



## Original Article



## Demographic and Clinical Factors Influencing the Peripheral Neuropathy in Anti-HCV Positive Patients

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## ABSTRACT

Peripheral neuropathy is a common complication affecting individuals with various underlying conditions, often influenced by factors such as age, gender, and disease duration. **Objectives:** To assess the prevalence of peripheral neuropathy by age, gender, and disease duration. **Methods:** It was a cross-sectional descriptive study conducted at the Neurology Department of Jinnah Postgraduate Medical Centre, from March 20, 2021, to September 19, 2021. The total number of patients was 164. The study enrolled patients aged 18-60 of either gender who had peripheral neuropathy. Patients with hepatitis other than hepatitis C, who received treatment for HCV, patients having diabetes mellitus, autoimmune disorder, kidney failure, vitamin B deficiency, thyroid disorders, hematological disorders, alcoholism, HIV infection, drug addiction or toxic agents were excluded. A questionnaire-based study was designed for the collection of data regarding demographics and clinical aspects. **Results:** The mean age of the study patients was  $42.7 \pm 18.2$  years. Peripheral neuropathy was found in 98 (59.8%) participants. Among 164 patients, 94 (57.3%) were male, while 70 (46.4%) were female. Diabetes mellitus and hypertension were documented in 63 (38.4%) and 85 (51.8%), respectively. **Conclusions:** It was concluded that gender is statistically significantly associated with the prevalence of peripheral neuropathy in anti-HCV positive patients, while a higher body mass index and extended duration of infection were also associated with peripheral neuropathy, but were not statistically significant.

## INTRODUCTION

Hepatitis C virus (HCV) infection continues to pose a significant global health challenge, with an estimated 58 million people living with chronic HCV worldwide as of 2022 [1]. Despite advancements in antiviral therapies, HCV remains a leading cause of liver-related morbidity and mortality. Beyond hepatic complications, HCV is associated with various extrahepatic manifestations, notably peripheral neuropathy, which significantly impacts patients' quality of life [2]. Peripheral neuropathy in HCV-infected individuals often presents as symmetrical axonal sensorimotor neuropathy, distal symmetric painful small-fiber neuropathy, mononeuritis multiplex, or, less commonly, demyelinating and autonomic neuropathies [3]. The prevalence of peripheral neuropathy among HCV

patients varies, with studies reporting rates ranging from 8% to 23% [4]. The pathogenesis is multifactorial, involving direct viral invasion, immune-mediated mechanisms, and neurotoxic effects of cryoglobulins. Hepatitis C virus (HCV) infection poses a significant public health challenge in Pakistan, where an estimated 9.8 million people are affected, marking a global peak prevalence rate of 7.5% [5]. The infection rate differs regionally, with Baluchistan showing the highest prevalence at 25.77%, followed by Khyber Pakhtunkhwa (6.07%), Punjab (5.46%), the Federally Administered Tribal Areas (3.37%), and Sindh (2.55%) [6]. This widespread transmission is largely attributed to poor healthcare practices, including the reuse of injection needles, insufficient sterilization protocols, and



transfusion of unscreened blood [7]. Among those infected with HCV, several demographic and clinical variables influence the likelihood of developing peripheral neuropathy. Advanced age and male sex have been linked to greater vulnerability [8], while coexisting conditions such as diabetes, kidney dysfunction, and high blood pressure further intensify neuropathic symptoms [9]. Additionally, mixed cryoglobulinemia notably raises neuropathy risk due to the deposition of immune complexes in nerve tissues [10]. The advent of direct-acting antivirals (DAAs) has revolutionized HCV treatment, achieving sustained virological response rates exceeding 95%. However, the impact of viral eradication on extrahepatic manifestations like peripheral neuropathy remains under investigation. Some studies suggest partial or complete resolution of neuropathic symptoms post-treatment, while others report persistent or even worsening symptoms, indicating possible irreversible nerve damage or ongoing immune-mediated processes [11, 12]. A prospective study involving 94 HCV-infected patients without systemic and metabolic diseases found that 23% had sensory-motor neuropathy at baseline. After DAA therapy, nerve amplitude parameters tended to improve, with a significant reduction in neuropathic pain and improved quality of life [10]. Another study reported that among 40 HCV-infected individuals, 22.5% exhibited signs of polyneuropathy. Post-treatment, some patients showed improvement in nerve conduction studies, suggesting potential reversibility of neuropathy after HCV eradication [3]. Understanding the demographic and clinical factors influencing peripheral neuropathy in anti-HCV-positive patients is crucial for early identification, prevention, and management of this debilitating complication. Comprehensive care strategies should include regular neurological assessments, especially for high-risk populations, and prompt initiation of antiviral therapy to mitigate the progression of neuropathic damage.

This study aimed to assess the prevalence of peripheral neuropathy by age, gender, and disease duration.

## METHODS

This descriptive cross-sectional study was conducted in the Department of Neurology at Jinnah Postgraduate Medical Centre (JPMC), Karachi, from March 20 2021, to September 19, 2021. A total of 164 patients were enrolled in the study. The sample size was calculated using the Open Epi sample size calculator, considering a previously reported prevalence of peripheral neuropathy in anti-HCV positive patients of 70.3% [13], with a 95% confidence interval and a 7% margin of error. Patients aged between 18 and 60 years, of either gender, with a confirmed diagnosis of hepatitis C virus (HCV) infection, were included in the study. HCV infection was confirmed through the patient's available medical records. A non-probability convenience

sampling technique was used to recruit participants from neurology outpatient and inpatient units. Informed written consent was taken from each participant before enrollment in the study. The study was approved by the College of Physicians and Surgeons, Pakistan via Letter No. CPSP/REU/NEU-2017-186-460. Exclusion criteria included individuals with viral hepatitis other than HCV, those who had previously received treatment for HCV, or those with coexisting diabetes mellitus, autoimmune disorders, nephropathy, thyroid dysfunction, hematological disorders, HIV infection, a history of alcoholism, drug addiction, or exposure to known neurotoxic agents. These conditions were excluded to reduce confounding factors that could independently contribute to peripheral neuropathy. Peripheral neuropathy was diagnosed based on a combination of self-reported symptoms, clinical neurological examination, and Nerve Conduction Studies (NCS). Symptoms included numbness, tingling, burning sensations, pins-and-needles, or a cold sensation in the extremities. All participants underwent a comprehensive neurological assessment by a resident neurologist, including testing for deep tendon reflexes, vibration sense, pin-prick sensation, temperature, and proprioception. Nerve Conduction Studies (NCS), as the gold standard for diagnosing peripheral neuropathy, were performed on all participants using standard protocols to assess motor and sensory nerve conduction velocities, amplitudes, and distal latencies. A structured questionnaire was administered by trained data collectors to gather information on demographic characteristics (age, gender, occupation, and residence) and clinical history (duration of HCV infection, comorbidities, and current symptoms). Data were entered and analyzed using the Statistical Package for Social Sciences (SPSS) version 21.0. Descriptive statistics, including means and standard deviations, were computed for continuous variables, while frequencies and percentages were calculated for categorical variables. Chi-square tests were applied to evaluate associations between demographic variables (age, gender) and the presence of peripheral neuropathy. A p-value  $\leq 0.05$  was considered statistically significant.

## RESULTS

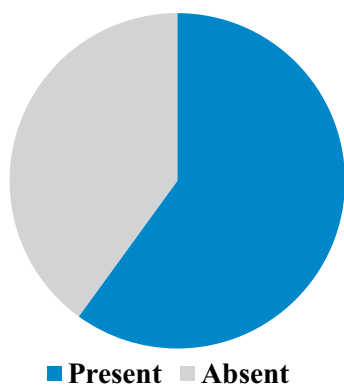
The demographic characteristics of the study population revealed a mean age of  $42.7 \pm 18.2$  years, indicating that the cohort predominantly comprised middle-aged individuals. Among the 164 participants, 94 (57.3%) were male and 70 (42.6%) were female, suggesting a slight male predominance. The majority of the patients were married (58.5%), while 41.5% were unmarried. In terms of educational status, 54.8% of participants were educated, whereas 45.1% had no formal education. The duration of disease ranged from 6 to 12 months, with a mean duration of  $10.2 \pm 4.1$  months, reflecting a subacute to chronic phase of illness at the time of evaluation (Table 1).

**Table 1:** Demographic Characteristics of Study Participants

Variables	n (%)
<b>Age</b>	
Mean $\pm$ SD	42.7 $\pm$ 18.2 years
<b>Gender Distribution</b>	
Male	94 (57.3%)
Female	70 (46.4%)
<b>Marital Status</b>	
Married	96 (58.5%)
Unmarried	68 (41.5%)
<b>Educational Status</b>	
Educated	90 (54.8%)
Uneducated	74 (45.1%)
<b>Duration of Disease (Months)</b>	
Minimum	6
Maximum	12
Mean $\pm$ SD	10.2 $\pm$ 4.1 (Months)

The prevalence of peripheral neuropathy among anti-HCV-positive patients was notably high, underscoring the significance of neurological complications in this population (Figure 1).

### Prevalence of Peripheral Neuropathy

**Figure 1:** Presence of Peripheral Neuropathy

Analysis of demographic factors revealed an increasing trend of peripheral neuropathy with advancing age, peaking in the 40–60 years' group; however, this was not statistically significant ( $p=0.082$ ). Gender showed a significant association ( $p=0.021$ ), with females having a higher proportion of neuropathy compared to males. BMI-wise, peripheral neuropathy was more prevalent in overweight and obese individuals, but this association did not reach statistical significance ( $p=0.312$ ) (Table 2).

**Table 2:** Relation of Demographic Factors with Peripheral Neuropathy

Variables	Peripheral Neuropathy		p-value
	Yes	No	
Age Group			
18–29	10 (6.1%)	14 (8.5%)	–
30–39	20 (12.2%)	20 (12.2%)	
40–49	34 (20.7%)	18 (11.0%)	

50-60	34 (20.7%)	14 (8.5%)	
Gender			
Male	49 (29.9%)	45 (27.4%)	-
Female	49 (29.9%)	21 (12.8%)	
BMI			
Underweight (<18.5)	6 (3.7%)	4 (2.4%)	-
Normal (18.5-24.9)	33 (20.1%)	39 (23.8%)	
Overweight (25.0-29.9)	40 (24.4%)	18 (11.0%)	
Obese (≥30.0)	19 (11.6%)	5 (3.0%)	

Clinical factors such as disease duration, diabetes mellitus, and hypertension were assessed for their association with peripheral neuropathy. A longer disease duration (>9 months) was more common among patients with neuropathy, but this association was not statistically significant ( $p=0.912$ ). Similarly, no significant relationship was observed between peripheral neuropathy and diabetes mellitus ( $p=0.860$ ) or hypertension ( $p=0.482$ ), possibly due to the exclusion of known diabetic patients and the multifactorial nature of neuropathy in HCV-positive individuals (Table 3).

**Table 3:** Relation of Clinical Factors with Peripheral Neuropathy

Variables	Peripheral Neuropathy		p-value
	Yes	No	
Duration of Disease (months)			
6-9	23 (14.0%)	15 (9.1%)	-
>9	75 (45.7%)	51 (31.1%)	
Diabetes Mellitus			
Present	39 (23.8%)	24 (14.6%)	-
Absent	59 (36.0%)	42 (25.6%)	
Hypertension			
Present	53 (32.3%)	32 (19.5%)	-
Absent	45 (27.4%)	34 (20.7%)	

## DISCUSSION

Peripheral neuropathy occurs when the nerves located outside of the brain and spinal cord are affected. This condition is often present with weakness, numbness, and pain, usually in the hands and feet. Hepatitis C presents with common neurological complications as peripheral neuropathy, spread by direct contact with infected blood through skin opening or the mucus membrane, sharing contaminated needles, and by sexual contact. Peripheral neuropathy is an extra-hepatic complication related to HCV through a vasculitis process caused by cryoglobulinemia. Age emerged as a significant factor, with an increasing trend of peripheral neuropathy observed in older age groups. This finding is consistent with earlier studies that have identified age as an independent predictor of peripheral neuropathy in HCV-infected individuals [14]. For instance, a multicenter study reported that the prevalence of peripheral neuropathy increased significantly with age, with an odds ratio (OR) of 1.10 for each additional year of age [15]. Similarly, a study conducted in

sub-Saharan Africa found that patients aged  $\geq 55$  years had a higher likelihood of developing peripheral neuropathy, with an adjusted odd ratio (AOR) of 6.25 [16]. Gender-based disparities were apparent in the prevalence of peripheral neuropathy, with a notably higher frequency among female than male. While certain investigations have not found statistically meaningful differences in neuropathy rates between genders in individuals with hepatitis C virus (HCV) infection [17], other research suggests that women may be more prone to developing neuropathic symptoms, possibly due to hormonal influences and immune system variations [10]. In terms of body mass index (BMI), although no statistically significant correlation was established in this analysis, a noticeable trend emerged, with overweight and obese participants experiencing higher rates of neuropathy. This observation supports previous studies indicating that elevated BMI might be linked to an increased likelihood of neurological issues among those with HCV [18]. Clinical characteristics such as the length of time since HCV diagnosis did not appear to influence the development of peripheral neuropathy in this group. This finding contrasts with prior studies suggesting that prolonged infection may elevate neuropathy risk [19]. The relatively brief average disease duration ( $10.2 \pm 4.1$  months) in the current study might account for this discrepancy. Additionally, common coexisting conditions like hypertension and diabetes mellitus showed no significant relationship with neuropathy, likely due to the deliberate exclusion of individuals with pre-existing diabetes, reducing potential bias. However, literature does emphasize that such comorbidities can heighten neurological complications in HCV patients [20]. Since cryoglobulinemia is often linked with HCV-induced neuropathy even in patients lacking overt symptoms, its exclusion may have prevented a full assessment of underlying immunologic mechanisms [21].

## CONCLUSIONS

It was concluded that gender is statistically significantly associated with the prevalence of peripheral neuropathy in anti-HCV-positive patients. Although a higher body mass index and extended duration of infection seemed to correspond with greater neuropathic involvement, these associations did not reach statistical significance within the scope of this study.

## Authors Contribution

Conceptualization: SHS

Methodology: SHS, MAL<sup>1</sup>, AHB, MAL<sup>2</sup>

Formal analysis: AHB

Writing review and editing: MAL<sup>1</sup>, AHB

All authors have read and agreed to the published version of the manuscript

## Conflicts of Interest

All the authors declare no conflict of interest.

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