis C virus (HCV) and its infective pathogenic role leads to the psychiatric and neurological signs and symptoms. Therefore, close monitoring and regular follow-up is warranted.

**Objective:** To find out the frequency of peripheral neuropathy among patients presenting at Liaquat University Hospital, Hyderabad, having Chronic Hepatitis C. **Methods:** The cross-sectional study included 359 patients with chronic HCV, aged 20 to 70 years, who presented to the Liaquat University Hospital's Hepatitis Clinic and Outpatient Department of General Medicine and Neurology. Non-probability - sequential sampling was used to choose patients. Patients were asked about demographic information and the duration of chronic HCV after giving informed written consent. The clinical examination was performed to see if there were any reduced tendon reflexes in all of the patient's extremities. To diagnose peripheral neuropathy based on nerve conduction velocity, all patients had an electrophysiological test using a simplified nerve conduction study (NCS) methodology (NCV). The research lasted six months, from June 2021 to December 2021. The information was examined via SPSS version 25.0. **Results:** There were 219 Men (61%) And 140 Females (39%) among the 359 Patients. The average age (SD) of the participants was 42.3 (8.7) years (range 22-70). HCV infection lasted 36 months on average (range 1-156). Out of 359 patients, 61 had clinical peripheral neuropathy (PN) (17%). Electrophysiological evidence of PN was present in all of these patients, electrophysiological investigation revealed subclinical PN in 19 more patients (5.3%). **Conclusion:** On the basis of the findings from this study, it can be concluded that a high prevalence of peripheral neuropathy is present among the patients with HCV in our locality. However, an electrophysiological examination should always be done to avoid underestimating PN, particularly in older HCV patients.

## INTRODUCTION

HCV infection accounts for up to 3% of global population. It is one of the major health related problem being faced by Pakistan [1]. Nearly 50-80% of individuals infected with HCV leads to chronic hepatitis, 20% of patients develop cirrhosis and 1-4% develop hepatocellular carcinoma (HCC). It is extensively prevalent around the globe and is leading cause of liver cirrhosis requiring liver transplantation [2]. However, disease burden varies among different countries being more among developing countries with low health and education standards [3]. HCV infection has hepatic and extrahepatic manifestation. It

involves the blood (mixed cryo-globulinaemia and porphyria cutanea tarda) lymphoid tissue (lymphoproliferation), kidney (membrano-proliferative glomerulonephritis), sicca syndrome, thyroid gland (thyroiditis and thyroid dysfunction) and nervous system (myopathy, mono and multiple mononeuritis and, sensory-motor polyneuropathy) [4]. HCV replicates and forms cold-precipitating immunoglobulins. These immunoglobulins form complexes which bypass the reticuloendothelial clearance mechanism and aggregate in the body in the form cryoglobulins. They deposit in various tissue of the

body inducing inflammatory response leading to tissue damage [5,7]. The pathogenesis involves damage of the endothelial cells by these complexes, eliciting inflammation of small and medium vessels and accumulation of perivascular mononuclear cells [8]. Therefore, neuropathy is attributed to multifactorial factors related to inflammation, direct HCV related damage and immune complex mediated damage [9]. Patients can present with clinical spectrum of features having symmetrical or asymmetrical presentation. They can be sensory, motor or mixed sensorimotor types. The patients usually present with paresthesia, weakness and gait difficulties [10,11]. Physicians caring for the patients HCV related chronic liver disease should always monitor them for its neurological manifestation [12]. As they may interfere or exacerbate with the HCV treatment, contributing to morbidity and poor health related quality of life [13,14]. Mapoure et al., found the incidence of neuropathy of peripheral nerves in people with positive HCV and found it to be 50.4% [15]. Thus, this study aimed to find out the prevalence of peripheral neuropathy among patients presenting at Liaquat University Hospital, Hyderabad, having Chronic HCV.

## METHODS

The cross-sectional study was conducted upon a sample of 359 patients having chronic HCV patients of either gender with aged between 20-70 years, presenting to Hepatitis Clinic and OPD of General Medicine and Neurology, at Liaquat University Hospital, Hyderabad. (The sample size was calculated via WHO open-epi calculator, by taking the margin of error as 5%, confidence interval as 95% and frequency of peripheral neuropathy in patient with HCV patients as 37%) [16]. Patients were chosen via non-probability - consecutive sampling. Patients with history of Diabetes Mellitus type II or Leprosy, Hypo or Hyperthyroidism, Acute or Chronic Demyelinating Neuropathy, Venous Thromboembolism, Fracture of Lower Limb, Vasculitis and Connective Tissue Disorder, Alcohol Use, Vitamin B 12 Deficiency and patient receiving Chemotherapy or having any other significant comorbidities like Stroke, COPD, Asthma, Myocardial Infarction, and Chronic Renal Failure were excluded from the study. After taking informed written consent, patients were inquired about demographic data, clinical history and duration of chronic HCV. Severity of Chronic HCV was measured through Child-Pugh Classification. Anthropometric and Clinical Examination were done to assess diminished tendon reflexes in all extremities. To diagnose peripheral neuropathy based on Nerve Conduction Velocity, all patients received an

electrophysiological test using a simplified nerve conduction study (NCS) methodology (NCV). The research lasted six months, from June 2021 to December 2021. SPSS 25.0 was used to analyze the data.

## RESULTS

Out of 359 patients, 219 (61%) were males and 140 (39%) were females. Mean age (SD) was 42.3 (8.7) years (range 22-70). Median duration of HCV infection was 36 months (range 1-156). Clinical peripheral neuropathy PN was diagnosed in 61 out of 359 patients (17%). All these patients had electrophysiological evidence of PN. Moreover, electrophysiological examination disclosed a subclinical PN in 19 additional patients (5.3%). An axonal sensory-motor polyneuropathy and mononeuropathy multiplex was diagnosed in (19/61) (31.1%) and (17/42) patients (68.9%), respectively. No electrophysiological signs of demyelination or cranial nerve involvement was found. The median HCV RNA level in the blood was 1.8 million of copies/ml (range 1800-42 000 000). No correlation was found between HCV-RNA levels and the presence of PN (Pearson  $\chi^2$ , 0.9;  $p = NS$ ). The main demographic, clinical, and laboratory features of patients with and without electro-physiologically defined PN" are shown in table 1.

Variable	Neuropathy			
	Yes		No	
	n	%	n	%
Total	61	17	298	87
Men	37	17	182	83
Women	24	17.15	116	82.85
<45	5	3.9	123	96.1
45-54	9	12.8	61	87.2
55-64	26	32.5	54	67.5
>65	21	30.4	48	69.6
<12	16	10.5	136	89.5
12-60	18	19	77	81
>60	27	24.1	85	75.9

**Table 1:** Characteristics of patients

## DISCUSSION

The current study aimed to "find out the prevalence of peripheral neuropathy among patients presenting to the study setting. The prevalence of electrophysiological PN in this population was 17%. Firstly, only 36 patients were clinically and electrophysiologically investigated and PN was detected in 8% of them [17] in the other large prospective study, Cacoub and colleagues diagnosed a peripheral neuropathy in 9% of 321 HCV patients on the

basis of clinical symptoms only. The prevalence of PN in our study (10.6%), if based on clinical assessment only, is very close to that of Cacoub and colleagues [18]. However, the electrophysiological examination revealed a subclinical neuropathy in 19 additional patients (5.3%). Therefore, pure clinical assessment tends to underestimate peripheral nervous system involvement in the HCV general population. As pointed out by England and colleagues [19], polyneuropathy occurs with a combination of multiple symptoms, signs, and abnormal electrodiagnostic studies, whereas symptoms alone have relatively poor diagnostic accuracy in predicting the presence of polyneuropathy. According to these criteria, PN could not be confirmed in all the patients complaining of pain, burning paresthesiae and fatigue in the absence of electrophysiological abnormalities. On the other hand, these symptoms are frequently described in HCV patients and they can be due to non-neurological (for example, rheumatological) causes or to a small fiber neuropathy [20]. A small fiber neuropathy could not be ruled out in our patients either by clinical examination or by conventional nerve conduction studies, but this was not an aim of the present study. Different mechanisms unrelated to the presence of PN, but possibly due to the direct or indirect effects of HCV infection, have been largely proposed in the pathogenesis of nerve damage [21-23]. Inflammatory vascular lesions and axonal degeneration, supporting an ischemic mechanism of nerve damage more than a direct role of the virus in HCV related PN, have been described in sural nerve biopsy of HCV patients. Under this assumption, the lack of correlation between type of PN and HCV duration is also in keeping with the current hypothesis that HCV related vascular nerve damage could be due to virus triggered immune mediated mechanisms [23]. Statistical analysis showed a strong correlation between older age and PN but not between PN and the known duration of HCV positivity. In keeping with these data, we found a strong correlation between older age and both PN and CG, which may be interpreted in the light of the emerging hypothesis of an immune mediated pathological mechanism of HCV related clinical manifestations [23]. At first sight, this latter observation might seem contradictory but the duration of HCV positivity was assessed from the first laboratory detection of HCV infection and it is likely different from the true duration of HCV infection, which might have actually occurred several years earlier. Some authors have already noted that older age is a major risk factor for the clinical and biological extrahepatic manifestations of HCV [20-24]. The study has several limitations. Firstly, although we elected to enroll consecutive patients which predisposes to selection bias towards more severe infection and

patients with neurological complications, this is not a population-based study. For this reason, our findings cannot be extended to HCV patients who do not seek care in secondary and tertiary centers. Although there were no significant differences between patients tested and not tested, we cannot exclude that their physicians decided to test patients at higher risk for PN.

## CONCLUSION

On the basis of the findings of this study, it can be stated that patients with HCV in the studied area have a significant prevalence of peripheral neuropathy. However, especially in older HCV patients, an electrophysiological evaluation should always be performed to prevent underestimating PN.

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