Platinum and Taxane-Induced Neuropathy and Its Impact on Quality of Life: A Single Institution Study

El-Morshidy SM[1], Haridy NAA[2], Mohamed TZ[1], Fathey WK[1], Hassan MA[1]

[1] Clinical Oncology Department, Faculty of Medicine, Assiut University
[2] Department of Neurology and Psychiatry, Faculty of Medicine, Assiut University

Abstract:

Background: Chemotherapy-induced peripheral neuropathy (CIPN) is a common and challenging complication of platinum and taxane agents and can have a significant impact on patients' quality of life (QoL).

Objective: This study aims to detect the frequency and severity of CIPN in patients receiving Platinum and Taxane compounds and their effect on QoL.

Methods: This prospective study enrolled 47 patients receiving neurotoxic chemotherapy (taxanes and platinum-based agents) at Assiut University Hospital's Clinical Oncology Department between March 2023 and July 2024, with a median 6-month follow-up. CIPN was detected, graded, and assessed clinically by using the NCI-CTCAE v5.0 criteria and electrophysiologically through nerve conduction studies conducted in collaboration with the Neurology Department. Health-related quality of life (HRQoL) was evaluated using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30).

Results: In this study, altered sensory symptoms occurred in 80-86.7% of patients across all regimens. Neuropathy grading revealed grade II in 44% of patients, grade I in 29%, and grade III in 25%. Platinum-based regimens were significantly associated with grade II neuropathy ($p<0.001$), while platinum+taxane combinations showed the highest rate of grade III neuropathy ($p=0.05$). Nerve conduction studies demonstrated significant post-chemotherapy reductions in sensory nerve action potential (SNAP) and motor conduction velocities (MCV) ($p<0.001$). Higher CIPN grades correlated significantly with worse global health status (commonly with patients received platinum + taxane combinations), reduced physical function, and increased symptom burden on both QLQ-C30 and NCI-CTCAE V5 scales ($p<0.014$).

Conclusion: CIPN is a frequent and devastating complication in patients receiving taxane and platinum-based chemotherapy, with significant clinical, neurophysiological, and QoL implications. Future research should focus on strategies to prevent and mitigate this debilitating side effect.

Trial Registration: (IRB 042023200122).

Keywords: Chemotherapy-induced peripheral neuropathy (CIPN), Platinum compounds, Taxanes, Quality of life (QoL), Nerve conduction studies

Received: 5 August 2025
Accepted: 1 September 2025

Authors Information:

Summar Mohamed El-Morshidy
Clinical Oncology Department, Faculty of Medicine, Assiut University
email: Summerelmorshidey@aun.edu.eg

Nourelhoda Ahmed Ahmed Haridy
Department of Neurology and Psychiatry, Faculty of Medicine, Assiut University
email: nourelhodaahmed@aun.edu.eg

Taha Zaki Mohamed
Clinical Oncology Department, Faculty of Medicine, Assiut University
email: taha_mohran@aun.edu.eg

Walaa Khalifa Fathey
Clinical Oncology Department, Faculty of Medicine, Assiut University
email: Walaa.14224161@med.aun.edu.eg

Mohamed Alaa Eldeen Hassan
Clinical Oncology Department, Faculty of Medicine, Assiut University
email: alaaoncology@aun.edu.eg

Corresponding Author:
Walaa Khalifa Fathey
Clinical Oncology Department, Faculty of Medicine, Assiut University
email: Walaa.14224161@med.aun.edu.eg

Introduction:

Chemotherapy-induced peripheral neuropathy (CIPN) is a prevalent and difficult complication arising from many commonly used antineoplastic drugs. A meta-analysis of randomized controlled trials and cohort studies indicated that nearly 50% of patients experience CIPN during their treatment [1, 2]. Peripheral neuropathy is a recognized side effect of chemotherapy that influences patients' physical, emotional, and cognitive well-being, leading to a decrease in their quality of life (QoL) and may be linked to pain. The onset of CIPN can lead to extended infusion times, dosage reductions, or the early termination of chemotherapy, which could adversely affect both treatment effectiveness and patient survival [3, 4].

The severity of polyneuropathy can last and even progress for months after chemotherapy had finished a phenomenon known as the “coasting effect”. The agents most commonly associated with neuropathy are

platinum-based compounds (eg,cisplatin, carboplatin, oxaliplatin) [5], antimitotic agents like taxanes (eg, paclitaxel, docetaxel) [6, 7], vinca alkaloids (eg, vincristine, vinblastine, vinorelbine, vinflunine) [8].

There is still no consensus on the ideal standardized assessment tool for evaluating CIPN in research and clinical practice. Currently, the most widely used measure is the neuropathy subscale of the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) , The latest version of the NCI-CTCAE (version 5.0) grades both motor and sensory neuropathy according to asymptomatic (grade 1), moderate (grade 2), severe (grade 3) or life-threatening (grade 4) neurotoxicity [9].

Nerve conduction studies (NCS) provide an unbiased assessment of large fiber function and are regarded as the gold standard for identifying large fiber involvement in CIPN. Demyelination of peripheral nerves results in slower conduction and increased latency, while axonal damage leads to a decrease in amplitude [10].

Although CIPN is a common, disabling toxicity of platinum and taxane agents that can impair function and QoL, data on post-treatment recovery, cumulative dose severity relationships, and QoL impact are limited, particularly in real-world settings from low- and middle-income countries. This study aims to detect the incidence of neuropathy and prospectively evaluate CIPN patterns, dose-response effects, recovery outcomes, and their impact on QoL.

Patients and Methods:

Study Design, Setting and Ethical approval

This prospective observational study was conducted at the Clinical Oncology Department of Assiut University Hospital, in collaboration with the Neurology Department for the conduction of nerve conduction studies. The study enrolled 47 patients between March 2023 and July 2024, and each participant was followed for a median duration of 6 months.

The study protocol was approved by the Assiut University Hospital's Ethics Committee (IRB 042023200122), and informed consent was obtained from all participants before inclusion.

Participants

Inclusion criteria were 1) adult patients aged 18 years or older and younger than 75 years, 2) both sexes were included, 3) patients with histopathologically confirmed solid tumors. 4) Patients were included regardless of whether they were receiving chemotherapy in the adjuvant or metastatic setting, provided their treatment regimens contained known neurotoxic agents such as oxaliplatin, carboplatin, cisplatin, docetaxel, or paclitaxel.

Patients were excluded if 1) they had concomitant neurologic conditions that might complicate the interpretation of neuropathic findings, 2) were receiving antiepileptic drugs, antidepressants, or major analgesics (unless on a stable regimen), or 3) had peripheral nerve damage resulting from illnesses unrelated to chemotherapy such as congenital neuropathies or diabetes mellitus. 4) Patients diagnosed with hematological malignancies were also excluded from the study.

Data collection

Our patients were indicated to receive regimens containing neurotoxic agents, including Paclitaxel, Cisplatin, Oxaliplatin, and Carboplatin.

These patients had CIPN identified, graded, and evaluated clinically as well as by nerve Conduction Studies.

A total of 47 patients were included in this study. All enrolled patients underwent a comprehensive baseline clinical assessment, including evaluation of performance status and documentation of chemotherapy-related variables. These included the type of chemotherapeutic agent administered categorized as either platinum-based or taxane-based the total number of chemotherapy cycles received, and the cumulative dose of the administered drugs.

Neurological evaluation was performed both before initiating chemotherapy and after the completion of 4 to 6 cycles. The clinical neurological examination focused on muscle strength, superficial and deep sensation, deep tendon reflexes, and signs or symptoms of autonomic involvement.

To complement the clinical evaluation, all patients underwent a standardized electrophysiological assessment. NCS were conducted for both sensory and motor nerves in the right upper and lower extremities. Specifically, the median, ulnar, posterior tibial nerve (PTN), and common peroneal nerve (CPN) were evaluated using the Nihon Kohden Machine model 9400 (Japan), following the methodology described by Carpenter and Reddi (2012) [11]. These neurophysiological studies were performed as early as possible after inclusion and were repeated after 4-6 cycles of chemotherapy to assess the progression or emergence of CIPN.

All pre-chemotherapy electrophysiological parameters were required to fall within normal physiological limits to ensure accurate identification of new-onset CIPN.

Outcome Assessment

The incidence and severity of CIPN were evaluated using the National Cancer Institute's Common Terminology Criteria for Adverse Events, version 5.0 (NCI-CTCAE v5.0) [12]. CIPN was assessed at three time points: at baseline, following completion of 4 to 6 chemotherapy cycles, and again at the end of the follow-up period.

Health-related quality of life (HRQoL) and the impact of CIPN were evaluated using validated patient-reported outcome measures. The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) Fayers et al., (2014) [13] was used to assess general HRQoL, while the QLQ-CIPN30 questionnaire was applied at the end of the follow-up period to specifically

evaluate the impact of peripheral neuropathy on quality of life.

Follow-up and Monitoring

Throughout the 6-month follow-up period, patients were systematically monitored for progression or improvement of neuropathy symptoms, the use of supportive treatments, and the effect of neuropathy on their quality of life. The primary outcomes of interest were the development and grading of CIPN, as well as patient-reported functional limitations due to neuropathic symptoms. The type of cancer was not considered a variable influencing outcomes and was thus not factored into the analysis.

Statistical analysis

All statistical calculations were done using SPSS (Statistical Package for the Social Sciences; SPSS Inc., Chicago, IL, USA) version 27. Data were statistically described in terms of mean ± standard deviation (±SD), or median and range when the data were not normally distributed, frequencies (number of cases), and relative frequencies (percentages) when appropriate. Comparison of quantitative variables was done using the Kruskal-Wallis test as the data were not normally distributed. The Wilcoxon signed-rank test was used for comparing paired continuous data. For comparing categorical data, a chi-squared ($\chi 2$) test was performed. The exact test was used instead when the expected frequency is less than 5, achieved by applying≥25% of cells, continuity correction, or the likelihood ratio. The p-value is always 2-tailed and set at a significance level of 0.05.

Results:

A total of 47 patients were enrolled in this prospective study to assess chemotherapy-induced neuropathy, its association with treatment regimens, follow-up outcomes, and management strategies. Of these, 42 patients completed follow-up and the EORTC QLQ-C30 questionnaire to evaluate health-related quality of life.

Demographic and clinical characteristics of the study participants

The study enrolled 47 patients, with a mean age of 51.9 ± 14.5 years; 68.1% of the patients were female. The majority had good performance status (PS). Our patients didn't receive previous chemotherapy, as they were de novo, and 44.7% had metastatic disease, with no comorbidity, with a median follow-up period of six months (Table 1).

The two most common cancers were breast cancer (27.7%) and colon cancer (21.3%), with mean ages of 41.6 and 45.7 years, respectively. The female-to-male ratio in colon cancer patients was 4:1. In contrast, lung cancer was the least common type (4.3%), with a mean age of 67.5 years, and all patients were male. Our patients received various chemotherapeutic regimens, most commonly cisplatin/gemcitabine in 34% of patients, followed by Paclitaxel only in 25.5% of patients and FOLFOX in 23%. In contrast, FOLFIRINOX was only received by three patients (6%). Sixteen patients (34%) received Cisplatin, fourteen patients (29.8%) received Oxaliplatin, and twelve patients (25.5%) received paclitaxel alone, however, only five patients (10.6%) received Carboplatin+paclitaxel

Chemotherapy-Induced Peripheral Neuropathy (CIPN) in the study participants

In term of symptoms of CIPN, after finishing the prescribed chemotherapy protocols, altered sensory symptoms were expressed in 86.7%, 83.3%, and 80% of patients receiving platinum only or combination (n=30), Taxanes only or combinations (n=12), and platinum + Taxanes combinations (n=5) respectively, while variable grades of weakness were detected in 60%, 25%, and 16.7% of platinum +Taxanes, Taxanes-based combination, and platinum-based combinations respectively.

Regarding the distribution of neuropathy grades, most patients developed grade II neuropathy (44%), followed by grade I (29%) and grade III (25%). Among those receiving platinum-based regimens, 16 patients (53.3%) developed grade II neuropathy compared to 4 patients (33.3%) on taxane-based and one patient (20%) on platinum + taxane regimens ($p < 0.001$). Grade III neuropathy occurred in 8 patients (26.7%) on platinum-based, two patients (16.7%) on taxane-based, and two patients (40%) on combined regimens ($p = 0.05$). However, no significant difference was observed among individual agents (cisplatin, oxaliplatin, carboplatin, paclitaxel) ($p = 0.27$) (Table 2).

Regarding the dose-response relationship, higher grades of neuropathy were associated with progressively increasing cumulative doses of chemotherapy, but this trend was significant only for cisplatin and oxaliplatin ($p = 0.006$ and $p = 0.003$, respectively). For both agents, patients with grade III neuropathy received the highest cumulative doses compared to those with grades I and II. No significant dose-related association was observed for paclitaxel ($p = 0.08$). The number of treatment cycles or weeks did not significantly differ across neuropathy grades for any drug (Table 3).

Pre- versus Post-Treatment Nerve Conduction Changes

Significant deterioration was observed in both motor and sensory studies after chemotherapy (Table 4). The median nerve showed the most significant changes, with prolonged distal latency, reduced CMAP amplitude, and slowed conduction velocity ($p < 0.001$). Ulnar nerve changes were similar but milder, while the common peroneal nerve showed isolated latency prolongation ($p < 0.001$). The posterior tibial nerve was largely unaffected. In sensory studies, the median and ulnar nerves exhibited marked latency prolongation and conduction slowing; the ulnar nerve also showed a significant reduction in SNAP amplitude ($p < 0.001$). Sural nerve involvement was minimal, limited to changes in latency. These findings indicate the multifocal, length-dependent, and predominantly mixed

(axonal and demyelinating) pattern of chemotherapy-induced peripheral neuropathy.

Post-Treatment Nerve Conduction by Chemotherapy Regimen

Differences across chemotherapy regimens are presented in Table 5. Combination therapy (platinum + taxane) produced the most significant reduction in CMAP amplitude (common peroneal nerve) and slowing of posterior tibial conduction velocity ($p = 0.010$). Ulnar nerve SNAP amplitude and sural SNAP amplitude were most severely reduced in the combination group ($p < 0.001$ and $p = 0.004$, respectively). These findings indicate that combined regimens exert the most pronounced neurotoxic effects.

Regarding treatment and recovery of CIPN, during a median follow-up of 6 months (range: 1–12), most patients (78.7%) received neurotonics, while those with moderate to severe neuropathy (grades 2–3) additionally received pregabalin.

Of the 47 enrolled patients, five (10.6%) died from causes unrelated to neuropathy and were excluded from outcome analysis. Recovery was significantly influenced by baseline severity ($p = 0.034$). Almost all patients with initial grade I (92.3%) and most with grade II (68.4%) achieved complete resolution. In contrast, only 40% of grade III cases fully recovered, while another 40% remained with residual grade II neuropathy (Table 6).

Analysis by chemotherapy regimen showed higher complete recovery rates in taxane-based regimens (81.8%) and carboplatin--taxane combinations (80%) compared with platinum-based therapy (61.5%), though this difference was not statistically significant ($p = 0.200$). Overall, these findings suggest that early-grade neuropathy is more likely to resolve, whereas severe neuropathy at onset carries a higher risk of persistent symptoms despite treatment (Table 6).

Health-Related Quality of Life (HRQoL)

The EORTC QLQ-C30 results (Table 7) showed that among functional domains, physical functioning scored the highest (mean 96.2 ± 7.1), indicating preserved mobility, whereas cognitive functioning was the lowest (81.0 ± 14.1). Among symptom scales, fatigue had the highest score (85.0 ± 16.2), representing the most burdensome symptom, while nausea and vomiting had the lowest (7.94 ± 9.2), indicating minimal impact. For single-item symptoms, financial difficulties had the highest mean score (18.3 ± 23.6), while dyspnea had the lowest (0.8 ± 5.1).

When comparing chemotherapy regimens (Table 8), global QoL was highest in patients receiving platinum-based therapy (84.44 ± 6.21) meaning that global QoL not severly affected in those patients with ($p = 0.05$). Physical functioning showed no significant variation between regimens ($p = 0.2$).

However, neuropathy severity significantly influenced physical functioning ($p = 0.014$), which declined progressively from grade I to III. In contrast, neither global QoL nor summary scores were significantly affected by neuropathy grade. These findings suggest that higher neuropathy grades mainly impaired physical functioning rather than overall QoL perception.

Table 1. Demographic characteristics of patients studied (N = 47)

Variable	Value
Age (years)	Mean ± SD 51.9 ± 14.5; median (range) 53 (24-74)
Sex, n (%)	Male: 15 (31.9%), Female: 32 (68.1)
Smoking Status, n (%)	Non-smoker: 32 (68.1%) Active: 6 (12.8%) Ex-smoker: 4 (8.5%) Passive: 5 (10.6%)
Body Surface Area (m²)	1.73 ± 0.15; median 1.73 (1.4-2.1)
ECOG Performance Status (PS), n (%)	PS= 0: 13 (22.7%) PS=1: 26 (55.3%) PS=2: 8 (17%)
Comorbidities	None
Previous Chemotherapy	None
Metastatic Disease, n (%)	Yes: 21 (44.7%), No: 26 (55.3%)
Chemotherapy Regimen, n (%)	Oxaliplatin: 14 (29.8%) Paclitaxel: 12 (25.5%) Cisplatin: 16 (34.0%) Carboplatin + Paclitaxel: 5 (10.6%)
Median No. of Chemotherapy Courses (range)	4-6
Median months follow-up (range)	6 (1-12)

Data are presented as mean ± SD and median (range) or number (percentage).

Table 2. Distribution of Neuropathy Grades Across Chemotherapy Regimens.

Neuropathy grade	Platinum-based	Taxane-based	Platinum + Taxane	p-value
Grade 1 (n=14)	6 (30%)	6 (50%)	2 (40%)	0.3
Grade 2 (n=21)	16 (53.3%)	4 (33.3%)	1 (20%)	**<0.001**
Grade 3 (n=12)	8 (26.7%)	2 (16.7%)	2 (40%)	**0.05**
p-value		0.27		

Data are expressed as numbers (percentages) and analyzed using a Chi-squared test with continuity correction.

Table 3: Dose-Response Relationship Between Cumulative Chemotherapy Dose and Neuropathy Grade

Drug	Parameter	Grade 1 Median (Range)	Grade 2 Median (Range)	Grade 3 Median (Range)	*p*-value
Cisplatin	Cumulative dose (mg/m²)	423.7 (420.3-427.14)	555.4 (482.4-656.7)	734.9 (513.81-806.1)	**0.006**
	No. of cycles	3 (3-4)	4 (3-5)	4 (4-6)	0.6
Oxaliplatin	Cumulative dose (mg/m²)	361.1 (336.5-424.3)	435.5 (383.5-513.81)	593.4 (465.6-635.3)	**0.003**
	No. of cycles	4 (4-4)	4 (4-6)	4 (4-6)	0.5
Paclitaxel	Cumulative dose (mg/m²)	1192.6 (385.4-1272.8)	1056.2 (389.6-1467.1)	1449.5 (1381.9-1517.2)	0.08
	No. of weeks	9 (9-12)	9 (9-11)	11 (9-12)	0.6

Data are expressed as median (range). Analysis conducted using the Kruskal-Wallis test. $p < 0.05$ is considered statistically significant.

Table 4. Pre- and Post-Chemotherapy Nerve Conduction Parameters (N = 47)

Nerve	Parameter	Pre-treatment	Post-treatment	p-value
		Motor Conduction		
Median	MDL (ms)	3.32 ± 0.41	3.60 ± 0.40	0.005
	CMAP (mV)	10.04 ± 3.73	7.33 ± 3.40	<0.001
	MCV (m/s)	61.2 ± 6.91	51.53 ± 17.53	0.002
Ulnar	MDL (ms)	2.55 ± 0.20	2.70 ± 0.30	0.012
	CMAP (mV)	8.34 ± 2.30	7.94 ± 9.50	0.800
	MCV (m/s)	65.94 ± 6.20	55.00 ± 16.00	<0.001
Posterior Tibial	MDL (ms)	4.02 ± 0.70	4.03 ± 0.61	0.900
	CMAP (mV)	8.40 ± 2.60	6.70 ± 6.45	0.090
	MCV (m/s)	48.9 ± 4.5	48.2 ± 5.5	0.500
Common peroneal	MDL (ms)	3.50 ± 0.8	4.0 ± 0.9	<0.001
	CMAP (mV)	4.84 ± 2.6	4.6 ± 2.4	0.6
	MCV (m/s)	52.2 ± 10.0	50.23 ± 8.8	0.3
		Sensory Conduction		
Median	SDL (ms)	3.25 ± 0.40	3.90 ± 0.52	<0.001
	SNAP (μV)	33.73 ± 19.3	50.73 ± 57.4	0.080
	SCV (m/s)	43.11 ± 6.2	36.74 ± 4.83	<0.001
Ulnar	SDL (ms)	2.91 ± 0.30	3.30 ± 0.51	<0.001
	SNAP (μV)	28.6 ± 25.4	14.9 ± 13.0	<0.001
	SCV (m/s)	46.65 ± 5.7	42.4 ± 5.4	<0.001
Sural	SDL (ms)	2.71 ± 0.91	3.70 ± 1.00	<0.001
	SNAP (μV)	12.2 ± 14.1	27.6 ± 53.9	0.080
	SCV (m/s)	45.9 ± 9.7	43.9 ± 23.2	0.600

Data are mean ± SD. Wilcoxon signed-rank test used. $p \leq 0.05$ is significant. Abbreviations: CMAP, compound motor action potential; MDL, motor distal latency; MCV, motor conduction velocity; SDL, sensory distal latency; SNAP, sensory nerve action potential; SCV, sensory conduction velocity.

Table 5. Post-Chemotherapy Nerve Conduction Parameters by Regimen (N = 47)

Nerve	Parameter	Platinum (n=30)	Taxane (n=12)	Combination (n=5)	p-value
Motor Conduction					
Median	MDL (ms)	3.6 ± 0.37	3.6 ± 0.48	3.4 ± 0.18	0.400
	CMAP (mV)	7.3 ± 3.1	7.8 ± 4.4	6.0 ± 3.0	0.200
	MCV (m/s)	48.2 ± 21.3	57.6 ± 4.7	56.6 ± 2.9	0.600
Ulnar	MDL (ms)	2.75 ± 0.25	2.6 ± 0.21	2.3 ± 0.20	0.001
	CMAP (mV)	8.5 ± 11.8	7.3 ± 1.5	6.3 ± 2.0	0.900
	MCV (m/s)	56.5 ± 13.5	48.1 ± 22.4	62.5 ± 2.0	0.200
Posterior Tibial	MDL (ms)	4.1 ± 0.7	4.2 ± 0.4	3.5 ± 0.3	0.060
	CMAP (mV)	7.7 ± 7.7	5.4 ± 2.5	3.7 ± 1.3	0.300
	MCV (m/s)	48.1 ± 4.5	50.9 ± 7.1	42.2 ± 0.8	0.010
Common Peroneal	MDL (ms)	4.0 ± 0.9	4.4 ± 0.8	3.1 ± 0.3	0.015
	CMAP (mV)	5.1 ± 2.4	4.6 ± 1.7	1.3 ± 0.2	0.003
	MCV (m/s)	48.1 ± 8.7	56.4 ± 6.1	44.5 ± 5.8	0.010
Sensory Conduction					
Median	SDL (ms)	4.0 ± 0.6	3.9 ± 0.5	3.6 ± 0.1	0.600
	SNAP (μV)	53.6 ± 55.7	30.2 ± 13.0	84.7 ± 109.7	0.300
	SCV (m/s)	37.5 ± 4.9	36.3 ± 4.7	33.6 ± 4.5	0.500
Ulnar	SDL (ms)	3.5 ± 0.5	3.1 ± 0.4	3.0 ± 0.3	0.019
	SNAP (μV)	50.0 ± 61.8	43.3 ± 52.4	13.5 ± 10.9	<0.001
	SCV (m/s)	41.1 ± 5.6	45.9 ± 4.6	41.8 ± 1.1	0.032
Sural	SDL (ms)	3.8 ± 1.0	3.4 ± 0.9	3.4 ± 0.0	0.600
	SNAP (μV)	34.3 ± 65.2	21.3 ± 21.3	2.0 ± 4.5	0.004
	SCV (m/s)	44.6 ± 27.1	40.0 ± 13.7	26.6 ± 47.7	0.400

Data are mean ± SD. Kruskal-Wallis test used. $p < 0.05$ is significant. Abbreviations: CMAP, compound motor action potential; MDL, motor distal latency; MCV, motor conduction velocity; SDL, sensory distal latency; SNAP, sensory nerve action potential; SCV, sensory conduction velocity.

Table 6. Neuropathy Outcomes at Follow-Up by Initial Grade and Chemotherapy Regimen

Variable	Neuropathy Outcome: n (%)	p-value
At the End of Follow-Up by Initial Neuropathy Grade		
Initial Grade 1 (n = 13)	Complete improvement: 12 (92.3%)	0.034
	Residual Grade 1: 1 (7.7%)	
Initial Grade 2 (n = 19)	Complete improvement: 13 (68.4%)	
	Residual Grade 1: 4 (21.1%)	
	Residual Grade 2: 2 (10.5%)	
Initial Grade 3 (n = 10)	Complete improvement: 4 (40.0%)	
	Residual Grade 1: 2 (20.0%)	
	Residual Grade 2: 4 (40.0%)	
At the End of the Treatment by the Chemotherapy Regimen		
Platinum-Based (n = 26)	Complete improvement: 16 (61.5%)	0.2
	Grade 1: 5 (19.2%)	
	Grade 2: 5 (19.2%)	
Taxane-Based (n = 11)	Complete improvement: 9 (81.8%)	
	Grade 1: 2 (18.2%)	
	Grade 2: 0 (0%)	
Carboplatin + Taxane (n = 5)	Complete improvement: 4 (80.0%)	
	Grade 1: 0 (0%)	
	Grade 2: 1 (20.0%)	

A total number of patients=42. Data expressed as numbers and percentages were analyzed using the likelihood ratio test. $p < 0.05$ is significant.

Table 7. EORTC QLQ-C30 Scores of Study Participants (n = 42)

Domain	Mean ± SD	Median (Range)
Functional Scales		
Physical Functioning	96.2 ± 7.1	100 (73.3–100)
Role Functioning	85.3 ± 10.5	83.3 (66.7–100)
Cognitive Functioning	81.0 ± 14.1	83.3 (16.7–100)
Emotional Functioning	83.7 ± 13.1	83.3 (22.2–100)
Social Functioning	85.0 ± 16.2	83.3 (33.3–100)
Global QoL	81.2 ± 5.8	83.3 (66.7–91.7)
Symptom Scales		
Fatigue	85.0 ± 16.2	83.3 (33.3–100)
Nausea/Vomiting	7.9 ± 9.2	0.0 (0.0–33.3)
Pain	27.5 ± 16.2	33.3 (0.0–67.7)
Single-Item Symptoms		
Loss of Appetite	8.7 ± 14.8	0.0 (0.0–33.3)
Diarrhea	3.3 ± 10.0	0.0 (0.0–33.3)
Constipation	1.6 ± 7.2	0.0 (0.0–33.3)
Dyspnea	0.8 ± 5.1	0.0 (0.0–33.3)
Insomnia	7.9 ± 14.4	0.0 (0.0–33.3)
Financial Impact	18.3 ± 23.6	0.0 (0.0–100)

Scores range from 0–100. For functional and global QoL scales, higher scores indicate better functioning; for symptom scales, higher scores indicate greater symptom burden.

.

Table 8. Impact of Chemotherapy Regimen and Neuropathy Grade on HRQoL Domains

QLQ-C30 Domain	Chemotherapy Regimen	p-value	Neuropathy Grade	p-value
Global QoL	Platinum: 84.4 ± 6.2 Taxane: 80.1 ± 2.5 Carboplatin + Taxane: 78.3 ± 7.5	0.05	Grade 1: 82.7 ± 2.3 Grade 2: 81.4 ± 5.5 Grade 3: 79.5 ± 8.7	0.6
Physical Function	Platinum: 95.4 ± 7.2 Taxane: 98.8 ± 2.7 Carboplatin + Taxane: 94.7 ± 11.9	0.2	Grade 1: 98.7 ± 5.0 Grade 2: 96.5 ± 3.7 Grade 3: 90.6 ± 10.2	0.014
Financial Impact	Platinum: 21.9 ± 26.7 Taxane: 12.1 ± 16.8 Carboplatin + Taxane: 13.3 ± 18.3	0.4	Grade 1: 17.9 ± 29.2 Grade 2: 22.3 ± 23.1 Grade 3: 12.1 ± 16.8	0.5
Summary Score	Platinum: 87.6 ± 4.4 Taxane: 90.5 ± 2.0 Carboplatin + Taxane: 88.9 ± 7.8	0.07	Grade 1: 88.8 ± 4.0 Grade 2: 88.7 ± 3.3 Grade 3: 87.7 ± 6.7	0.8

Data were expressed as Mean ± SD. The Welch test is used for comparisons. $p < 0.05$ is considered significant.

Discussion:

The occurrence of CIPN varies based on the specific agent used, with incidence rates ranging between 19% and more than 85%. The highest incidence is observed with platinum-based agents (70–100%), followed by taxanes (11–87%), and thalidomide along with its derivatives (20–60%) (2). Our findings showed that (80-86.7%) of patients across all regimens experienced altered sensory symptoms while motor weakness of any grade was detected in (16%) of taxane-based, (25%) of platinum-based and (60%) of platinum+taxane combination groups.

Similarly, A study by Argyriou et al., supported our findings that sensory symptoms, such as numbness and tingling, were highly prevalent regardless the regimens while motor weakness was more common in platinum + taxane combinations [1].

Our patient characteristics showed that the mean age of patients was (51.9) years old and patients were divided by sex (32 females to 15 male). We included both metastatic (44.7%) and non- metastatic (55.3%) cases. As regard CIPN, patients received different

chemotherapy protocols and developed different grades of neuropathy where (44%) of them developed grade II neuropathy followed by grade I (29%) and (25%) developed grade III.

A study by Ahmed et al showed that the incidence of CIPN reached (46.8%), where most of them (70%) were grade I, and only (4.4%) developed grade III [14].

More specifically, a statistically significant association was observed between regimen type and the development of grade II neuropathy ($p<0.001$) with the highest proportion occurring in the platinum based group (53.3%), suggesting a stronger link between platinum compounds and moderate CIPN. For grade III neuropathy, a borderline significant difference was noted ($p=0.05$) with the combination regimen showing the highest proportion (40%), possibly reflecting a synergistic neurotoxic effect.

Likewise, Park et al showed that patients receiving platinum + taxane combinations had a lower rate of grade II neuropathy (20%), but a higher rate of grade III neuropathy (40%), which was statistically significant with p value =0.05 [15].

The severity of both cisplatin and oxaloplatin induced neuropathy are mainly determined by their cumulative doses ($p=0.006$), with a stepwise increase in median cumulative dose of cisplatin from grade I (423.7mg/m2) to grade III (734.9mg/m2), however, the number of cycles was not statistically significant, similarly cumulative doses of oxaloplatin demonstrated a statistically significant association with neuropathy severity. The ranges also support a dose dependent pattern. As with cisplatin the number of cycles did not significantly correlate with neuropathy grade. ($p=0.5$)

On the contrary, a study by Loprinzi et al reported that this relationship between dose and higher neuropathy grades was not linear. Some patients receiving higher doses with milder neuropathy. The study suggested that individual factors, such as genetic predisposition, preexisting conditions, and metabolic differences, might influence the severity of neuropathy more than cumulative dose [16].

We performed nerve conduction studies at baseline and after 4-6 cycles of chemotherapy, and significant sensory conduction changes were observed post-chemotherapy, with distinct patterns across nerves. The median nerve showed significant SDL prolongation and SCV reduction ($p<0.001$) with preserved SNAP amplitude. The ulnar nerve demonstrated comprehensive impairment with increased SDL, decreased SNAP amplitude, and reduced SCV (all $p<0.001$). The sural nerve exhibited isolated SDL prolongation ($p<0.001$) with maintained amplitude and conduction velocity.

In a study by Blerim et al, initial (pre-chemotherapy) assessment, sensory and motor responses were within normal limits in 120 examined patients. The SNAPs and velocities of the median, tibial, peroneal (P-value<0.001), and ulnar ($P<0.01$) nerves were significantly lower and slower, respectively. The SNAPs of all sensory nerves were significantly lower ($P<0.001$) and the conduction velocities of the sensory median ($P<0.001$), and ulnar ($P<0.05$) nerves were significantly slower [17].

Notably in our study, nearly all patients with grade I and grade II achieved complete improvement. In contrast, 40% of patients with grade III neuropathy still had residual grade II at the end of the follow-up period. overall, all patients experienced variable degrees of improvement, with a statistically significant impact ($p = 0.034$).

Comparable to our findings, a study by Rodwin et al found that while most patients with mild neuropathy achieved complete recovery, those with severe neuropathy often had persistent symptoms, even after treatment [18].

As regard Quality of life, physical functioning scored highest in functional scale. Fatigue, however, remained the most prevalent symptom, with the highest score in the three-item scale. This suggests that while our patients' physical daily activities and mobility were minimally affected, fatigue persisted as a dominant concern. Notably, patients receiving platinum-based combinations had the highest global QoL scores ($p = 0.05$), indicating that their overall quality of life was minimally impaired. Furthermore, the high score on financial impact underscores the significant financial burden that cancer patients face during their treatment journey.

A study by Deerasamee S. found that physical functioning often scores higher than other functional scales, cognitive functioning tends to be more severely affected and the fatigue is one of the most common and debilitating symptoms reported by cancer patients, supporting our findings [19].

A study by Bottomley et al investigated the impact of chemotherapy regimens on global QoL using the EORTC QLQ-C30, found that platinum-based regimens, alone or in combination, were associated with higher global QoL scores. Global QoL was a more sensitive indicator of overall treatment impact, supporting our observation [20].

Ethical approval: was obtained with a local approval number. (IRB 042023200122).

Conflicts of interest of each author/contributor: None

Funding: None

Availability of data and material: On reasonable request, the corresponding author will make the data used and/or analyzed during the current work available.

Acknowledgement: None

References:

[1] Argyriou AA, Bruna J, Marmiroli P, et al. Chemotherapy-induced peripheral neurotoxicity (CIPN): an update. Critical reviews in oncology/hematology. 2012;82(1):51-77.

[2] Seretny M, Currie GL, Sena ES, et al. Incidence,

prevalence, and predictors of chemotherapy-induced peripheral neuropathy: a systematic review and meta-analysis. Pain®. 2014;155(12):2461-2470.

[3] Addington J, Freimer M. Chemotherapy-induced peripheral neuropathy: an update on the current understanding. F1000Research. 2016;5:F1000 Faculty Rev-1466.

[4] Cavaletti G. Chemotherapy-induced peripheral neurotoxicity (CIPN): The dilemma of proper assessment. Journal of the peripheral nervous system. 2018;23(4):388-388.

[5] Burgess J, Ferdousi M, Gosal D, et al. Chemotherapy-induced peripheral neuropathy: epidemiology, pathomechanisms and treatment. Oncology and therapy. 2021;9(2):385-450.

[6] Quasthoff S, Hartung HP. Chemotherapy-induced peripheral neuropathy. Journal of neurology. 2002;249(1):9-17.

[7] Hilkens P, Verweij J, Vecht CJ, et al. Clinical characteristics of severe peripheral neuropathy induced by docetaxel (Taxotere). Annals of oncology. 1997;8(2):187-190.

[8] Paulson JC, McClure WO. Inhibition of axoplasmic transport by colchicine, podophyllotoxin, and vinblastine: an effect on microtubules. Annals of the New York Academy of Sciences. 1975;253:517-527.

[9] Park SB, Alberti P, Kolb NA, et al. Overview and critical revision of clinical assessment tools in chemotherapy-induced peripheral neurotoxicity. Journal of the Peripheral Nervous System. 2019;24:S13-S25.

[10] Kandula T, Farrar MA, Kiernan MC, et al. Neurophysiological and clinical outcomes in chemotherapy-induced neuropathy in cancer. Clinical Neurophysiology. 2017;128(7):1166-1175.

[11] Carpenter R, Reddi B. Neurophysiology: a conceptual approach. CRC Press. 2012;8(2):54-59.

[12] Tan AC, McCrary JM, Park SB, et al. Chemotherapy-induced peripheral neuropathy patient-reported outcomes compared with NCI-CTCAE grade. Supportive Care in Cancer. 2019;27(12):4771-4777.

[13] Fayers P, Aaronson N, Bjordal K, et al. The EORTC QLQ-C30 Scoring Manual. Published by: European Organisation for Research and Treatment of Cancer, Brussels 2001. Accessed Oct. 2014;8(3):54-59.

[14] Ahmed G, Shafik A, Elhusseiny K, et al. Chemotherapy-induced peripheral neuropathy in Egyptian patients: Single institution retrospective analysis. Asian Pacific journal of cancer prevention: APJCP. 2018;19(8):22-23.

[15] Park SB, Goldstein D, Krishnan AV, et al. Chemotherapy-induced peripheral neurotoxicity: a critical analysis. CA: a cancer journal for clinicians. 2013;63(6):419-437.

[16] Loprinzi CL, Lacchetti C, Bleeker J, et al. Prevention and management of chemotherapy-induced peripheral neuropathy in survivors of adult cancers: ASCO guideline update. Journal of Clinical Oncology. 2020;38(28):3325-3348.

[17] Blerim M, Hundozi Z, Sermaxhaj F, et al. Chemotherapy-induced peripheral neuropathy (CIPN) in patients receiving 4– 6 cycles of platinum-based and Taxane-based chemotherapy: a prospective, single-center study from Kosovo. Medical Science Monitor: International Medical Journal of Experimental and Clinical Research. 2022;28:e937856-937851.

[18] Rodwin RL, Siddiq NZ, Ehrlich BE, et al. Biomarkers of chemotherapy-induced peripheral neuropathy: Current status and future directions. Frontiers in Pain Research. 2022;3:864910.

[19] Deerasamee S. Asian Pacific Organization for Cancer Prevention (APOCP) Founding Conference- The APOCP and Regional Collaboration for Cancer Prevention. Asian Pac J Cancer Prev. 2000;1:263-267.

[20] Bottomley A, Tridello G, Coens C, et al. An international phase 3 trial in head and neck cancer: quality of life and symptom results: EORTC 24954 on behalf of the EORTC Head and Neck and the EORTC Radiation Oncology Group. Cancer. 2014;120(3):390-398.