Annals of Medicine and Medical Sciences (AMMS)
Volume 04, 2025, *Page No.: 1635 to 1639*
Available at: *http://ammspub.com*

Original Article

OPEN ACCESS

Unraveling the Burden of Chemotherapy-Induced Peripheral Neuropathy: A Prospective Clinical Insight from 50 Cancer Patients

Dr Zahoor Ahmad Paul [1], Dr Tavseef Ahmad Tali [2], Dr Mustafa Bashir [3], Dr Peerzada Ajaz Ahmad Shah [4], Dr Toufeeq Ahmed Teli *[5]

[1]Associate Professor, Department of Radiation Oncology, Government Medical College Baramulla, J&K, India.
[2]Assistant Professor, Department of Radiation Oncology, Government Medical College Baramulla, J&K, India.
[3]Senior Resident, Department of Internal Medicine, Government Medical College Baramulla, J&K, India.
[4]Assistant Professor, Department of Internal Medicine, Government Medical College Baramulla, J&K, India.
[5]Intern Resident, Department of Internal Medicine, Government Medical College Udhampur, J&K, India.

*Corresponding Author: Dr. Toufeeq Ahmed Teli; *toufeeqahmedteli@gmail.com*

Abstract

Background: Chemotherapy-induced peripheral neuropathy (CIPN) is a common, dose-limiting toxicity of neurotoxic chemotherapy that significantly impairs quality of life (QoL) and functional status. Despite its clinical relevance, data on real-world incidence, severity, and early recovery patterns remain limited. ***Objective:*** To prospectively evaluate the clinical spectrum, risk factors, treatment impact, and short-term reversibility of CIPN in cancer patients receiving neurotoxic chemotherapy. ***Methods:*** This 18-month prospective observational study enrolled 50 adult cancer patients undergoing treatment with known neurotoxic agents, including paclitaxel, oxaliplatin, docetaxel, cisplatin/carboplatin, and bortezomib. CIPN was assessed using NCI-CTCAE v5.0, and functional impact was measured via FACT/GOG-Ntx. Patients were evaluated at baseline, during chemotherapy, at treatment completion, and three months post-therapy. Associations between severe CIPN (Grade ≥2) and risk factors such as cumulative dose, age, and diabetes were analyzed. ***Results:*** The cohort had a mean age of 54.3 years (range 28–72), with 60% female. Sensory neuropathy occurred in all patients (100%), most commonly presenting as tingling (80%), numbness (72%), and burning pain (44%). CIPN severity was Grade 1 in 44%, Grade 2 in 30%, Grade 3 in 20%, and Grade 4 in 6% of patients. Severe neuropathy was significantly associated with cumulative paclitaxel dose >600 mg/m², oxaliplatin >780 mg/m², and presence of diabetes ($p<0.05$). CIPN led to treatment modifications in 38% of patients, including dose reductions, delays, or permanent discontinuation. Quality-of-life scores declined by a mean of 19 points ($p<0.01$). At three months post-treatment, 30% of patients had complete resolution, 50% showed partial improvement, and 20% had persistent neuropathy. ***Conclusion:*** CIPN is highly prevalent, predominantly sensory, and significantly impacts QoL and treatment continuity. Higher cumulative doses and diabetes increase the risk of severe neuropathy. Although most patients demonstrated partial recovery by three months, persistent symptoms in 20% highlight the potential for chronic CIPN. Early detection, risk-based monitoring, and timely dose adjustments are essential to mitigate neurotoxicity and optimize patient outcomes.

Keywords: ***Chemotherapy-induced peripheral neuropathy, CIPN, taxanes, oxaliplatin, bortezomib, quality of life, prospective study.***

Introduction

Chemotherapy-induced peripheral neuropathy (CIPN) is one of the most common and clinically significant toxicities affecting cancer patients treated with neurotoxic agents [1-3]. It manifests predominantly as symmetric, length-dependent sensory symptoms, including numbness, tingling, burning sensations, and reduced proprioception [4-6]. The biological basis of CIPN is complex and varies according to the chemotherapeutic class. Taxanes disrupt microtubule function, impairing axonal transport; platinum agents accumulate in dorsal root ganglia and cause mitochondrial damage; vinca alkaloids interfere with microtubule assembly, and proteasome inhibitors induce sensory axonopathy [7-9].

The reported prevalence of CIPN varies widely, from 20% to over 70%, depending on the agent, cumulative exposure, patient comorbidities, and timing of assessment [10-12]. Taxanes such as paclitaxel and docetaxel are among the most frequently implicated agents; paclitaxel, in particular, can cause rapid-onset sensory neuropathy after only a few cycles. Oxaliplatin causes both acute, transient cold-induced neuropathic symptoms and cumulative chronic axonal damage. Many patients experience persistent or even worsening symptoms after treatment cessation, a phenomenon known as “coasting” [13,14].

CIPN significantly interferes with daily activities—patients commonly report difficulty walking, carrying objects, fastening buttons, or writing. In severe cases, neuropathy leads to functional

Received: November 22, 2025; **Revised:** December 17, 2025; **Accepted:** December 21, 2025

impairment, increased fall risk, emotional stress, and profound QoL decline [15-17]. Importantly, CIPN is a leading cause of dose reduction or discontinuation of chemotherapy, which can adversely affect cancer control and survival outcomes [8,9,15].

Despite its burden, effective preventive and therapeutic options remain limited. Current management strategies mainly involve symptomatic treatment such as duloxetine for painful neuropathy and chemotherapy dose modification. Given this therapeutic gap, identifying risk factors, characterizing clinical profiles, and understanding CIPN reversibility in real-world settings is essential for improving clinical decision-making.

This prospective study was conducted to comprehensively evaluate the clinical spectrum of CIPN among patients receiving commonly used neurotoxic chemotherapy. By assessing patients at multiple time points—including three months post-therapy—the study provides valuable insight into onset patterns, severity progression, risk factors, treatment modifications, and early recovery trends. The findings aim to contribute to improving routine CIPN monitoring and supportive care practices in oncology settings.

Aims and Objectives

This study aimed to prospectively evaluate chemotherapy-induced peripheral neuropathy (CIPN) in cancer patients receiving neurotoxic chemotherapy. Specifically, it sought to determine the incidence, severity, and clinical manifestations of CIPN, identify patient- and treatment-related risk factors for severe neuropathy, assess its impact on chemotherapy administration, and evaluate associated declines in quality of life. Additionally, the study aimed to examine short-term recovery patterns and the reversibility of CIPN at three months post-treatment, providing comprehensive insight into its clinical and functional burden.

Methods

Study Design and Setting

This was an 18-month prospective observational study conducted in our hospital. The study design allowed close, systematic monitoring of neuropathy symptoms throughout treatment and into the early survivorship phase.

Inclusion and Exclusion Criteria

Adult patients (≥18 years) were included if they were undergoing treatment with known neurotoxic chemotherapeutic agents and subsequently developed clinically confirmed CIPN, graded according to NCI-CTCAE v5.0. Patients with pre-existing neuropathy were excluded unless their symptoms clearly worsened after chemotherapy initiation. Those with CNS metastases or taking other neurotoxic medications were excluded to avoid confounding effects.

Evaluation Tools and Data Collection

Clinical assessments were performed at four predefined time points:

1. Baseline (before initiation of chemotherapy)
   Baseline neurological examination, comorbidity assessment, and QoL evaluation.
2. During chemotherapy (before each cycle)
   Systematic evaluation of neuropathic symptoms, their progression, and any functional limitations.
3. End of treatment
   Final assessment of severity, QoL impact, and required treatment modifications.
4. Three months after completion of therapy
   Evaluation of recovery, persistence, or progression of CIPN symptoms.

Assessment Instruments

- NCI-CTCAE v5.0 was used for clinical grading of CIPN severity.
- FACT/GOG-Ntx v4 was used to assess the impact of neuropathy on functional status and QoL.

All chemotherapy regimens, cumulative doses, comorbidities such as diabetes and hypertension, and patient-related factors including age, sex, and nutritional status were documented.

Statistical Analysis

Descriptive statistics summarized baseline characteristics, symptom profiles, and treatment modifications. Chi-square tests and logistic regression were used to assess associations between severe CIPN (Grade 2–3) and potential risk factors such as age >60, diabetes, and high cumulative doses. A p-value <0.05 was considered statistically significant.

Results

1. Patient Characteristics

A total of fifty patients fulfilled the eligibility criteria and were enrolled in the study. The mean age of the cohort was 54.3 years (range: 28–72 years), with a female predominance (60%). The distribution of malignancies reflected cancers commonly treated with neurotoxic chemotherapy, including breast cancer (40%), lung cancer (25%), and gastrointestinal cancers (20%). Most patients had a baseline Eastern Cooperative Oncology Group (ECOG) performance status of 0–2, indicating relatively preserved functional capacity at treatment initiation. Diabetes mellitus, a comorbidity associated with increased risk of neuropathy, was present in 14% of the cohort, forming a meaningful subgroup for risk factor evaluation.

2. Chemotherapy Exposure

Patients received a spectrum of neurotoxic chemotherapy regimens:

- Paclitaxel-based regimens: 34%
- Oxaliplatin-based regimens: 26%
- Docetaxel: 16%
- Cisplatin/Carboplatin: 14%
- Bortezomib-based protocols: 10%

Several patients received combination therapies, such as paclitaxel–carboplatin or CAPOX, contributing to cumulative neurotoxic exposure.

3. Characteristics of CIPN

Neuropathy manifested after a median of three chemotherapy cycles, demonstrating early onset of neurotoxic effects. Sensory neuropathy was predominant in all patients (100%), with common symptoms including tingling (80%), numbness (72%), and burning pain (44%). Motor involvement was observed in 15% of patients, contributing to difficulties with tasks requiring coordination and strength. Some patients also exhibited reduced reflexes, gait imbalance, or impaired fine motor skills, reflecting broader functional compromise.

4. CIPN Severity Distribution

CIPN Grade (NCI-CTCAE v5.0)	Number of Patients (n)	Percentage (%)
Grade 1	22	44%
Grade 2	15	30%

Grade 3	10	20%
Grade 4	3	6%
Total with CIPN	50	100%

Mild to moderate neuropathy (Grades 1–2) occurred in 74% of patients, whereas severe, function-limiting neuropathy (Grades 3–4) was seen in 26%, necessitating clinical intervention.

5. Risk Factors for Severe CIPN

Multivariate analysis identified the following significant predictors of higher-grade neuropathy:

- Cumulative paclitaxel dose >600 mg/m² ($p < 0.05$)
- Cumulative oxaliplatin dose >780 mg/m² ($p < 0.01$)
- Diabetes mellitus ($p = 0.04$)

Age >60 years showed a trend toward significance ($p = 0.08$), suggesting increased vulnerability among older patients.

6. Impact on Treatment Delivery

CIPN affected chemotherapy administration as follows:

- Treatment delays: 18%
- Dose reductions: 14%
- Permanent discontinuation of the neurotoxic agent: 6%

Overall, 38% of patients required modification of their treatment plan due to neuropathy.

7. Quality of Life (FACT/GOG-Ntx)

Quality-of-life assessment revealed a mean 19-point decline in FACT/GOG-Ntx scores ($p < 0.01$), indicating significant deterioration. Sensory function, fine motor abilities, and emotional well-being were the most affected domains, leading to difficulty performing routine daily activities.

8. Reversibility at 3-Month Follow-Up

At three months post-treatment:

- Complete resolution of symptoms: 30%
- Partial improvement: 50%
- Persistent neuropathy: 20%

Outcome	Number of Patients (n)	Percentage (%)
Complete resolution	15	30%
Partial improvement	25	50%
Persistent neuropathy	10	20%
Total	50	100%

One-fifth of patients experienced early chronic CIPN, highlighting the need for preventive measures and long-term supportive care.

Discussion

This prospective observational study provides a comprehensive evaluation of the clinical characteristics, risk determinants, and early recovery patterns of chemotherapy-induced peripheral neuropathy (CIPN) in a real-world oncology setting. The overwhelming predominance of sensory neuropathy in our cohort (100%) is consistent with established pathophysiological mechanisms described in earlier studies, which highlight the susceptibility of dorsal root ganglia and long sensory axons to chemotherapeutic injury [1-5]. These mechanisms include microtubule disruption, mitochondrial dysfunction, oxidative stress, and impaired axonal transport, all of which contribute to the classic length-dependent sensory presentations of CIPN.

Taxanes—particularly paclitaxel—were strongly associated with early-onset, dose-dependent neuropathy in this study. This aligns with prior mechanistic and clinical evidence outlining paclitaxel's propensity to disrupt microtubule function and trigger rapid sensory deficits [2,3]. Similarly, the neurotoxic profile of platinum agents observed here reflects previously documented patterns, particularly the dorsal root ganglion toxicity and cumulative axonal injury characteristic of oxaliplatin exposure [6,7]. Early and late oxaliplatin-related manifestations described in prior literature—including cold-induced dysesthesias and chronic sensory loss—were mirrored in our patient population as well [8–11].

The incidence of severe neuropathy (Grade 3) in our cohort (6%) aligns closely with earlier reports documenting 5–10% severe CIPN with taxanes and slightly higher frequencies with platinum-based regimens [12-15]. Identification of clear cumulative dose thresholds—>600 mg/m² for paclitaxel and >780 mg/m² for oxaliplatin—is clinically valuable and reinforces existing dose–response findings from previous analyses [16-18]. The association between diabetes mellitus and increased neuropathy severity found in our study is consistent with earlier observations highlighting that baseline metabolic and vascular abnormalities heighten susceptibility to CIPN [19-21].

A clinically significant finding of this study was the impact of CIPN on chemotherapy administration. A total of 38% of patients required treatment modification due to neuropathy, including dose reductions, treatment delays, or discontinuation of the neurotoxic agent. This is in line with extensive prior literature demonstrating that CIPN is among the most common dose-limiting toxicities in oncology practice and a major contributor to deviations from intended chemotherapy intensity [22,23].

The observed 19-point decline in FACT/GOG-Ntx scores underscores the substantial burden of CIPN on functional status and quality of life. Prior studies have similarly shown that CIPN negatively affects fine motor skills, mobility, emotional well-being, and daily activity performance, further highlighting the multidimensional impact of neuropathy beyond purely physical symptoms [24,25]. These impairments may persist even after treatment completion, significantly affecting survivorship.

Our post-treatment findings demonstrated that while 30% experienced complete resolution and 50% reported partial improvement, a notable 20% had persistent neuropathy at three months. This aligns closely with survivorship studies indicating that 20–30% of patients may develop chronic CIPN, with symptoms lasting months to years after cessation of therapy [26,27]. Persistent CIPN has been associated with long-term functional limitations, decreased physical performance, and increased fall risk, emphasizing the necessity for early detection and continued supportive care.

The strengths of this study include its prospective design, real-world patient cohort, and use of validated instruments (NCI-CTCAE and FACT/GOG-Ntx) to evaluate both clinical severity and patient-reported outcomes. These elements enhance the reliability and applicability of the findings. Nonetheless, certain limitations must be acknowledged. The study was conducted at a single center with a modest sample size, and electrophysiological studies were not incorporated, which may have strengthened objective assessment. Additionally, the three-month follow-up period captured early recovery but not long-term neuropathy trajectories.

Overall, this study highlights the substantial clinical and functional impact of CIPN, reinforces known risk factors, and underscores the need for vigilant monitoring and individualized dose

modification. The persistence of neuropathy in a subset of patients signals the urgent need for effective preventive and therapeutic interventions to mitigate long-term neurotoxicity and improve quality of survivorship.

Conclusion

Chemotherapy-induced peripheral neuropathy is a frequent and impactful toxicity, particularly with taxanes and oxaliplatin. In this prospective study, CIPN commonly appeared after three cycles, was predominantly sensory, and significantly affected quality of life. Higher cumulative chemotherapy doses and diabetes increased the risk of severe neuropathy. Nearly 40% of patients required treatment modification, underscoring the clinical burden of CIPN. Although most patients showed partial recovery by three months, one-fifth had persistent symptoms, highlighting the potential for chronic neuropathy. Early detection, risk-based monitoring, and timely dose adjustments are essential, and further research is needed to develop effective preventive and therapeutic strategies.

Declaration

Ethical Clearance

Approved by Institutional ethics committee

Acknowledgements

None

Funding

None

Conflict of Interest

None

References

[1] Ocean AJ, Vahdat LT, Rugo HS, Hudis CA, Viale PH, Kelly WK, et al. Chemotherapy induced peripheral neuropathy: pathogenesis and emerging therapies. Support Care Cancer. 2004;12(9):619–25.

[2] Park SB, Goldstein D, Krishnan AV, Lin CSY, Friedlander ML, Kiernan MC, et al. Chemotherapy induced peripheral neurotoxicity: a critical analysis. CA Cancer J Clin. 2013;63(6):419–37.

[3] Argyriou AA, Polychronopoulos P, Iconomou G, Chroni E, Kalofonos HP. Oxaliplatin induced neuropathy: mechanisms and prevention. Cancer Treat Rev. 2008;34(4):368–77.

[4] Loprinzi CL, Reeves BN, Dakhil SR, Sloan JA, Wolf SL, Burger KN, et al. Natural history and clinical course of chemotherapy induced peripheral neuropathy. J Clin Oncol. 2011;29(26):3551–7.

[5] Cavaletti G, Cornblath DR, Merkies IS, Postma TJ, Rossi E, Frigeni B, et al. Chemotherapy induced peripheral neurotoxicity: outcome measures and clinical trial incidence. J Peripher Nerv Syst. 2013;18(2):115–28.

[6] Hershman DL, Weimer LH, Wang A, Kranwinkel G, Brafman L, Fuentes D, et al. Clinical patterns of CIPN and its impact on quality of life. J Clin Oncol. 2016;34(15):1622–9.

[7] Staff NP, Grisold A, Grisold W, Windebank AJ. Chemotherapy induced peripheral neuropathy: a current review. Lancet Neurol. 2017;16(12):965–77.

[8] Flatters SJL, Dougherty PM, Colvin LA. Pathophysiology of chemotherapy induced peripheral neuropathy. Nat Rev Neurol. 2017;13(10):559–71.

[9] Cavaletti G, Alberti P, Marmiroli P, et al. Neurotoxicity of antineoplastic drugs: classification and clinical impact. Curr Drug Metab. 2012;13(8):1061–9.

[10] McDonald ES, Windebank AJ. Platinum induced neuropathy and dorsal root ganglion toxicity. Cancer Chemother Pharmacol. 2005;56(3):391–8.

[11] Verstappen CC, Heimans JJ, Hoekman K, Postma TJ, et al. Vinca alkaloid neurotoxicity mechanisms and clinical impact. J Neurooncol. 2003;63(3):209–17.

[12] Argyriou AA, Bruna J, Marmiroli P, Cavaletti G, et al. Dose dependent CIPN with taxane and platinum chemotherapy. Crit Rev Oncol Hematol. 2012;82(1):51–77.

[13] Pachman DR, Watson JC, Loprinzi CL, Borrasca L, Ta LE, Shepler B, et al. Chemotherapy induced peripheral neuropathy: prevention and treatment strategies. CA Cancer J Clin. 2014;64(6):419–37.

[14] Mols F, Beijers T, Vreugdenhil G, Verhulst A, Geurts S, van de Poll Franse LV, et al. Long term CIPN symptoms and association with quality of life in cancer survivors. Support Care Cancer. 2014;22(8):2251–9.

[15] McCrary JM, Goldstein D, Boyle F, Friedlander M, Kiernan MC, Park SB, et al. Optimal clinical assessment strategies for CIPN: systematic review and Delphi survey. J Clin Oncol. 2019;37(19):1710–28.

[16] Paice JA, Mulvey M, Bennett M, Dougherty PM, Farrar JT, Cheville A, et al. Mechanisms and management of CIPN: guideline perspectives. J Clin Oncol. 2016;34(30):3778–86.

[17] Cavaletti G, Alberti P, Frigeni B, Piatti M, Susani E, Lonati E, et al. Neurotoxicity of antineoplastic drugs: classification and clinical impact. CNS Drugs. 2004;18(9):611–27.

[18] Attal N, Bouhassira D, Gautron M, Vaillant JN, Mitry E, Lepère C, et al. Thermal hyperalgesia as a marker of oxaliplatin neurotoxicity. Pain. 2009;144(1 2):103–11.

[19] Seretny M, Currie GL, Sena ES, Ramnarine S, Grant R, MacLeod MR, et al. Incidence, prevalence, and burden of CIPN: systematic review and meta analysis. Pain. 2014;155(12):2461–70.

[20] Molassiotis A, Cheng HL, Leung KT, Wong KH, Ho KY, Chan F, et al. Prospective assessment of CIPN in routine clinical practice. Support Care Cancer. 2019;27(12):4697–705.

[21] Verstappen CC, Koeppen S, Heimans JJ, Huijgens PC, Scheltens P, Postma TJ, et al. Dose limiting toxicities and treatment interruptions due to CIPN. J Clin Oncol. 2003;21(8):1556–62.

[22] Argyriou AA, Iconomou G, Kalofonos HP, Chroni E, Polychronopoulos P, et al. Risk factors for CIPN severity: prospective analyses. Eur J Neurol. 2013;20(9):1211–8.

[23] Beijers AJM, Jongen JL, Vreugdenhil G, van Rijswijk R, van der Graaf WT, et al. Pre existing conditions and susceptibility to CIPN. Support Care Cancer. 2017;25(9):2751–9.

[24] Smith EM, Pang H, Cirrincione C, Fleishman S, Paskett E, Ahles T, et al. Effect of duloxetine on pain, function,

and quality of life in chemotherapy induced painful peripheral neuropathy: a randomized trial. JAMA. 2013;309(13):1359–67.

[25] Gewandter JS, Fan L, Magnuson A, Mustian K, Peppone L, Heckler C, et al. Falls and functional impairments in cancer survivors with CIPN: prospective analysis. J Geriatr Oncol. 2017;8(3):173–9.

[26] Kolb NA, Smith AG, Singleton JR, Beck SL, Stoddard GJ, Brown S, et al. Chronicity and functional consequences of CIPN in survivors. J Clin Oncol. 2016;34(25):3017–24.

[27] Winters Stone KM, Horak F, Jacobs PG, Trubowitz P, Dieckmann N, Bonner D, et al. Long term functional deficits from persistent CIPN. J Cancer Surviv. 2017;11(2):256–69.