

Impact of chemotherapy-induced peripheral neuropathy upon quality of life for patients with cancer receiving neurotoxic anticancer drugs

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ABSTRACT

Chemotherapy-induced peripheral neuropathy is a common side effect caused by neurotoxic anticancer drugs that leads to nerve damage, degeneration, and inflammation. Its incidence ranges from 10% to 100% of patients receiving certain chemotherapeutic agents. Limited research has investigated the association between CIPN and QOL, with most studies assessing these concepts separately. This study aims to determine the impact of chemotherapy-induced peripheral neuropathy upon quality of life for patients with cancer receiving neurotoxic anticancer drugs. The study utilized a descriptive cross-sectional design and was conducted at two oncology centers. A purposive sampling method was used to collect data from 102 breast or lung cancer patients receiving neurotoxic chemotherapy from the period of December 2022 to May 2023. The questionnaire was divided into three sections. The first part included demographic and clinical data, while the second and third parts, EORTC QLQ-CIPN-20 and EORTC QLQ-C30, respectively, were used to assess CIPN and evaluate QoL. The present study has shown a highly significant negative correlation ($P < 0.01$) between chemotherapy-induced peripheral neuropathy and quality of life. Recommendations include providing free cancer diagnosis, medication, CIPN assessment, and psychological support by the Ministry of Health and nursing staff in oncology centers.

Key words: impact, chemotherapy-induced peripheral neuropathy, quality of life, cancer, neurotoxic anticancer drugs

INTRODUCTION

Cancer is the second cause of death and one of the main public health problems universally [1, 2]. Cancer is responsible for a substantial burden on communities and, mainly, on less developed countries [3]. Over the past ten years, cancer rates have increased among people in the Middle East, especially in Iraq [4]. The current rise in incidence is correlated with population growth and aging and due to the increment of the risk factors, such as low physical activity, smoking, and obesity, as a result of western lifestyle adoption [5-8]. Chemotherapy is one of the primary treatments for cancer, and it can be administered as the primary therapy or in combination with other treatments such as radiation therapy or surgical resection. It may also be given before or after the primary treatment [9]. However, the antineoplastic agents are initially developed and intended to target malignant cells primarily, the harmful effect also involves the host cells, as evidenced by systemic unpleasant side effects. Chemotherapy-induced peripheral neuropathy is one of the most common dose-limiting and long-standing side effect caused by several chemotherapeutic agents [10]. The neurotoxic antineoplastic drugs lead to nerve fibers damage, degeneration, and inflammation [10]. Oncology nurses frequently report this treatment-related adverse effect when caring for patients with cancer. CIPN has been reported to occur in a range of 10% to 100% of patients undergoing platinum, taxane, and plant alkaloid treatments [11, 12]. A tendency to develop CIPN is generally observed in nerves that were previously affected by inherited neuropathy, diabetes mellitus, alcohol use, and thyroid dysfunction [13]. The CIPN can result in sensory loss, hypersensitivity, and functional deficits such as tingling, numbness, and discomfort [14]. While some patients experience severe neuropathic pain, others may experience sensory loss without pain [15]. The impairment of both gross and fine motor skills can occur, along with loss of proprioception and numbness in the hands and feet, leading to an increased risk of falls and injuries [16]. In addition to physical symptoms and loss of function, CIPN may also cause psychological symptoms that can interfere with daily activities [17]. Although many studies have been conducted, there is currently no consensus on how to prevent CIPN. Furthermore, managing CIPN remains a difficult task, and there is no universally accepted and proven treatment. With the increasing use of chemotherapy in cancer treatment, CIPN has become a significant concern that may extend to affect individuals' aims, expectations, and functioning, which can negatively impact patients' quality of life [1]. Many

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studies found that CIPN was associated with increased healthcare costs, decreased work productivity, higher rates of disability and early retirement. In addition to direct healthcare costs, such as increased medication and hospitalization expenses, CIPN can also lead to indirect costs, such as lost wages and reduced quality of life [18]. The rising incidence and prevalence of cancer, coupled with the absence of proven preventative or treatment options for CIPN, means that more patients are facing the consequences of this condition. As a result, CIPN is likely to become a significant issue with a notable social and economic impact on society [1]. The present study aims to determine the impact of chemotherapy-induced peripheral neuropathy upon quality of life for patients with cancer receiving neurotoxic anticancer drugs.

Hypothesis of the study

There is impact of chemotherapy-induced peripheral neuropathy upon the quality of life for patients with cancer who receive neurotoxic anticancer drugs.

METHODOLOGY

The study utilized a descriptive cross-sectional design and was conducted at two oncology centers in Babylon Province: the Babylon Oncology Center and the Imam Al-Sadiq Hospital/ Oncology and Radiotherapy Center. A purposive sampling method was used to collect data from 102 breast or lung cancer patients receiving neurotoxic chemotherapy from the period of December 2022 to May 2023. About the ethical consideration, the study respondent gave their written agreement to the researcher after the College of Nursing Council at the University of Baghdad and the Ethical Research Committee accepted it. The instrument of the study was divided into three parts. The first part included demographic and clinical data, the demographic data which consists of (five) items including age, gender, occupation,

BMI, and smoking. While the clinical data which consists of five items including site of cancer, stage of cancer, chemotherapeutic agent, number of chemotherapy cycles, and a cumulative dose. The second part include 20-item EORTC QLQ-CIPN20 was utilized to evaluate CIPN symptoms. The third part EORTC QLQ-C30 is a comprehensive 30-item questionnaire designed to assess the multidimensional nature of the quality-of-life construct. The permission for use Arabic version of EORTC QLQ-C30 was obtained from the copyright owner EORTC by Email. The Arabic version of the EORTC QLQ-C30 questionnaire is reliable and valid. Regarding the EORTC QLQ-CIPN-20 permission was obtained from the copyright owner EORTC by Email then translated and back-translated by bilingual physicians and a native speaker. Content validity was evaluated by 12 experts using the content validity index, aiming for at least 95% of items to receive a rating of 4 or higher. A pilot study with 11 patients was conducted to assess the reliability of the Arabic version of the EORTC QLQ-CIPN20. The Cronbach alpha reliability coefficient was 0.8, indicating that the instrument is reliable for measuring the study phenomenon in the future. Statistical data analysis Descriptive and inferential statistics and SPSS (version 26) were used to analyse the data of the study.

RESULTS

In table 1, the results showed the age for 102 participants at most (41.2%) were from 51 years-60 years with mean 56.90 years. Regarding the gender, the majority (82.4%) of the patients were female and the most (74.5%) were not work/ housewife. According to the smoking, the most (74.5%) from the study samples were not smoking. The results also showed the BMI for patients with cancer at most (39.2%) were overweight.

In table 2, the results showed for 102 participants, the site of the cancerous tumor at most (72.5%) in the breast. Regarding the

Tab. 1. Distribution of the participants according to their socio demographic data characteristics

Demographic Characteristics	Subgroup	f.	%
Age group	30- 40 years	8	7.8
	41- 50 years	18	17.7
	51- 60 years	42	41.2
	60 years and above	34	33.3
	Total	102	100
Mean ± SD 56.90 ± 9.973			
Min- Max 31-75 years			
Gender	Male	18	17.6
	Female	84	82.4
	Total	102	100
Occupation	Student	0	0
	Employer	8	7.9
	Earnier	0	0
	Retired	18	17.6
	Not work/ housewife	76	74.5
Total	102	100	
Body Mass Index	Underweight	0	0
	healthy weight	20	19.6
	Overweight	40	39.2
	Obesity class I	34	33.3
	Obesity class II	8	7.9
	Obesity class III	0	0
Total	102	100	
Smoking	No	76	74.5
	Yes	26	25.5
	Total	102	100

f= frequencies, %=Percentages, M = Mean of score, S.D = Standard Deviation, Min= Minimum and Max= Maximum

Tab. 2. Distribution of the participants according to their clinical data characteristics

Clinical data characteristics	Subgroup	f.	%
The site of the cancerous tumor	Breast	74	72.5
	Lung	28	27.5
	Total	102	100
Tumor stage	First	20	19.6
	Second	32	31.4
	Third	20	19.6
	Fourth	30	29.4
	Total	102	100
Chemotherapy Drug	Cisplatin	14	13.8
	Paclitaxel	80	78.4
	Docetaxel	8	7.8
	Total	102	100
The number of chemotherapy cycles	Mean ± SD 3.55 ± 2.272 Min-Max 1-12 cycles		
Cumulative dose	Mean ± SD: 934.33 ± 945.457 Min- Max 220 mg/m ² - 6288 mg/m ²		

f= Frequencies, %=Percentages, M = Mean of score, S.D = Standard Deviation, Min= Minimum and Max= Maximum

Tab. 3. Assess the chemotherapy-induced peripheral neuropathy for patients with cancer receiving neurotoxic anticancer drugs

Domain	Patients' scores				
	Range	T	Raw score	Transformed score (0-100)	
Sensory (9 items)	Sep-36	19.33	2.14	38.27	
Motor (8 items)	Aug-32	15.12	1.89	29.66	
Autonomic	(3 items)	12-Mar	5.47	1.82	27.45
	Female (2 items)	8-Feb	4.84	2.42	47.39
Total	(20 items)	20-80	39.92	1.99	33.2
	Female (19 items)	19- 76	39.29	2.06	35.6

*Higher scores represent more complaints

Tab. 4. Evaluate the quality of life for patients with cancer receiving neurotoxic anticancer drugs

Scale	Items (N)	Range	CL	Mean	SD	TS 0-100
Physical functioning	5	20-May	3	11.13	3.833	59.08
Role functioning	2	8-Feb	3	4.92	1.71	51.31
Emotional functioning	4	16-Apr	3	12.39	2.618	30.07
Cognitive functioning	2	8-Feb	3	4.71	1.816	54.9
Social functioning	2	8-Feb	3	6.16	1.795	30.72
Functional scales	15	15-60	3	28.18	6.42	45.22
Fatigue	3	12-Mar	3	8.67	2.554	62.96
Nausea and vomiting	2	8-Feb	3	4.2	2.106	53.59
Pain	2	8-Feb	3	5.22	1.772	22.22
Dyspnea	1	4-Jan	3	1.67	0.947	36.6
Insomnia	1	4-Jan	3	2.31	1.134	43.79
Appetite loss	1	4-Jan	3	2.49	1.167	49.67
Constipation	1	4-Jan	3	1.73	1.016	24.18
Diarrhea	1	4-Jan	3	1.69	1.005	22.88
Financial difficulties	1	4-Jan	3	3.2	0.89	73.2
Symptom scales/ items	13	13-52	3	31.16	8.08	43.23
Global health status	2	14-Feb	6	7.39	3.419	44.93

tumor stage, the most (31.4%) of the patients at second stage and the majority (78.4%) were use Paclitaxel chemotherapy. According to the number of chemotherapy cycles, the Min- Max 1-12 cycles with mean 3.55. The results also had shown the cumulative dose, the Min- Max 220 mg/m²-6288 mg/m² with mean 934.33 mg/m².

The results in table 3 showed the chemotherapy-induced peripheral neuropathy for patients with cancer receiving neurotoxic anticancer drugs more complaints in female from than male (transformed score 35.6), and regarding the subscale more complaints in sensory from than motor (transformed score 38.27), and according to the autonomic less complaints in male and more complaints in female (transformed score 47.39).

Category length, Transformed score, M=Mean of score, S.D= Standard Deviation, a high score for a functional scale represents

a high / healthy level of functioning, a high score for the global health status / QoL represents a high QoL, but a high score for a symptom scales / items represents a high level of symptomatology / problems.

The results in Table 4 showed that the quality of life for patients with cancer receiving neurotoxic anticancer drugs was at its best in terms of physical functioning (mean ± SD 11.13 ± 3.833) and total score 59.08. However, it was the worst in emotional functioning with (mean ± SD 12.39 ± 2.618) and total score 30.07. Furthermore, the results in the table also revealed that the least problematic symptom was pain with (mean ± SD 5.22 ± 1.772) and total score 22.22, while the most problematic issue was financial difficulties with (mean ± SD 3.20 ± .890) and total score 73.20.

Tab. 5. Impact of chemotherapy-induced peripheral neuropathy upon quality of life for patients with cancer receiving neurotoxic anticancer drugs

EORTC QLQ-C30		Functional scales	Symptom scales/ items	Global health status	QoL
EORTC QLQ - CIPN20					
Sensory	Cc	-.677.**	-.630.**	-.831.**	-.795.**
	P. value	0	0	0	0
	N	102	102	102	102
Motor	Cc	-.718.**	-.620.**	-.719.**	-.756.**
	P. value	0	0	0	0
	N	102	102	102	102
Autonomic male	Cc	-.410.**	-.324.**	-.430.**	-.432.**
	P. value	0	0.001	0	0
	N	102	102	102	102
Autonomic female	Cc	-.512.**	-.458.**	-.545.**	-.559.**
	P. value	0	0	0	0
	N	102	102	102	102
Total CIPN	Cc	-.739.**	-.657.**	-.826.**	-.823.**
	P. value	0	0	0	0
	N	102	102	102	102
Total CIPN female	Cc	-.739.**	-.664.**	-.828.**	-.826.**
	P. value	0	0	0	0
	N	102	102	102	102

*Cc= Correlation Coefficient, P=Probability value, NS: Non-Significant at P>0.05, S: Significant at P<0.05, HS: Highly Significant at P<0.01.

In Table 5, the results showed highly significant negative statistical correlations between Chemotherapy-Induced Peripheral Neuropathy (CIPN) and quality of life, with a p-value of P<0.01. This means that the impact of CIPN on the quality of life of patients with cancer receiving neurotoxic anticancer drugs was strong and inverse. The higher the CIPN, the lower of the quality of life, and the sensory factor had the most significant impact.

DISCUSSION

According to the study findings in Table 1, more than one third of study participants fell within the age range of 51 years-60 years, with a mean age of 56.9 years. This suggests that the study population was predominantly middle-aged, this finding was consistent with study conducted in Virginia which investigate the prevalence, pattern, and impact of CIPN on the QoL of women treated for breast cancer in a community oncology practice. Where the mean age of the study samples was 56.6 years [19]. Our study reported 82.4% of participants were female, and 17.6 % were male. This finding consists with study conducted on African American cancer survivors, to identify non-genetic risk factors and comorbidities associated with CIPN. The participant of this study was 76.1 % female and 23.9 % male [20,21]. Related to the occupation of cancer patients in this study, the results show that approximately three-quarters of patients were not working or were housewives, this result is supported by a study conducted to assess CIPN and general quality of life levels. The study found that the majority of participants (71%) did not work [22]. The results of the present study revealed that more than one-third of patients fell into the overweight category based on body mass index classification, Similar findings were reported in a longitudinal study involving women diagnosed with invasive breast cancer, where 65.6% of study participants were found to be overweight [23,24]. The present study shows that 74.5% of participants do not smoke, which is consistent with the findings of study conducted on CIPN evaluation after initiating chemotherapy administration, and reported that 78% of their participants were non-smokers [25]. According to the study findings in Table 2, the majority of participants 72.5% had breast cancer, while a smaller percentage 27.5% had lung cancer. The researcher justifies the reason for the emergence of these results to the higher prevalence of breast cancer globally and locally compared to other types of cancer [26, 27]. Regarding the tumor

stage, the most 31.4% of the patients at second stage. This finding was consistent with study conducted to investigate the predictors of incident chemotherapy-induced peripheral neuropathy claims among 11,149 women who were 66 years or older and diagnosed with American Joint Commission on Cancer (AJCC) stage II to IV breast cancer. According to the findings of the study, the distribution of participants across tumor stages revealed that the majority 47% of the study sample were at the second stage [28]. The results regarding chemotherapeutic agents showed the majority 78.4% of participants use Paclitaxel. This finding similar to several studies in related literature [29]. The results showed the mean of number of chemotherapy cycles was 3.55, this result is consistent with the study conducted on women with breast cancer who had received paclitaxel in a prospective observational study. Their results show the mean of number of chemotherapy cycles was 2.59 [30, 31]. The results also showed that the mean cumulative dose was 934.33 mg/m². This finding is consistent with a study to evaluate neuropathy development from weekly paclitaxel treatment and assessed the impact of dose reduction on post-treatment neuropathy outcomes. Their study reported a similar outcome, with a mean cumulative dose of 848.9 mg/m² [32]. Regarding the spectrum of CIPN manifestations, the present study has shown that sensory peripheral neuropathy is the most commonly reported type of peripheral neuropathy among participants with a mean transformed score of 38.27. This finding is consistent with many previous studies [22, 17, 33]. Regarding autonomic symptoms, our study showed that females report more complaints than males, with a mean transformed score of 47.39. This result is consistent with who also found that females are more likely to experience autonomic symptoms related to CIPN [24]. The study results presented in Table 4 demonstrate that the quality of life for cancer patients receiving neurotoxic anticancer drugs was best in terms of physical functioning (mean ± SD 11.13 ± 3.833) and a total score of 59.08. This finding is consistent with recent research conducted to evaluate the effect of acupuncture treatment on neurological symptoms of CIPN and the QoL of oncological patients. Their results showed

that the acupuncture group had better outcomes than the control group in the physical domains of the EORTC QLQ-C30 [34]. The present study results also demonstrated that the emotional domain was the worst performing domain in the functional scales, with a mean \pm SD score of 12.39 ± 2.618 and a total score of 30.07. This finding is similar to the results of a study conducted to determine the incidence and severity of TIPN in individuals with breast cancer. Their findings revealed that the emotional functioning domain had the lowest subscale scores (mean \pm SD 65.93 ± 8.72) [35]. The study results indicate that the most problematic issue was financial difficulties, with a mean \pm SD of $3.20 \pm .890$ and a total score of 73.20. This finding is consistent with the results of a study conducted to evaluate the impact of chemotherapy-induced peripheral neuropathy on patients' quality of life and resilience after treatment with platinum and taxane-based chemotherapy drugs. They found that financial difficulties (mean=19.0) were one of the most significant issues affecting quality of life [36]. According to the study findings in Table 5, there were highly significant negative correlations between chemotherapy-induced peripheral neuropathy and quality of life, with a p-value <0.01 . This means that the impact of chemotherapy-induced peripheral neuropathy upon quality of life for cancer patients receiving neurotoxic anticancer drugs was strong and inverse, where the higher the impact of CIPN, the lower the quality of life. These findings are consistent with study conducted to investigate CIPN and its relationship with QoL among cancer patients. They found a significant negative correlation between symptoms severity related

to neurotoxic anticancer drugs and patients' QoL ($p=.000^*$), as manifested by sensory, motor, and autonomic neuropathy [37]. Another studies had same findings [18, 19].

CONCLUSION

There is a negative correlation between CIPN and QoL in cancer patients receiving neurotoxic chemotherapy, with sensory symptoms most problematic. CIPN affects patients' functional roles, emotional well-being, and financial state and overall quality of life.

RECOMMENDATIONS

A recommendation for the Ministry of Health to provide all diagnostic measures and cancer-related medications free of charge for all cancer patients to minimize the financial burden on patients and their families.

Encourage nurses in the oncology ward to provide psychological support for their patients to maintain good emotional well-being, which is crucial for the quality of life.

STATEMENT OF CONFLICT OF INTEREST

Members of the committee declare that they have no conflict of interest.

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