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# Occurrence and Severity of Chemotherapy-Induced Peripheral Neuropathy and Its Association with Comorbidities in Patients Receiving Cytotoxic Chemotherapy: A Prospective Observational Study

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## Abstract

**Background:** Chemotherapy-induced peripheral neuropathy (CIPN) is a common and dose-limiting adverse effect of cytotoxic chemotherapy that can significantly impair quality of life (QoL), compromise functional status, and affect treatment adherence. Early recognition is essential to improve patient outcomes.

**Objectives:** To evaluate the occurrence and severity of CIPN using clinician-based NCI-CTCAE grading and patient-reported FACT/GOG-Ntx scores, and to identify associated risk factors, including co morbidity burden.

**Methods:** In this prospective observational study, 200 patients receiving cytotoxic chemotherapy were assessed for CIPN using NCI-CTCAE version 5.0, the FACT/GOG-Ntx questionnaire, and the Charlson Comorbidity Index.

**Results:** CIPN was observed in 124 (62.0%) patients. According to NCI-CTCAE grading, 73 (36.5%) patients had grade 1 neuropathy, 44 (22.0%) had grade 2 neuropathy, and 7 (3.5%) had grade 3 neuropathy. The prevalence increased with age, reaching 13 (81.3%) patients in the 74–83-year age group, and was higher among females. A cumulative effect of chemotherapy was observed with increasing treatment cycles. Platinum-based agents, taxanes, and proteasome inhibitors were most commonly associated with CIPN. Quality of life was adversely affected in 144 (72.0%) patients. CTCAE grading showed a significant association with FACT/GOG-Ntx scores ($p < 0.001$), although agreement between the assessment tools was low ($\kappa = 0.025$). Mandeep Singh Juneja

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**Conclusion:** CIPN is a common and clinically relevant toxicity influenced by cumulative chemotherapy exposure, neurotoxic drug class, and increasing age. Combining clinician-based toxicity grading with patient-reported outcome measures may improve early detection, comprehensive assessment, and management of CIPN while supporting treatment continuation and improving quality of life.

**Keywords:** CIPN, CTCAE, FACT-GOG-Ntx, Charlson Comorbidity Index, ROC analysis, QOL, Neurotoxicity

## Introduction

Chemotherapy-induced peripheral neuropathy (CIPN) is one of the most common and clinically significant adverse effects of cytotoxic chemotherapy, affecting approximately 30–70% of patients receiving neurotoxic anticancer agents. It is an important dose-limiting toxicity that may result in chemotherapy dose reduction, treatment delays, or premature discontinuation, potentially affecting treatment outcomes. Clinically, CIPN commonly presents as a symmetrical, length-dependent sensory neuropathy, with symptoms such as numbness, tingling, burning pain, paraesthesia, impaired sensation, and gait instability. In severe cases, motor dysfunction may also occur.[1-5] The development of CIPN is multifactorial and varies according to the chemotherapeutic agent involved. Platinum compounds primarily affect the dorsal root ganglia through mechanisms involving DNA damage, oxidative stress, mitochondrial dysfunction, and neuronal apoptosis, whereas taxanes interfere with microtubule dynamics and axonal transport, contributing to distal axonal degeneration. Neuroinflammation, altered ion channel activity, calcium dysregulation, and impaired neuronal repair may further contribute to peripheral nerve injury and the persistence of neuropathic symptoms. Although the underlying mechanisms differ between drug classes, these processes ultimately lead to peripheral nerve dysfunction that may persist even after completion of chemotherapy.[1-5]

Beyond the neurological symptoms themselves, CIPN can have a considerable impact on patients' daily lives. It may affect physical functioning, psychological well-being, routine activities, and overall health-related quality of life. In some patients, neuropathic symptoms continue for months or years after treatment, potentially limiting functional independence and affecting adherence to planned chemotherapy. Thus, CIPN represents an important concern not only during active cancer treatment but also during survivorship. Despite increasing understanding of its pathophysiology, effective preventive and disease-modifying treatments remain limited, emphasizing the importance of early recognition and systematic assessment.[6–10]

Current clinical guidelines emphasize regular assessment of neuropathic symptoms during chemotherapy to allow early recognition and appropriate management. The American Society of Clinical Oncology (ASCO) recommends duloxetine as the only pharmacological treatment with moderate evidence for established painful CIPN, while no intervention has consistently demonstrated efficacy for preventing CIPN. Consequently, treatment modification when clinically necessary, patient education, symptom monitoring, and supportive care remain important components of CIPN management.[11–18]

Several patient- and treatment-related factors have been associated with the development of CIPN. Older age, cumulative chemotherapy exposure, longer treatment duration, diabetes mellitus, obesity, pre-existing neuropathy, and exposure to neurotoxic agents such as platinum compounds, taxanes, and proteasome inhibitors have been reported as potential risk factors. However, the importance of individual risk factors varies across patient populations, cancer types, and treatment regimens. Sánchez-Barroso et al. also demonstrated that patient characteristics and concomitant medications may contribute to differences in CIPN risk, highlighting the importance of considering individual patient factors when assessing susceptibility to neuropathy.[19–23,33]

Accurate assessment of CIPN remains challenging because no single assessment tool captures all aspects of the condition. The National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) is commonly used to grade clinician-reported neurotoxicity, whereas the Functional Assessment of Cancer Therapy/Gynecologic Oncology Group–Neurotoxicity (FACT/GOG-Ntx) questionnaire provides a patient-reported assessment of neuropathic symptoms and their effect on daily functioning. Previous studies have demonstrated that CIPN can adversely affect health-related quality of life, including physical, emotional, and

social well-being. Clinician-reported grading and patient-reported outcome measures may capture different aspects of neuropathy; therefore, using both approaches can provide a broader understanding of the patient's neurological toxicity and its functional consequences.[24–31]

Although considerable progress has been made in understanding the epidemiology, risk factors, and management of CIPN, prospective real-world data evaluating its occurrence, severity, comorbidity burden, and the relationship between clinician-reported and patient-reported assessments remain limited in Indian oncology practice. Furthermore, most studies have evaluated either clinician-reported toxicity or patient-reported outcomes independently, with limited evidence comparing both approaches in routine clinical practice. Recent evidence has also emphasized the value of individualized risk prediction approaches that consider patient characteristics and treatment-related factors to identify individuals at greater risk of taxane-induced peripheral neuropathy.[32],[33] Therefore, this prospective study was conducted to comprehensively evaluate the occurrence and severity of CIPN using both clinician-reported (NCI-CTCAE version 5.0) and patient-reported (FACT/GOG-Ntx) assessment tools, identify demographic and treatment-related risk factors, assess the influence of comorbidity burden, and generate real-world evidence to support early detection and individualized management of CIPN in an Indian tertiary cancer care setting.

Accordingly, the primary objective of this study was to determine the occurrence and severity of chemotherapy-induced peripheral neuropathy among patients receiving cytotoxic chemotherapy using NCI-CTCAE version 5.0 and the FACT/GOG-Ntx questionnaire. The secondary objectives were to identify demographic, clinical, and treatment-related factors associated with CIPN, evaluate the association between comorbidity burden and neuropathy severity, and examine the relationship between clinician-reported toxicity and patient-reported neuropathy symptoms.

## Methodology

### Study Design and Setting

A Prospective observational study was carried out over six month period (January 2025-June2025) in the oncology department of a tertiary teaching hospital, ESIC hospital, Rajajinagar, Bengaluru, India

### Study Population

A total of 458 patients were screened for study eligibility, a total of 458 patients were screened for study eligibility, of whom 200 eligible patients were prospectively enrolled after providing written informed consent.

### Sample Size Justification

The sample size was determined based on the primary and secondary objectives of the study. Previous studies have reported a 40–60% incidence of chemotherapy-induced peripheral neuropathy (CIPN) among patients receiving neurotoxic chemotherapy. Assuming an expected incidence of 50%, a sample size of 200 patients was considered adequate to estimate the primary outcome with acceptable precision.

For the secondary objective, a sample of 190–200 participants was estimated to provide 80% power at a two-sided α level of 0.05 to evaluate the diagnostic performance of the FACT/GOG-Ntx questionnaire against NCI-CTCAE version 5.0 using ROC curve analysis (assuming an AUC of 0.75 based on the Hanley and McNeil method).

The sample size was also considered adequate for planned subgroup analyses according to the Charlson Comorbidity Index (CCI). Assuming a 20% difference in the incidence of clinically significant CIPN between high- and low-co morbidity groups, 200 participants provided sufficient statistical power for these comparisons A sample size of 200 patients was considered appropriate to reliably estimate the occurrence of CIPN, evaluate the performance of FACT/GOG-Ntx against CTCAE grading using ROC analysis, and identify meaningful differences in risk across patient subgroups, including those with varying co morbidity burden.

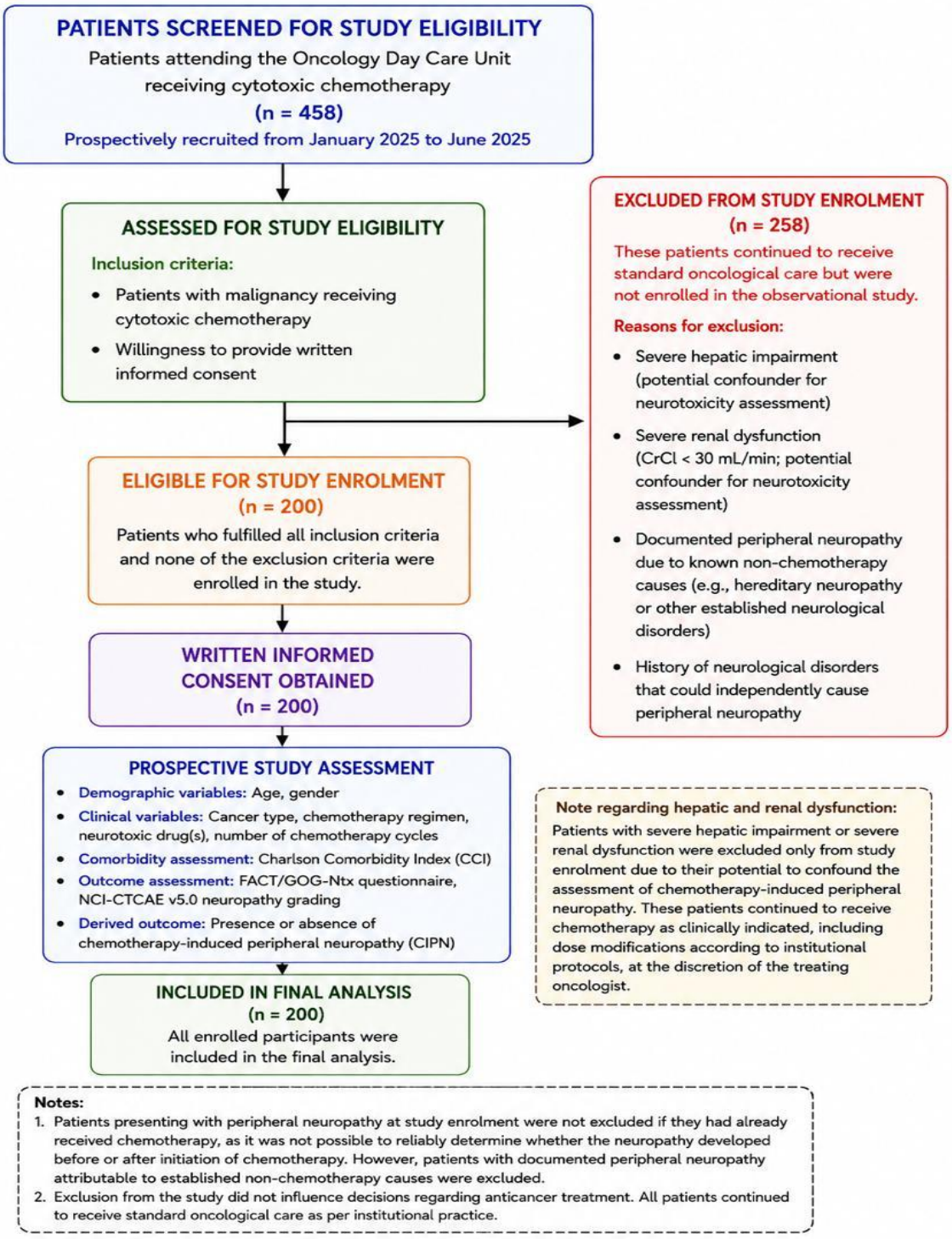


**Figure 1:** Flow diagram of patient screening, enrolment, prospective study assessment, and inclusion in the final analysis.

## Study Assessment (Study Variables)

Baseline demographic, clinical, and treatment-related characteristics were collected prospectively for all enrolled participants. Demographic variables included age and sex. Clinical variables included cancer type, chemotherapy regimen, neurotoxic anticancer agents received, number of chemotherapy cycles, treatment duration, and relevant laboratory parameters, including renal and hepatic function status.

Lifestyle and social variables, including smoking and tobacco exposure, were recorded. Smoking was defined as the use of combustible tobacco products, whereas tobacco exposure included other forms of tobacco use, such as chewing tobacco. Beedi smoking was categorized as smoked tobacco exposure.

## Assessment of Chemotherapy-Induced Peripheral Neuropathy (CIPN)

The occurrence and severity of CIPN were assessed using the Functional Assessment of Cancer Therapy/Gynecologic Oncology Group-Neurotoxicity (FACT/GOG-Ntx) questionnaire. Neurotoxicity severity was graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 5.0 as Grade 1 (mild), Grade 2 (moderate), Grade 3 (severe), Grade 4 (life-threatening), and Grade 5 (death). The onset of CIPN was determined based on patient-reported symptoms and clinical assessment during chemotherapy exposure.

### *Assessment of Comorbidity*

Pre-existing chronic medical conditions were recorded and categorized individually. The overall co morbidity burden was assessed using the Charlson Comorbidity Index (CCI). The CCI was included to evaluate whether underlying co morbidity burden was associated with the occurrence and severity of CIPN.

### *Quality of Life Assessment*

Neurotoxicity-related quality of life was assessed using the FACT/GOG-Ntx questionnaire. Scores were calculated according to validated scoring guidelines, with higher scores indicating better quality of life and lower neurotoxicity-related impairment.

## Ethical Considerations

The study protocol was approved by the Institutional Ethics Committee of ESIC Medical College and PGIMSR, Bengaluru (Approval No. 532/L/11/12/Ethics/ESICMC&PGIMSR/Estt. Vol. IV/2D1/2025, dated 02 August 2025). The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and applicable institutional guidelines. Written informed consent was obtained from all participants before enrollment. Participant confidentiality and anonymity were maintained throughout the study.

## Statistical Analysis

- Continuous variables were assessed for normality and summarized as mean ± standard deviation (SD) for normally distributed data or median with interquartile range (IQR) for non-normally distributed data.
- Categorical variables were summarized as frequencies and percentages.
- Associations between categorical variables were evaluated using the Chi-square test or Fisher's exact test, as appropriate.
- Differences in continuous or ordinal outcome measures between two independent groups were analyzed using the Mann–Whitney U test.
- Comparisons of continuous or ordinal outcome measures across three or more independent groups were performed using the Kruskal–Wallis test. Where appropriate, Bonferroni-adjusted pairwise Mann–Whitney U tests were conducted for post hoc comparisons.
- Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated to assess the association between co-morbidity status and clinically significant chemotherapy-induced peripheral neuropathy (CIPN).
- Binary logistic regression analysis was performed to identify independent predictors of CIPN, and results were reported as ORs with 95% CIs.
- Receiver operating characteristic (ROC) curve analysis was performed to determine the optimal FACT/GOG-Ntx score cut-off for identifying clinically significant CIPN. Diagnostic performance was evaluated using the area under the ROC curve (AUC), and the optimal threshold was determined using the Youden Index.
- Cohen's kappa coefficient was used to assess the agreement between FACT/GOG-Ntx questionnaire scores and NCI Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 5.0 neuropathy grading.
- A two-sided p-value <0.05 was considered statistically significant

## Results

**Table 1:** Baseline demographics and clinical characteristics of study population.

| Characteristics | Category | Overall n(%) | CIPN n(%) | No CIPN n(%) |
|---|---|---|---|---|
| **Age** | 24-33 | 6(3.0) | 4(66.7) | 2(33.3) |
| | 34-43 | 30(15.0) | 15(50.0) | 15(50.0) |
| | 44-53 | 70(35.0) | 44(62.9) | 26(37.1) |
| | 54-63 | 50(25.0) | 33(66.0) | 17(34.0) |
| | ≥ 64 | 44(22.0) | 28(63.6) | 16(36.4) |
| **Gender** | Male | 76(38.0) | 41(53.9) | 35(46.1) |
| | Female | 124(62.0) | 83(66.6) | 41(33.1) |
| **Social factors** | None | 147(73.5) | 93(64.6) | 54(36.7) |
| | Smoking only | 9(4.5) | 4(44.4) | 5(55.6) |
| | Tobacco/Beedi only | 16(8.0) | 12(75) | 4(25) |
| | Alcohol only | 5(2.5) | 4(80) | 1(20) |
| | Multi-Factorial | 23(11.5) | 8(34.7) | 15(65.2) |
| **Diagnosis** | Breast cancer | 68(34.0 ) | 43(63.2) | 25(36.8) |
| | Esophageal cancer | 19(9.5) | 13(68.4) | 6(31.6) |
| | Ovarian cancer | 13(6.5) | 11(84.6) | 2(15.4) |
| | Colorectal cancer | 12(6.0) | 4(33.3) | 8(66.7) |
| | Stomach cancer | 12(6.0) | 6(50.0) | 6(50.0) |
| | Cervical cancer | 10(5.0) | 5(50.0) | 5(50.0) |
| | Lung cancer | 10(5.0) | 7(70.0) | 3(30.0) |
| | Lymphoma | 8(4.0) | 4(50.0) | 4(50.0) |
| | Buccal mucosa cancer | 7(3.5) | 3(42.9) | 4(57.1) |
| | Multiple myeloma | 6(3.0%) | 5(83.3) | 1(16.7) |
| | Others | 35(17.5) | 24(68.6) | 11(31.4) |
| **Chemotherapy cycles** | ≤13 | 165(82.5) | 98(59.4) | 67(40.6) |
| | 14-25 | 26(13.0) | 19(73.1) | 7(26.9) |
| | ≥26 | 9(4.5) | 8(88.9) | 1(11.1) |
| **Chemotherapy Drug** | | | | |
| **Platinum-based agents** | Carboplatin | 54(27.0) | 42(62.7) | 12(17.9) |
| | Oxilaplatin | 15(7.5) | 4(26.7) | 11(73.3) |
| | Cisplatin | 15(7.5) | 9(60.0) | 6(40.0) |
| | Total | 84(42.0) | 55(65.5) | 29(34.5) |
| **Taxel based agents** | Paclitaxel | 52(26.0) | 35(67.3) | 17(32.7) |
| | Docetaxel | 24(12.0) | 13(54.2) | 11(45.8) |
| | Total | 76(38.0) | 48(63.2) | 28(36.5) |
| **Anthracyclines** | Doxorubicin | 26(13.0) | 16(61.5) | 10(38.5) |
| | Epirubicin | 1(0.5) | 1(100.0) | 0(0.0) |
| | Total | 27(13.5) | 17(63.0) | 10(37.0) |
| **Alkylating agent** | Bendamustine | 4(2.0) | 4(100.0) | 0(0.0) |
| | Dacarbazine | 1(0.5) | 1(100.0) | 0(0.0) |
| | Cyclophosphamide | 23(11.5) | 11(47.8) | 12(52.2) |
| | Temzolomide | 1(0.5) | 0(0.0) | 1(100.0) |

| | | | | |
|---|---|---|---|---|
| | Total | 29(14.5) | 16(55.2) | 13(44.8) |
| **Antimetabolites** | Pemetrexed | 2(1.0) | 2(100.0) | 0(0.0) |
| | 5-Fluorouracil | 14(7.0) | 6(42.9) | 8(57.1) |
| | Gemcitabine | 6(3.0) | 6(100.0) | 0(0.0) |
| | Capcitabine | 2(1.0) | 1(50.0) | 1(50.0) |
| | Tegafur | 1(0.5) | 1(100.0) | 0(0.0) |
| | Methotrexate | 2(1.0) | 2(100.0) | 0(0.0) |
| | Total | 27(13.5) | 18(66.7) | 9(33.3) |
| **Vinca alkaloids** | Vincristine | 2(1.0) | 0(0.0) | 2(100.0) |
| | Vinblastin | 1(0.5) | 1(100.0) | 0(0.0) |
| | Total | 3(1.5) | 1(33.3) | 2(66.7) |
| **Topoisomerase inhibitors** | Irinotecan | 6(3.0) | 5(83.3) | 1(16.7) |
| | Etopside | 2(1.0) | 0(0.0) | 2(100.0) |
| | Total | 8(4.0) | 5(62.5) | 3(37.5) |
| **Proteosome inhibitors** | Bortezomib | 3(1.5) | 3(100.0) | 0(0.0) |
| **HER2- targeted Monoclonal antibodies** | Trastuzumab | 36(18.0) | 27(75.0) | 9(25.0) |
| | Pertuzumab | 24(12.0) | 20(83.3) | 4(16.7) |
| | Total | 60(30.0) | 47(78.3) | 13(21.7) |
| **EGFR- targeted monoclonal antibodies** | Panituzumab | 2(1.0) | 1(50.0) | 1(50.0) |
| | Nimotuzumab | 3(1.5) | 2(66.7) | 1(33.3) |
| | Cetuximab | 1(0.5) | 0(0.0) | 1(100.0) |
| | Total | 6(3.0) | 3(50.0) | 3(50.0) |
| **VEGF/VEGFR - targeted monoclonal antibodies** | Bevacizumab | 15(80.0) | 12(80.0) | 3(20.0) |
| | Raamucirumab | 7(3.5) | 4(57.1) | 3(42.9) |
| | Total | 22(11.0) | 16(72.7) | 6(27.3) |
| **Anti-CD20 monoclonal antibodies** | Rituximab | 7(3.5) | 3(42.9) | 4(57.1) |
| | Obinutuzumab | 1(0.5) | 1(10.0) | 0(0.0) |
| | Total | 8(4.0) | 4(50.0) | 4(50.0) |
| **Immune checkpoint inhibitors** | Pembrolizumab | 17(8.5) | 13(76.5) | 4(23.5) |
| | Nivolumab | 13(6.5) | 8(61.5) | 5(38.5) |
| | Atezolizumab | 5(2.5) | 5(100.0) | 0(0.0) |
| | Total | 35(17.5) | 26(74.3) | 9(25.7) |
| **Other monoclonal** | Daratumumab | 2(1.0) | 2(100.0) | 0(0.0) |
| **Tyrosine kinase inhibitor** | Lenvatinib | 1(0.5) | 0(0.0) | 1(100.0) |
| | Gefitinib | 3(1.5) | 3(100.0) | 0(0.0) |
| | Axitinib | 1(0.5) | 1(100.0) | 0(0.0) |
| | Total | 5(2.5) | 4(80.0) | 1(20.0) |
| **Immunomodulatory agents** | Lenalidomide | 1(100.0) | 0(0.0) | 1(100.0) |
| **CCI Category** | | | | |
| **Mild** | 1-2 | 43(21.5) | 23(18.5) | 20(26.3) |
| **Moderate** | 3-4 | 69(34.5) | 46(37.1) | 23(30.3) |
| **Severe** | ≥5 | 88(44.0) | 55(44.4) | 33((43.4) |

Table 1 summarizes the demographic and clinical characteristics of the study population according to the presence or absence of CIPN. CIPN was observed in 62.0% of patients. Higher proportions of CIPN were observed among females, patients receiving a greater number of chemotherapy cycles, and those with moderate-to-severe comorbidity. The highest proportions of CIPN were observed among patients with ovarian cancer and multiple myeloma.

**Table 2:** Clinical characteristics of chemotherapy induced peripheral neuropathy (CIPN)

| Characteristics | Category | N (%) / Median (IQR) |
|---|---|---|
| **CIPN** | Present | 124(62.0) |
| | Absent | 76(38.0) |
| **CTCAE Neurotoxicity Grading** | Grade 1 | 76(38.0) |
| | Grade 2 | 73(36.5) |
| | Grade 3 | 44(22.0) |
| | Grade 4 | 7(3.5) |

Table 2 summarizes the clinical outcomes of chemotherapy-induced peripheral neuropathy (CIPN). Overall, CIPN was observed in 124 (62.0%) of the 200 patients. Grade 1 neurotoxicity was the predominant severity category, followed by Grade 2, whereas Grade 3 neurotoxicity was uncommon, indicating that most cases were mild to moderate in severity.

**Table 3:** FACT/GOG-NTX scores according to neuropathy severity

| NTx severity | N (%) | FACT/GOG-NTX Total, Median (IQR) | No Functional + Social, Median (IQR) | Functional + Social, Median (IQR) |
|---|---|---|---|---|
| **No/minimal symptoms** | 76 (38.0) | 57 (52.75–61) | 14 (10–18.25) | 44 (38–48) |
| **Mild neuropathy** | 73 (36.5) | 62 (56–67) | 24 (20–28) | 38 (33–43) |
| **Moderate neuropathy** | 44 (22.0) | 72.5 (68.75–80) | 39 (34.75–47.25) | 31.5 (28.75–40) |
| **Severe neuropathy** | 7 (3.5) | 92 (87.5–100) | 70 (64–72) | 28 (15.5–32.5) |
| **Overall** | 200 (100) | 62 (56–71) | 24 (15–35) | 38.5 (32–44) |

Table 3 summarizes the FACT/GOG-Ntx quality-of-life scores according to the severity of chemotherapy-induced peripheral neuropathy. The overall median FACT/GOG-Ntx score was 62 (IQR: 56‑71). The Functional + Social score decreased with increasing neuropathy severity, from 44 (IQR: 38‑48) in patients with no or minimal symptoms to 28 (IQR: 15.5‑32.5) in those with severe neuropathy, indicating poorer functional and social well-being with increasing neuropathy severity.

**Table 4:** Association of clinical characteristics with neurotoxicity severity (FACT/GOG-Ntx and CTCAE)

| Variable | Test | FACT/GOG-NTX P-value | CTCAE P-value |
|---|---|---|---|
| **Chemotherapy cycles quartiles** | Kruskal-wallis test | 0.932 | 0.542 |
| **Chemotherapy drug groups** | Kruskal-wallis test | 0.110 | 0.281 |
| **CCI category** | Kruskal-wallis test | 0.422 | 0.230 |
| **Cancer diagnosis** | Kruskal-wallis test | 0325 | 0.607 |

**Footnote:** Kruskal–Wallis test was used to compare neurotoxicity severity scores across clinical and treatment-related subgroups. A p value <0.05 was considered statistically significant.

Table 4 summarizes the association between clinical and treatment-related characteristics and neurotoxicity severity assessed using FACT/GOG-Ntx scores and CTCAE grading. No statistically significant differences were observed across chemotherapy cycle quartiles (FACT/GOG-Ntx, p = 0.932; CTCAE, p = 0.542),

chemotherapy drug groups (FACT/GOG-Ntx, p = 0.110; CTCAE, p = 0.281), CCI categories (FACT/GOG-Ntx, p = 0.422; CTCAE, p = 0.230), or cancer diagnosis (FACT/GOG-Ntx, p = 0.325; CTCAE, p = 0.607). These findings indicate that neurotoxicity severity was comparable across the evaluated clinical and treatment-related subgroups.

## Discussion

### Occurrence and Severity of CIPN

In this prospective study of 200 patients receiving cytotoxic chemotherapy, CIPN was observed in 124 patients (62.0%). Most affected patients had mild-to-moderate neuropathy, while severe neurotoxicity was uncommon. The occurrence observed in this study is within the range reported in previous studies, although differences in cancer type, chemotherapy regimen, assessment methods, and timing of assessment can contribute to variation between studies.[6–8]

### Treatment-Related Factors

The relatively high occurrence of CIPN in our cohort should not be attributed solely to individual neurotoxic agents such as oxaliplatin or paclitaxel. Platinum compounds and taxanes are well-established causes of CIPN, but the development and severity of neuropathy are influenced by cumulative exposure, treatment schedule, patient characteristics, and other clinical factors.[3–5] In the present study, no significant association was observed between chemotherapy drug groups and neuropathy severity using either FACT/GOG-Ntx (p = 0.110) or CTCAE (p = 0.281).

### Age and Patient-Related Factors

Age did not demonstrate a significant relationship with neuropathy severity in our cohort. Although older patients showed relatively higher proportions of CIPN, the findings suggest that age alone may not adequately predict neuropathy risk. Sánchez-Barroso et al. emphasized that CIPN risk is influenced by multiple patient-related factors and concomitant medications, supporting a broader approach to individual risk assessment rather than relying on age alone.[33]

### Chemotherapy Exposure and Time-Dependent Factors

Chemotherapy cycle quartiles were not significantly associated with FACT/GOG-Ntx (p = 0.932) or CTCAE severity (p = 0.542). This finding should be interpreted cautiously because the number of cycles may not accurately represent cumulative dose or dose intensity. CIPN is a time-dependent toxicity, and differences in drug exposure and treatment schedules may influence symptom development.[3,19–22] Recent evidence from Trivedi et al. further supports the use of multivariable risk prediction rather than relying on a single treatment-related variable.[32]

### Comorbidity Burden

No significant association was observed between CCI category and neuropathy severity using FACT/GOG-Ntx (p = 0.422) or CTCAE (p = 0.230). This may indicate that an overall comorbidity index does not adequately capture the specific conditions that influence CIPN risk. Individual factors such as diabetes, pre-existing neuropathy, and other neurological vulnerabilities may be more informative than overall comorbidity burden.[19–23]

### CIPN and Quality of Life

An important finding was the relationship between neuropathy severity and patient-reported functioning. The median FACT/GOG-Ntx score was 62 (IQR: 56–71), while the Functional + Social score decreased from 44 in patients with no/minimal symptoms to 28 in those with severe neuropathy. This indicates increasing impairment in functional and social well-being with greater neuropathy severity. These findings are consistent with previous evidence showing that CIPN can negatively affect physical functioning, daily activities, and quality of life.[25–30] However, previous studies have reported variability in the strength of this

relationship, possibly because quality of life is also influenced by cancer-related and treatment-related factors.[25–29]

### FACT/GOG-Ntx and CTCAE Assessment

The use of both CTCAE and FACT/GOG-Ntx provides complementary information. CTCAE captures clinician-assessed neurotoxicity, whereas FACT/GOG-Ntx reflects the patient's experience and functional impact.[24],[31] Hertz highlighted the complexity of the relationship between chemotherapy exposure and neuropathy, particularly with taxanes, suggesting that drug exposure alone may not fully explain patient-reported neurotoxicity.[31] Therefore, incorporating patient-reported outcomes alongside conventional clinical grading may provide a more clinically meaningful assessment of CIPN.

### Clinical Implications

The findings support the importance of routine CIPN assessment during chemotherapy, particularly because mild symptoms may progress and affect patients' daily functioning. Combining clinician-reported grading with patient-reported assessment may allow clinically relevant symptoms to be identified earlier. A multidimensional approach incorporating patient characteristics, treatment exposure, comorbidities, and patient-reported symptoms may be more useful than relying on a single risk factor.[32,33]

## Conclusion

In this study, CIPN was predominantly mild to moderate, while severe neurotoxicity was less frequently observed. Increasing neuropathy severity was accompanied by poorer functional and social well-being, indicating that CIPN can have meaningful effects on patients' daily lives beyond neurological symptoms. Previous literature similarly demonstrates that CIPN can adversely affect functional status and quality of life.
No significant association was observed between neuropathy severity and chemotherapy cycle groups, chemotherapy drug groups, cancer diagnosis, or comorbidity categories. These findings suggest that CIPN is a multifactorial toxicity and that its severity may not be adequately explained by a single patient or treatment-related characteristic. The combined use of clinician-based assessment and patient-reported outcomes provides a more comprehensive evaluation of neuropathy and its functional consequences. Overall, systematic and patient-centred monitoring during chemotherapy may support earlier recognition of clinically relevant CIPN and facilitate individualized supportive care.

## Limitations

This study has several limitations. First, it was conducted at a single tertiary cancer centre, which may limit the generalizability of the findings to other oncology populations and healthcare settings. Second, the study included patients receiving heterogeneous chemotherapy regimens, and some individual drug groups had relatively small sample sizes, limiting meaningful comparisons between specific anticancer agents. Third, although the number of chemotherapy cycles was assessed, the relatively small numbers in the higher-cycle categories may have limited the ability to detect associations between treatment exposure and CIPN severity.
Fourth, the Charlson Comorbidity Index (CCI) was used to assess overall comorbidity burden; therefore, the individual contribution of specific comorbidities to CIPN could not be evaluated in detail. Fifth, cancer stage was not included in the present analysis, limiting assessment of its potential influence on CIPN. CIPN assessment was based on NCI-CTCAE v5.0 and FACT/GOG-Ntx, which provide complementary clinician- and patient-reported information but do not replace objective neurophysiological investigations. Finally, the present study was primarily designed to evaluate the occurrence, severity, and association of CIPN with comorbidity burden and was not powered to develop or validate a predictive model. Therefore, the findings should be considered a basis for future development of validated predictive and clinical decision-support approaches.
Future studies should include larger multicentre populations and longer follow-up to validate these findings and better characterize the development and persistence of CIPN.

## Future Directions

Future studies should include larger multicentre populations and longer follow-up to confirm these findings and better understand the development and persistence of CIPN. Further research should focus on developing and validating predictive models using clinical characteristics, chemotherapy-related factors, CCI, and patient-reported outcomes. Kaplan–Meier analysis and other time-to-event methods could be used to evaluate the timing and persistence of CIPN. In the longer term, pharmacometric modelling could be incorporated into these predictive approaches to support the development of clinical decision-support systems for early identification and individualized monitoring of patients at risk of CIPN.

## Clinical Trial Registration:

Not applicable, as it is prospective observational study

## Conflicts of Interest:

None declared by any author.

## Contribution Details

- ✓ **Mandeep Singh Juneja**: Study design, data acquisition, data analysis, manuscript preparation, manuscript editing
- ✓ **Armagan Shahid**: Data collection, data entry, data segregation, interpretation and manuscript review.
- ✓ **Nandhana Rajesh**: Data collection, literature review, data analysis, report drafting and manuscript review
- ✓ **Dr. Laigin Sebastian**: Academic guidance, study design support, biostatistical analysis and manuscript approval
- ✓ **Dr. ShivaShankar**: Academic oversight and manuscript review
- ✓ **Dr. Shwetha:** Study supervision, clinical guidance, and manuscript approval

## Authorship Criteria

All authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship, including substantial contributions to study design, data collection, analysis, manuscript drafting/revision, and final approval.

## Author Declaration

All authors have read and approved the final manuscript and confirm that it represents original and honest research work.

## Ethical Approval

Approved by the Institutional Ethics Committee, ESIC Medical College & PGIMSR, Rajajinagar, Bengaluru (Approval No.532/L/11/12/Ethics/ESICMCPGIMSR/Estt.Vol IV/2D/2025 dated 02.08.2025). Written informed consent was obtained.

## References

1. Zajączkowska R, Kocot-Kępska M, Leppert W, Wrzosek A, Mika J, Wordliczek J. Mechanisms of chemotherapy-induced peripheral neuropathy. Int J Mol Sci. 2019;20(6):1451. https://doi.org/10.3390/ijms20061451
2. Mattar M, Umutoni F, Hassan MA, Wamburu MW, Turner R, Patton JS, et al. Chemotherapy-induced peripheral neuropathy: A recent update on pathophysiology and treatment. Life (Basel). 2024;14(8):991. https://doi.org/10.3390/life14080991
3. Egashira N. Pathological mechanisms and preventive strategies of oxaliplatin-induced peripheral neuropathy. Front Pain Res (Lausanne). 2021;2:804260. https://doi.org/10.3389/fpain.2021.804260
4. Yang Y, Zhao B, Gao X, Sun J, Ye J, Li J, et al. Targeting strategies for oxaliplatin-induced peripheral neuropathy: Clinical syndrome, molecular basis, and drug development. J Exp Clin Cancer Res. 2021;40(1):331. https://doi.org/10.1186/s13046-021-02141-z
5. Wu S, Xiong T, Guo S, Zhu C, He J, Wang S. An up-to-date view of paclitaxel-induced peripheral neuropathy. J Cancer Res Ther. 2023;19(6):1501-1508. https://doi.org/10.4103/jcrt.jcrt_1982_22
6. Ocean AJ, Vahdat LT. Chemotherapy-induced peripheral neuropathy: Pathogenesis and emerging therapies. Support Care Cancer. 2004;12(9):619-625. https://doi.org/10.1007/s00520-004-0657-7

7. Haryani H, Fetzer SJ, Wu CL, Hsu YY. Chemotherapy-induced peripheral neuropathy assessment tools: A systematic review. Oncol Nurs Forum. 2017;44(3):E111-E123. https://doi.org/10.1188/17.ONF.E111-E123
8. Burgess J, Ferdousi M, Gosal D, Boon C, Matsumoto K, Marshall A, et al. Chemotherapy-induced peripheral neuropathy: Epidemiology, pathomechanisms and treatment. Oncol Ther. 2021;9(2):385-450. https://doi.org/10.1007/s40487-021-00168-y
9. Mezzanotte JN, Grimm M, Shinde NV, Nolan T, Worthen-Chaudhari L, Williams NO, et al. Updates in the treatment of chemotherapy-induced peripheral neuropathy. Curr Treat Options Oncol. 2022;23(1):29-42. https://doi.org/10.1007/s11864-021-00926-0
10. Wang C, Chen S, Jiang W. Treatment for chemotherapy-induced peripheral neuropathy: A systematic review of randomized control trials. Front Pharmacol. 2022;13:1080888. https://doi.org/10.3389/fphar.2022.1080888
11. Molinares D, Kurtevski S, Zhu Y. Chemotherapy-induced peripheral neuropathy: Diagnosis, agents, general clinical presentation, and treatments. Curr Oncol Rep. 2023;25(11):1227–35. Available from: https://doi.org/10.1007/s11912-023-01449-7
12. Loprinzi CL, Lacchetti C, Bleeker J, Cavaletti G, Chauhan C, Hertz DL, et al. Prevention and management of chemotherapy-induced peripheral neuropathy in survivors of adult cancers: ASCO guideline update. J Clin Oncol. 2020;38(28):3325–48. Available from: https://doi.org/10.1200/JCO.20.01399
13. Preti K, Davis ME. Chemotherapy-induced peripheral neuropathy: Assessment and treatment strategies for advanced practice providers. Clin J Oncol Nurs. 2024;28(4):351–7. Available from: https://doi.org/10.1188/24.CJON.351-357
14. Batash R, Asna N, Ali SH, Charkovsky T, Asali M, Pelles S, et al. Management of chemotherapy-induced peripheral neuropathy (CIPN) in oncologic patients—A new promise? Preliminary results. Cancers (Basel). 2025;17(20):3321. Available from: https://doi.org/10.3390/cancers17203321
15. Sałat K. Chemotherapy-induced peripheral neuropathy—Part 2: Focus on the prevention of oxaliplatin-induced neurotoxicity. Pharmacol Rep. 2020;72(3):508–27. Available from: https://doi.org/10.1007/s43440-020-00106-1
16. Donovan HS, Campbell GB. Persistent chemotherapy-induced peripheral neuropathy: Are dose reductions and drug modifications our only options? Gynecol Oncol. 2018;149(3):433–4. Available from: https://doi.org/10.1016/j.ygyno.2018.05.003
17. Gießen-Jung C, von Baumgarten L. Peripheral neuropathy as a side effect of chemotherapy and targeted therapy. Dtsch Med Wochenschr. 2018;113(13):970–8. Available from: https://doi.org/10.1055/s-0043-120839
18. Saad M, Tafani C, Psimaras D, Ricard D. Chemotherapy-induced peripheral neuropathy in the adult. Curr Opin Oncol. 2014;26(6):634–41. Available from: https://doi.org/10.1097/CCO.0000000000000139
19. Wang RY, Lin XL, Xiang ST, Sun QH, Ding XH. Risk factors for oxaliplatin-induced peripheral neuropathy: A systematic review and meta-analysis. Eur Rev Med Pharmacol Sci. 2022;26(11):4028–43. Available from: https://doi.org/10.26355/eurrev_202206_28973
20. Pulvers JN, Marx G. Factors associated with the development and severity of oxaliplatin-induced peripheral neuropathy: A systematic review. Asia Pac J Clin Oncol. 2017;13(6):345–55. Available from: https://doi.org/10.1111/ajco.12694
21. Lixian S, Xiaoqian Y, Luyan G, Lizhi Z, Rui D, Hongyue Y, et al. Risk factors of paclitaxel-induced peripheral neuropathy in patients with breast cancer: A prospective cohort study. Front Oncol. 2024;14:1327318. Available from: https://doi.org/10.3389/fonc.2024.1327318
22. Hiramoto S, Asano H, Miyamoto T, Takegami M, Kawabata A. Risk factors and pharmacotherapy for chemotherapy-induced peripheral neuropathy in paclitaxel-treated female cancer survivors: A

retrospective study in Japan. PLoS One. 2021;16(12):e0261473. Available from: https://doi.org/10.1371/journal.pone.0261473

23. St Germain DC, O'Mara AM, Robinson JL, Torres AD, Minasian LM. Chemotherapy-induced peripheral neuropathy: Identifying research gaps and associated changes to clinical trial design. Cancer. 2020;126(20):4602–13. Available from: https://doi.org/10.1002/cncr.33108
24. Postma TJ, Heimans JJ. Grading of chemotherapy-induced peripheral neuropathy. Ann Oncol. 2000;11(5):509–13. Available from: https://doi.org/10.1023/a:1008345613594
25. Mols F, Beijers T, Vreugdenhil G, van de Poll-Franse L. Chemotherapy-induced peripheral neuropathy and its association with quality of life: A systematic review. Support Care Cancer. 2014;22(8):2261–9. Available from: https://doi.org/10.1007/s00520-014-2255-7
26. Beijers A, Mols F, Dercksen W, Driessen C, Vreugdenhil G. Chemotherapy-induced peripheral neuropathy and impact on quality of life 6 months after treatment. J Community Support Oncol. 2014;12(11):401–6. Available from: https://doi.org/10.12788/jcso.0086
27. Scheel A, Beijers AJM, Mols F, Faber CG, Vreugdenhil G. Chemotherapy-induced peripheral neuropathy: Impact on quality of life. Ned Tijdschr Geneeskd. 2014;158:A7455 27. Scheel A, Beijers AJM, Mols F, Faber CG, Vreugdenhil G. Chemotherapy-induced peripheral neuropathy: Impact on quality of life. Ned Tijdschr Geneeskd. 2014;158:A7455. Available from: https://pubmed.ncbi.nlm.nih.gov/25270958/
28. Hung HW, Liu CY, Chen HF, Chang CC, Chen SC. Impact of chemotherapy-induced peripheral neuropathy on quality of life in advanced lung cancer patients receiving platinum-based chemotherapy. Int J Environ Res Public Health. 2021;18(11):5677. Available from: https://doi.org/10.3390/ijerph18115677
29. Matsuoka H, Nakamura K, Matsubara Y, Ida N, Saijo M, Ogawa C, et al. Influence of chemotherapy-induced peripheral neuropathy on quality of life of gynecologic cancer survivors. Int J Gynecol Cancer. 2018;28(7):1394–402. Available from: https://doi.org/10.1097/IGC.0000000000001320
30. Tofthagen C. Patient perceptions associated with chemotherapy-induced peripheral neuropathy. Clin J Oncol Nurs. 2010;14(3):E22–8. Available from: https://doi.org/10.1188/10.CJON.E22-E28
31. Hertz DL. Exploring pharmacogenetics of paclitaxel- and docetaxel-induced peripheral neuropathy by evaluating the direct pharmacogenetic-pharmacokinetic and pharmacokinetic-neuropathy relationships. Expert Opin Drug Metab Toxicol. 2021;17(2):227-239. https://doi.org/10.1080/17425255.2021.1856367
32. Trivedi MS, Unger JM, Henry NL, Darke AK, Hertz DL, Brannagan TH, et al. Risk prediction model for taxane-induced peripheral neuropathy in early-stage cancer. JAMA Netw Open. 2026;9(4):e264901. https://doi.org/10.1001/jamanetworkopen.2026.4901
33. Sánchez-Barroso L, Apellaniz-Ruiz M, Gutiérrez-Gutiérrez G, et al. Concomitant medications and risk of chemotherapy-induced peripheral neuropathy. *The Oncologist*. 2019;24(8):e784-e792. https://doi.org/10.1634/theoncologist.2018-0418

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