ORIGINAL RESEARCH

Chemotherapy-induced peripheral neuropathy and its association with quality of life among cancer patients

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ABSTRACT

Background and objective: Chemotherapy-induced peripheral neuropathy (CIPN) is a common incapacitating complication of various chemotherapeutic agents that severely impact the patient's quality of life. Most of patients treated with anticancer agents develop CIPN early after treatment and may necessitate dose modification or termination, which can increase cancer-related morbidity and mortality. Aim: investigate the Chemotherapy-Induced Peripheral Neuropathy and its Association with Quality of Life among Cancer patients.

Methods: A descriptive study design was applied in this study, on a purposeful sample of 250 adult patients diagnosed with chemotherapy induce peripheral nephropathy. The study instruments were the demographic and medical history questionnaire, PNQ, EORTC CIPN20 and EORTC30.

Results: Symptoms severities mean score is 5.58 ± 2.97. Sensory neuropathy registered the highest mean at 21.23 points, followed by motor (17.33) and autonomic (5.11). About one quarter of participants reported poor global quality of life. Poor physical function was reported by 22.3% of all participants. Fatigue, pain and insomnia were the most common symptoms suffered by patients. There is a relation between CIPN and duration of cancer diagnosis, type of cancer, intervention, gender, and other condition.

Conclusions: CIPN is the furthermost common complication of chemotherapy that affects patient's QoL. Assessment of chemotherapy-related peripheral neuropathy helps clinicians to develop and evaluate much needed targeted therapies and to help improving QoL.

Key Words: Chemotherapy, Peripheral neuropathy, Quality of life

1. INTRODUCTION

While quality of life (QOL) is the primary immediate objective for most cancer patients after diagnosis, soon after quality of life becomes more important. Nevertheless, cancer prevalence increase, additional patients are living with the long-term cancer and cancer related complications which can have a destructive influence on QOL. One of those potential complications is chemotherapy-induced peripheral neuropathy (CIPN).[1]

Cancer-related neuropathy is a major adverse outcome for cancer patients that delay functional recovery, decrease treatment tolerability, and causing symptom distress in cancer patients.[2] CIPN characterized by the presence of somatic or autonomic peripheral nerve dysfunction, whether, resulting from damage to the peripheral or the autonomic nervous systems caused by anti-cancer drugs.[3]

CIPN incidence and severity are directly related to dose, duration of therapy, previous or simultaneous administra-

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tion of neurotoxic agents and the type of impaired nervous fiber. Consequently, the occurrence of CIPN approaches nearly 100% for some agents at higher doses.[4] CIPN is seen by care givers as acceptable, unavoidable complication of chemotherapy, that is often important to save patients' life.[2] In contrast, CIPN seen by cancer patients as mostly difficult chemotherapeutic complication that affects their quality of life.[3] chemotherapeutic dose modification required in patients with acute neuropathy, which could have had an influence on whether chronic neuropathy occurs later on.[5] It appears to be of vital importance to replace the patients' unnecessary suffering and loss of function by early and accurate diagnosis.[6]

The most frequent agents causing CIPN are Platinum compounds, Taxane Derivatives, Vinca Alkaloids, Epothilones, Thalidomide and Bortezomib, which adversely affect the peripheral nervous system through dissimilar mechanisms.[7] Platinum-based therapies cause bursts of Reactive Oxygen Species (ROS), which can trigger structural changes in peripheral nerves including neuronopathy, axonopathy and/or myelinopathy. Glutathione, an antioxidant, plays an important role in redox homeostasis.[8]

Preexisting neuropathy either from treatment with neurotoxic agents, or from comorbid conditions like, diabetes mellitus, alcohol, or inherited neuropathies, may predispose to more severe CIPN. Age-related axonal loss may also predispose to more severe symptoms. Prior chemotherapy can also be predisposing towards CIPN.[9] The incidence of CIPN varies with dose per cycle, duration of infusion, cumulative dose, and treatment schedule.[10]

Assessment tools for CIPN are either objective, subjective, or a combination of both. Additionally, several neuropathy manifestations are subjective, that needs assessment with a self-reported questionnaire, to help understanding the effects of CIPN and its related symptoms on QOL, which could be implemented by different health professionals taking care of those patients.[11] our study provides a vital contribution to the limited data existing on CIPN and its effect on health related quality of life. Aim: The current study aimed to investigate the Chemotherapy-Induced Peripheral Neuropathy and its Association with Quality of Life among Cancer patients.

1.1 Research questions

- What are peripheral neuropathy related characteristics induced by chemotherapy?
- Is neuropathy induced by chemotherapy affect on quality of life?

1.2 Statement of the problem

CIPN is a serious problem affecting the cancer patients' QoL. Therefore, early detection CIPN is needed to avoid long term damage. Additionally, nursing researchers using subjective measures and patient reported outcomes to help guide clinicians to choose suitable therapeutic intervention thus preventing permanent complications, functional disabilities and impaired QoL from CIPN

2. METHODOLOGY

2.1 Research design

A descriptive design was used in this study, to help provide answers to the questions associated with a research problem, and to obtain information concerning the current status of the phenomena and to describe "what exists" with respect to variables or conditions in a situation.

2.2 Subjects

A purposeful sample of 250 adult patients with CIPN, enrolled in Mansoura Oncology Center, Mansoura University, Egypt, between March, 2017 and March, 2018.

The inclusion criteria included adult patients aged between 20-60 years old, from both sexes, diagnosed with cancer; had received at least 3 prior sessions of chemotherapy, be able to speak and willing to participate in this study. The sample size for this study calculated using the following Equation:

$$\textit{Margin of error} = Z * (\frac{SD}{\sqrt{n}})$$

Z = 1.960 for 95% confidence interval, SD = Standard deviation, n = Sample size.

So, a sample size of 107 yields a two-sided 95% confidence interval with a distance from the mean to the limits that is equal to 4.025 when the estimated standard deviation is 21.000. Therefore, a minimum of 108 patients will be selected for this study.

2.3 Setting

This study was carried out in the Mansoura Oncology Center, Mansoura University, Egypt.

2.4 Instruments

Four tools were used to collect the necessary data.

Tool I: Demographic and Medical History Questionnaire: designed by the researchers after reviewing the recent related literature. It includes the following parts:

Part (1): Included demographic data as age, sex, and marital status, level of education, occupation, income.

Part (2): Included clinical characteristics as, diagnosis, duration of cancer, tumor differentiation, and characteristics

related to peripheral neuropathy as duration of peripheral neuropathy (month), status of chemotherapy, period after recent chemotherapy, and response of medical team to symptom.

Tool II: Patient's Neurotoxicity Questionnaire (PNQ).[12] The PNQ was designed to obtain clinically relevant and quantifiable information directly from the patient regarding the subjective symptoms (e.g., tingling, pain and numbness) and activities of daily living (e.g., walking, eating). The PNQ is comprised of two clinically defined symptom areas relevant to CIPN, namely, sensory (numbness, tingling, and pain) and motor (weakness), with a clear demarcation between interference and noninterference in daily activities. This questionnaire has been revealed to be valid, reliable and reactive to change. It has been used to detect short- and long-term effects in different cancer types and stages of the disease

Scoring system: These two items are rated 1-5 on the following scale: 1 = No, 2 = Mild, 3 = Moderate, 4 = Moderate-to-Severe, and 5 = Severe. The CIPN was assessed by summing the two items' scores, with the ending score being called the PNQ total score, ranges from 2 to 10, defined as grade A: 3-4, grade B: 5-6, grade C: 7-8, and grade D: 9-10 with a high total score representing severe CIPN symptoms.

Tool III: Chemotherapy Induced Peripheral Neuropathy 20 (EORTC CIPN20).[13] It was developed by European Organization for Research and Treatment of Cancer (EORTC). This instrument has three subscales sensory, motor, and autonomic, and 20 questions, 9 items related to sensory nerves, 8 items related to motor nerves, and 3 items related to autonomic nerves. According to the scoring manual, 100 points are converted into full marks. The higher the score, the lower the quality of life.

Tool IV: EORTC QLQ-C30 (version 3).[14,15] EORTC QLQ-C30 is a validated 30-item questionnaire encompassing both single- and multi-item measures, for all cancer patients. it is a questionnaire assessing HRQL. 30 items arranged into five functional scales (Physical, Role, Cognitive, Emotional, and Social Functioning), three symptom scales (Fatigue, Pain, and Nausea/Vomiting), a Global Health Status/QoL scale, and six single items (Constipation, Diarrhea, Insomnia, Dyspnea, Appetite Loss, and Financial impact of the disease). Each item takes four response: 1) "not at all", 2) "a little", 3) "quite a bit", and 4) "very much", and for the global health-status/quality of life scale, options ranging from 1) "very poor" to 7) "excellent".

Scoring system: All questionnaire answers were converted into scores on a linear 0 to 100 scale according to the EORTC scoring manual. Mean scores with standard deviations (SDs) were calculated. Responses were dichotomized into "good" versus "poor" for function scales, and into "no or minor symptoms" versus "symptomatic" for symptom scales and single items. People who responded 3 "quite a bit" or 4 "very much" on an item within a scale or for a single item were included in the "poor" function or "symptomatic" groups. Otherwise the person was categorized as having "good" function or "no symptoms to facilitate interpretation of the data. A high score for functional scales and for Global Health Status/QoL denote better HRQoL, whereas a high score for symptom scales and single items denotes significant symptomatology.

EORTC QLQ-C30 (version 3). The reliability was assessed with Cronbach's alpha for all scales, yielded a coefficient greater than 0.8 for all functional scales, except the cognitive scale (alpha 0.6), and all symptoms scales except for nausea and vomiting (alpha 0.6).

Patient Neurotoxicity Questionnaire (PNQ). PNQ appears to have an applicable and practical level of feasibility and validity for CIPN diagnosis and grading in the clinical setting, not only for the identification of CIPN-related symptoms, but also to aid treatment-related decisions.

2.5 Validity

Chemotherapy Induced Peripheral Neuropathy 20 (EORTC CIPN20). The reliability were tested by a Cronbach's alpha coefficient of 0.82, 0.73 and 0.76 for the sensory, motor and autonomic scales. Validity was studied by using expert opinion.[16]

2.6 Pilot study

A pilot study was carried out on 25 patients (10% of sample size) to ascertain the clarity and applicability of the study tools, also for estimation of the approximate time needed to complete the study tools. In light of the findings of the pilot study, the necessary modifications were done. Those patients were excluded in the study.

2.7 Research procedures

Step 1: (Agree)

- During this stage, an oral agreement were obtained by the researchers from the patient after explaining the goal from the study.
- Agreement from the hospital administration were obtained to carry out the study. The researchers assured that participation in the study was voluntary and they have the right to withdraw at any time.

Step 2: (Assess)

The data of the admitted patients, structured questionnaires, interviews, and electronic record were collected for patients

who matched the study subjects. General characteristics, questions about peripheral neuropathy, and quality of life were directly answered by the patient.

2.8 Ethical considerations

Ethical approval from Mansoura University Faculty of Nursing Ethic Committee was obtained to carry out the study, the researchers introduced themselves to all the studied patients and the aim of the study was explained prior their participation to obtain their acceptance and cooperation as well as their written consent. Confidentiality of data was assured to all the participants.

2.9 Data analysis

statistical analyses were carried out using Statistical Package for Social Science (SPSS V 20.0 for windows; SPSS Inc, Chicago, IL, 2001). The results obtained were interpreted and descriptive statistics (mean, median, standard deviation, and percentages) were applied whenever feasible. The chi-square test and one way ANOVA test were used for interpretation of qualitative data. p-value of .05 or less was taken as significant value and < .01 as highly significant, whereas p-value > .05 was taken as non-significant.

3. Results

Demographic characteristics of studied samples are outlined in Table 1. The age of the studied sample ranged from 20 to 60 years. The mean age was 49.9 $\pm$ 10.18. females were more included (52.8%). Most of them (85.6%) were married and unemployed (72.4). Illiteracy was prevailing among 55.2%. The most frequent diagnosis was breast and Colon cancer (29.6% and 21.6 respectively). Most of studied sample diagnosed with cancer less than 12 month (72.4%).

Table 1. Demographic characteristics of studied sample (N = 250)

Variables	Characteristics	Number	%
Age			
(Mean ± Std. Deviation)	49.9 ± 10.18		
Minimum	20		
Maximum	60		
Gender	Male	132	52.8
	Female	118	47.2
Marital status	Married	214	85.6
	Single	24	9.6
	Others	12	4.8
Job	Yes	69	27.6
	No	181	72.4
Education	Literate	138	55.2
	Illiterate	112	44.8
Income	Enough	204	81.6
	Not enough	46	18.4
Diagnoses	Gastric cancer	23	9.2
	Lung cancer	33	13.2
	Liver cancer	54	21.6
	Breast cancer	74	29.6
	Lymphoma	35	14
	Colon cancer	31	12.4
Duration of cancer diagnosis (Month)	Less than 12	181	72.4
	13-24	39	15.6
	25-36	12	4.8
	49-60	11	4.4
	More than 60	7	2.8

Table 2 illustrates peripheral neuropathy related Characteristics. Concerning other health problems, it was noticed that 45.2% of studied sample suffering DM, whereas 28.0% suffering hypertension. The same table reveals that 47.6 suffer neuropathy 6-11 month and 41.6 of patients suffer neuropathy less than or equal 5 months. 77.6% were currently receiving chemotherapy, and 2-6 months period after recent chemotherapy was documented by 54% of studied sample. About three fourth (74%) of respondents appreciate active response of medical team, whereas one third (32%) treated pharmacologically and 26% use both pharmacological and non-pharmacological intervention compared to 24.4% aware of symptoms without any intervention.

Table 2. Clinical characteristics of studied sample (N = 250)

Variables	Characteristics	Number	%
TNM staging	Stage 1	23	9.2
	Stage 2	62	24.8
	Stage 3	15	6
	Stage 4	31	12.4
	Unknown	119	47.6
Tumor differentiation	Grade 1	12	4.8
	Grade 2	54	21.6
	Grade 3	36	14.4
	Grade 4	30	12
	Unknown	118	47.2
Other health problems	Hypertension	70	28.0
	Osteoarthritis	8	3.2
	Heart disease	5	2.0
	DM	113	45.2
	DM and hypertension	54	21.6
Duration of neuropathy (Month)	Less than or equal 5	104	41.6
	6-11	119	47.6
	12-17	21	8.4
	More than or equal 24	6	2.4
Status of chemotherapy	Current	194	77.6
	Past	56	22.4
Period after recent chemotherapy (Month)	Less than or equal 2	75	30
	2-6	135	54
	7-12	35	14
	More than or equal 13	5	5
Response of medical team	Active	190	76
	Inactive	44	17.6
	Apathy	4	1.6
	Non-responsive	12	4.8
Intervention	Pharmacological	80	32
	Non-pharmacological	44	17.6
	Dual	65	26
	None	61	24.4

Figure 1 shows the distribution of studied sample according to symptoms severity using patient neurotoxicity questionnaire (PNQ). It can be noticed that, the proportion of patients with PNQ of grades A, B, C, D, and E was respectively, 27.2%, 20.0%, 20.0%, 12.2%, and 20.8%. with mean score is 5.58 ± 2.97.

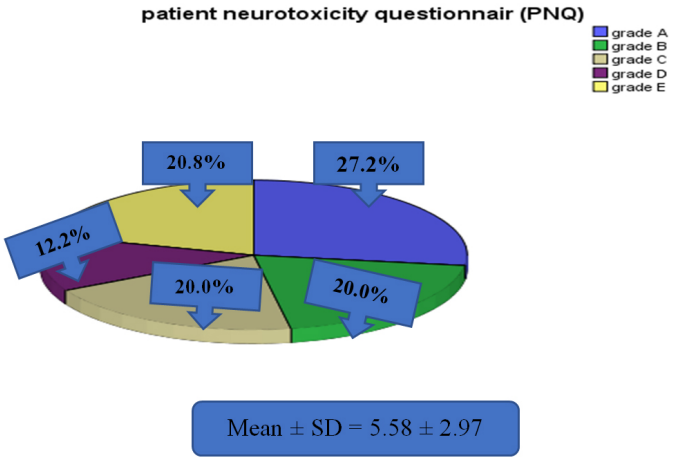

Figure 1. Distribution of studied sample according to symptoms severity using patient neurotoxicity questionnaire (PNQ) (N = 250)

Figure 2 shows that, the sensory area registered the highest mean score (21.23), followed by motor area (17.33) with lowest mean score in autonomic area (5.11), representing statistical significant effect on quality of life.

Figures 3, 4 and 5 show the score and frequency per question of EORTC CIPN20 for patients with peripheral neuropathy. among sensory symptoms, the incidence of tingling in the fingers and hands/toes and feet increased followed by numbness, aching, and burning pain. problems in standing or walking because of difficulty feeling the ground under feet and difficulty distinguishing between hot and cold water were also reported by the majority of patients. Regarding motor symptoms, difficulty manipulating small objects, walking, climbing stairs and getting up out of a chair were most reported motor difficulties.

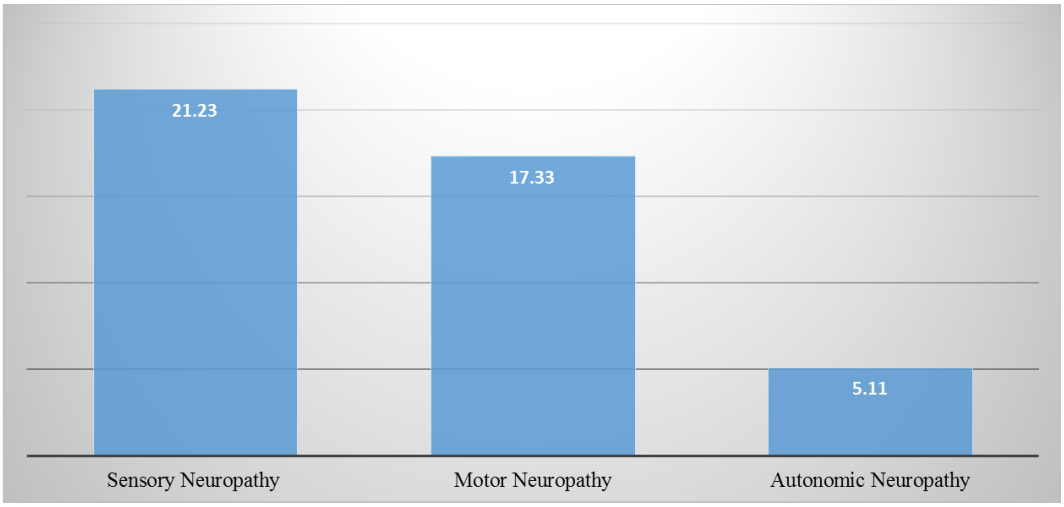

Figure 2. Mean Score of EORTC CIPN20

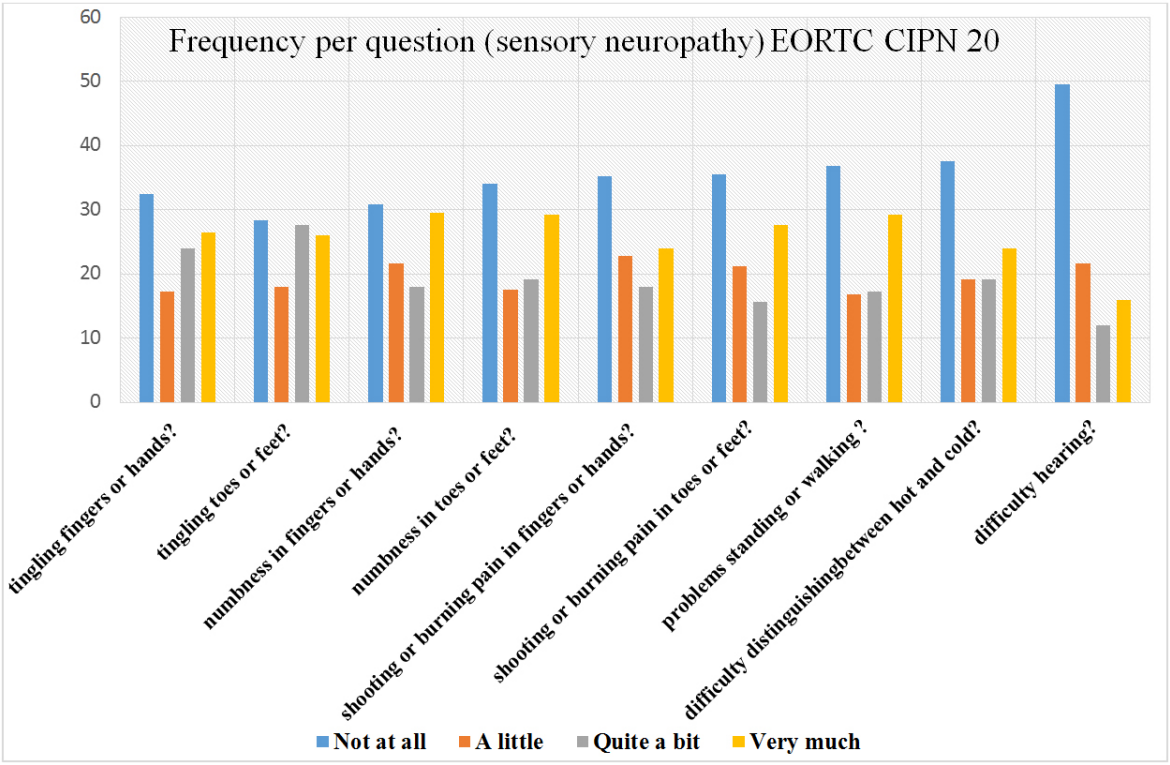

Figure 3. Score and frequency per question of EORTC CIPN20

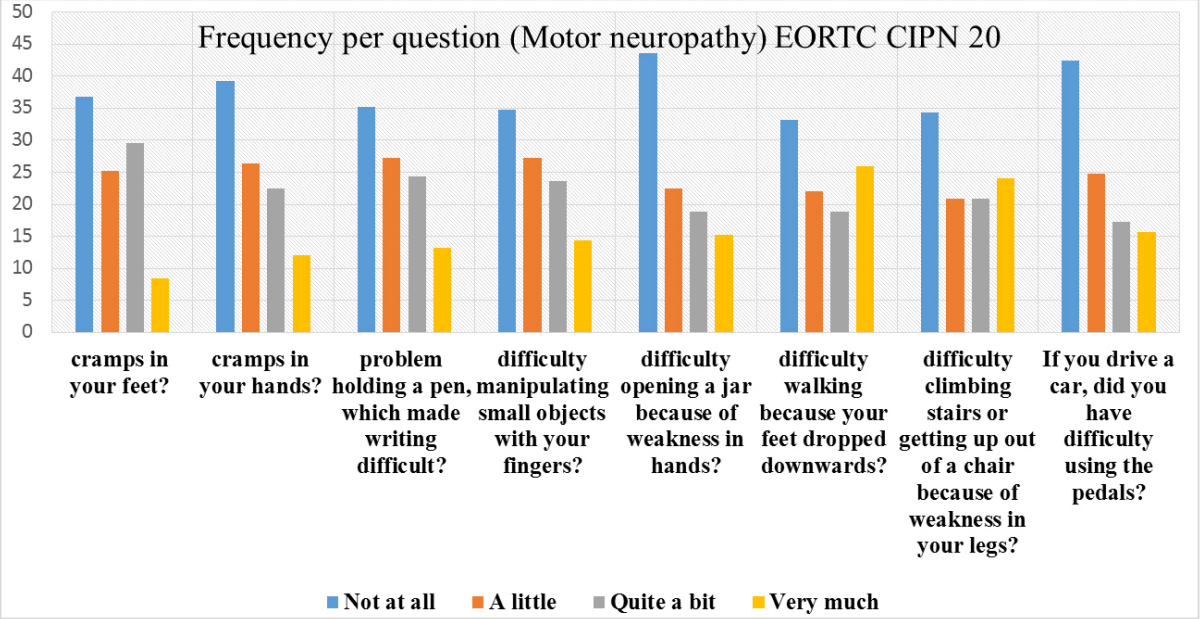

Figure 4. Score and frequency per question of EORTC CIPN20

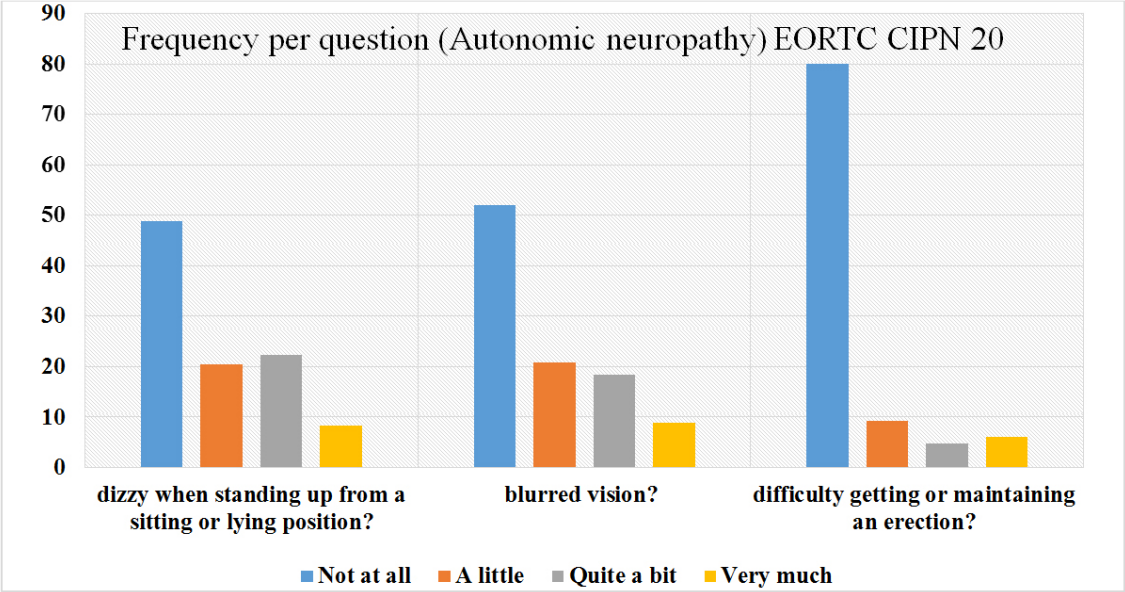

Figure 5. Score and frequency per question of EORTC CIPN20

Table 3 shows that about one fourth of respondents reported poor global quality of life (17.2%). Poor physical function were reported by 22.3% of all participants. fatigue, pain and Insomnia were the most common symptoms suffered by patients (18.6% and 18.7% and 12.2% respectively).

Table 4 shows a significant relation between duration of cancer diagnosis (month) founded in patients diagnosed more than 24 months previously and appearance of sensory symptoms (.01*). Concerning patient's diagnosis, neuropathy significantly related to diagnosis (p = .000*). Also, a relation founded intervention (p = .000), gender(p = .000*), other diseases suffered by the patient (p = .014) especially DM and the presence of neuropathy.

Table 5 demonstrates correlation between symptoms severity related to neurotoxicity and patients' QoL, our study revealed that there was a significant correlation between symptoms severity related to neurotoxicity and patients' QoL (p = .000*) as manifested by sensory, motor, and autonomic neuropathy.

Table 3. EORTC QLQ-C30 score presented with mean, standard deviation (SD), median and frequencies

Scale	Mean score ± SD	Median	Poor quality of life/function (%)
Global health status/QoL	55.47 ± 26.11	50.00	17.2
Functional scales			
Physical functioning	67.69 ± 18.99	73.33	22.3
Roll functioning	62.21 ± 29.50	66.67	14.6
Emotional functioning	56.62 ± 23.14	62.5	13.5
Cognitive functioning	69.21 ± 24.03	66.67	9.5
Social functioning	72.01 ± 27.17	83.33	7.9
Symptoms scales			Symptomatic (%)
Fatigue	47.15 ± 23.46	38.89	18.6
Nausea/Vomiting	23.72±25.19	16.67	4.1
Pain	33.87±26.94	33.33	18.7
Single items			Symptomatic (%)
Dyspnea	24.73 ± 27.35	33.33	1.1
Insomnia	47.65 ± 32.38	33.33	12.2
Appetite Loss	48.50 ± 31.07	33.33	2.5
Constipation	34.40 ± 29.67	33.33	2.8
Diarrhea	31.42 ± 28.56	33.33	3.7
Financial difficulties	23.72 ± 25.19	16.67	2.9

Table 4. Relationship between peripheral neuropathy-related characteristics and peripheral neuropathy-related quality of life (CIPN20)

Variables		Sensory neuropathy	Motor neuropathy	Autonomic neuropathy
Duration of cancer diagnosis (month)	*F* or *t*	3.400	2.062	2.250
	p	0.01*	0.08	.06
Patients' Diagnosis	*F* or *t*	14.193	12.370	5.063
	p	0.000*	0.000*	.000*
Status of chemotherapy	*F* or *t*	2.715	.010	.029
	p	0.10	0.91	.86
Neuropathy related Intervention	*F* or *t*	26.926	9.043	1.626
	p	0.000*	0.000*	0.18
Gender	*F* or *t*	11.261	7.423	4.547
	p	0.001*	0.007*	.03*
Most frequent condition	*F* or *t*	2.910	1.432	1.209
	p	0.014*	0.21	.305

Note. F: One Way ANOVA; *t*: samples *t*-test; *$p < .05$ (significant).

Table 5. Correlation between Patient neurotoxicity and EORTC CIPN20

		Patient neurotoxicity questionnaire PNQ	Total sensory	Total motor	Total autonomic
Patient neurotoxicity questionnaire PNQ	Pearson Correlation	1	.817**	.624**	.252**
	Sig. (2-tailed)		.000	.000	.000
Total sensory	Pearson Correlation	.817**	1	.638**	.386**
	Sig. (2-tailed)	.000		.000	.000
Total motor	Pearson Correlation	.624**	.638**	1	.379**
	Sig. (2-tailed)	.000	.000		.000
Total autonomic	Pearson Correlation	.252**	.386**	.379**	1
	Sig. (2-tailed)	.000	.000	.000	

**Correlation is significant at the 0.01 level (2-tailed).

4. DISCUSSION

CIPN is a common restricting complication of many anticancer therapy that rigorously affects the patient's QoL. Generally, about 68% of those patients suffering CIPN early after treatment,[4, 17] requiring dose modification or termination, resulting in increased cancer-related morbidity and mortality.[18, 19]

Using self-administered questionnaires has now become standard practice in oncological research to assess patients' QoL and is increasingly achieving significance as an evaluation tool used in clinical decision-making. So, it is crucial to deliver a further accurate measure of the prevalence of CIPN to permit proper resource allocation and research planning, informed decision making regarding treatment plan, furthermore understanding risk factors to guide future research and treatment.[1, 18]

Based on the above results, we will discuss the relationship between the characteristics of peripheral neuropathy experienced by cancer patients receiving chemotherapy, quality of life, and related factors.

The current study found that, the age of the studied sample extended from 18 to 60 years. The mean age was 49.9 $\pm$ 10.18, mostly diabetic, and females were more included. According to American cancer society, Cancer Facts & Figures 2017[20] Cancer risk increases with age; an estimated 80% of all cancers in the world are diagnosed in people 50 years of age or older, with increased incidence in females than males. The most common types of cancers are breast and liver cancer, in this respect Ibrahim, Khaled & Mikhail, 2014[21] documented that, approximately one third of cancer in males diagnosed as liver and bladder cancers. Whereas breast and liver cancer occupied the top ranks in females, of all cancers in Egypt. These could be attributed to the high prevalence of hepatitis C viral infection (HCV), which is more frequent in Nile delta.

Regarding symptoms severity the majority of our studied sample suffering grad II, III, and V according to PNQ scale with a greater impact on activities of daily living. This is in accordance with a studies carried out by Driessen et al. (2012) and Gaballah, Shafik & Elhusseiny (2018)[22, 23] reported that of the patients experiencing neurotoxicity, the majority had severe and moderate symptoms. Another study by Argyriou et al. (2013) and Brewer, Morrison & Dolan (2016)[24, 25] showed that CIPN develops coincidently with accumulating doses of neurotoxic agents with aggressive deterioration, depending on type of chemotherapeutic agent, cumulative dose applied, and duration of administration as the most important factors affecting the severity of neuropathy.

Quality of life indicators measure disease and its treatment related impact on the patient's mental and physical well-being. These indicators assess the non- therapeutic aspects of care and explore deep into life of the patients to understand their own perception of the disease and identify associated problems,[26] that negatively affect patients' quality of life, functional ability, sleep, balance, and influence adhesion to anticancer therapy.[27]

Our results revealed that, the sensory symptoms are the most commonly founded symptoms in our studied sample, followed by motor and autonomic symptoms. This may accredited to the effect of chemotherapeutic agents that interfere with axonal transport, target the sensory cell bodies and nerve axons, and induce neuronal cell death.[28] In this respect studies by Cavaletti and Marmiroli, 2015; Dermitzakis, Kimiskidis & Lazaridis, 2016 and Boland, Sherry, and Polomano, 2017[29–31] reported that, clinically, CIPN presents as deficits in sensory, motor, and autonomic function but sensory symptoms are far more common than motor or autonomic.

Moreover the results of our study reveal that, among sensory symptoms, the incidence of tingling in the fingers and hands/toes and feet increased followed by other symptoms of numbness, aching, and burning pain. These phenomena described in the study by Baptista-de-Souza et al. (2014)[32] reported that, neuropathy affecting nerves, and excite extracellular calcium, interfering with sensory neurons depolarization with consequent membrane hyperexcitability. These findings are similar to the findings of Cavaletti, and Marmiroli (2015)[29] who reported that numbness and aching/burning pain in toes and feet were significantly worse in patients managed with chemotherapy. Moreover studies by Dermitzakis et al. (2016);[30] and Starobova and Vetter (2017)[33] clarify that the sensory subscale of the EORTC QLQ-CIPN20 showing clearly CIPN related manifestations that appears initially in the feet and hands as numbness, tingling, paresthesia and dysesthesias induced by touch, warmer cool temperatures, compromised vibration and changed touch sensations.

Patients under potentially neurotoxic chemotherapy are at higher risk for falls, which increases at every chemotherapy cycle.[34] In the same contexts our results revealed that, CIPN patients suffering difficulty feeling the ground under feet resulting in standing or walking problems. Difficulty distinguishing between hot and cold water were also reported by the majority of patients. Also studies carried out by Simão, Murad, and Martins (2015)[35] showed that, sensory symptoms are described as bilateral paresthesia, often reported as numbness and tingling in 90% of CIPN cases and commonly

reported as "difficulty to hold things" and to discriminate shape, texture and/or temperature. These findings are in agreement with the findings of Cavaletti et al. (2013)[36] clarify that, chemotherapeutic agents were positively associated with tingling, numbness, and aching or burning pain in toes or feet that affecting standing or walking ability.

Regarding motor symptoms, the finding of the present study showed that, difficulty manipulating small objects with fingers, walking, and climbing stairs or getting up out of a chair were most reported motor difficulties by studied patients. This may attributed to decreased strength of distal muscle, resulting in weakness in dorsiflexion of the feet, athetoid movements and muscle cramps in the calf with subsequent foot drop.[37] This is in accordance with a study by Mols et al. (2016)[38] who reported that CIPN related motor symptoms include distal weakness, gait and balance disturbances and impaired fine movements can progress to paralysis with significant functional disruption. Also studies carried out by Speck et al. (2012) & Mols et al. (2013)[5,39] showed that CIPN results in serious limitations in daily functioning manifest as feet weakness, gait and balance disorders, and difficulties with fine movements (writing, buttoning clothes, cutting and sewing),with significant impact on QL, directly interfering with daily activities, and behavior of cancer patients.

In our study autonomic symptoms documented low scores. In the same way Mols et al. (2016)[38] denoted that autonomic symptoms occur less frequently in cancer patients treated with chemotherapy including orthostatic hypotension, constipation and altered sexual or urinary function.

HRQL is progressively predicted as a significant measure in cancer research. In our study results related to EORTC QLQ-C30 subscales poor physical function and global quality of life were reported by participants. This is primarily owing to adverse change in sensory and/or motor function caused by toxic or physical nerve damage, which results in serious limitations in daily functioning. In the same vein Kirchheiner, Nout and Pötter (2015)[40] stated that cancer-related neuropathy affecting global health status, and physical and role functioning that poses a barrier to recovery of function and treatment tolerability, causing a highly significant decline, in quality of life. Furthermore, study by Hong and Tian (2014)[41] confirmed that CIPN has a negative influence on QOL as a consequence of social role impairment, due to functional skills changes, in addition to disappointment and loss of objectives due to the need to give up some activities. While these findings are different from the findings of a study by Pasek, Suchocka and Urbanski (2013)[42] found that patients diagnosed with CIPN were satisfied with their Global Quality of Life.

In relation to symptoms subscale of EORTC QLQ-C30, insomnia, appetite loss, bowel elimination problems (diarrhea and constipation), fatigue, pain and insomnia were the most common symptoms suffered by patients. This is primarily due to direct toxic effect of chemotherapeutic agents and other neuropathic related symptoms. These findings match the findings of Mols, Beijers, Vreugdenhil and Kirchheiner (2014)[43] they noted that, patients treated with a variety of neurotoxic agents can experience fatigue and malaise, anxiety, depression and sleep disorders, which were worsened by neuropathic pain. Another study by Simão et al. (2012)[34] showing that according to the EORTC QLQ-C30, CIPN fatigue, pain, poor physical functioning, appetite reduction, and reduced overall health, are issues of major concern for cancer patients with CIPN.

Driessen et al. (2012)[22] reported undesirable influence of CIPN on patients' regular activities and QOL. Additionally, Patients complain from feelings of frustration, and hopelessness, resulting from inability to carryout enjoyable activities. In the same direction study by Mols et al. (2013)[5] stated that, patients with severe neuropathic symptoms documented statistically significant worse scores on all EORTC QLQ-C30 subscales compared to those with less neuropathy symptoms.

The present study found a significant relation between duration of cancer diagnosis (month) and CIPN, as patients diagnosed more than 24 months suffering more symptoms, this my attributed to anticancer agent, the duration of therapy, combinations of chemotherapeutic agents and the cumulative dose applied. Our results goes in line with the report of Gaballah et al. (2018)[23] who stated that a significant percentage of CIPN cases persisted for more than 12 months. These results suggest that patients who have been on chemotherapy for a long time using various anticancer drugs and because of the nature of peripheral neuropathy, symptoms may persist for months to years after the treatment or may remain irreversible. In this respect Park et al. (2011), Kautio 2017 and Starobova & Vetter (2017)[33,44,45] reported that, development of CIPN is closely linked to both single as well as cumulative drug doses of chemotherapeutic agents at the end of cancer therapy, differently from other adverse effects, CIPN symptoms may not stop and may even worsen. Therefore, the medical staff should continue to evaluate and manage peripheral neuropathy even if the chemotherapy is terminated.

In relation to age it was founded that recorded significant relation between age and sensory neuropathy as it increased with age. Study carried out by Tofthagen (2010)[46] showed that with increased age most of CIPN symptoms are age-related

and not certainly associated with cancer or its treatment. Another research carried out by Balayssac et al. (2011)[47] denoted that patients' characteristics as age, is among the influencing factors to develop CIPN.

Concerning patient's diagnosis, it is clear that neuropathy significantly related to diagnosis. In the same way Argyriou, Bruna and Marmiroli (2012)[44] documented that CIPN is a common complication among patients treated with chemotherapy for most malignancies. taxanes, platinums, bortezomib, thalidomide, lenolidamide, and vinca alkaloids are anticancer agents used to manage numerous types of cancers and linked to sever neurotoxicity.

In relation to chemotherapy related interventions, patients choose to use intervention other than pharmacological therapy suffering sensory and motor neuropathy compared to other patients treated with pharmacological therapy. This is in accordance with a study carried out by Kautio, Haanpaa and Saarto (2007)[45] who stated that pharmacological therapy is effective in treatment of peripheral neuropathy especially in diabetic patients. Concerning Gender, the findings of the present study reveal that female patients recorded significant relation between gender and peripheral neuropathy including sensory, motor, and autonomic neuropathy. There were no studies found for the relation between the gender related to peripheral neuropathy.

In the present study DM, followed by Hypertension recorded a significant relation with sensory neuropathy. These findings goes well together with Starobova and Vetter (2017)[33] who stated that numerous cases as pre-existing nerve impairment, as in diabetic patients, can be associated with an increased risk of developing CIPN. Another study by Gaballah et al. (2018)[23] confirmed that systemic diseases, such as diabetes, related to higher risk of peripheral neuropathy, predispose the onset of more frequent and severe symptoms, even with the use of low doses of anticancer agents.

Concerning correlation between symptoms severity and peripheral neuropathy related QoL, the findings of the present study revealed that there was a significant correlation between symptoms severity and impaired QoL. This was also found in a study by Driessen et al. (2012)[22] who showed a strong negative correlation between QOL and CIPN as assessed during chemotherapy treatment. Another study by Griffith et al. (2014)[46] confirmed that more CIPN symptoms were correlated with a lower QOL. This is in accordance with a study carried out by Carlson and Ocean (2011)[47] who reported that CIPN symptoms may evolve to a point in which people can no longer live with them being necessary to decrease anticancer agent dose or even discontinue treatment.

5. Conclusion/Recommendations

Treatment is not the only aspect of health care services. It also includes detecting and addressing problems affecting patients' QoL. Peripheral neuropathy is the most common complication affecting the cancer patients' QoL treated with chemotherapy, where the incidence of CIPN reached a significant percentage of patients and affects their QoL, therefore, early detection CIPN is needed to avoid long term damage. Many neuropathy symptoms are subjective in nature, assessing them with a self-reported questionnaire is necessary to gathering information from patients who are the most reliable source of information needed to help clinicians to use this data as a guidance to develop and evaluate much needed targeted therapies, thus preventing permanent complications, functional disabilities and help improving QoL.

Future research and clinical application

Future research involving a larger study sample would help in doing some stratified analysis. It should help in differentiating the findings among different participants with various cancer types, and various chemotherapy agents.

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Conflicts of Interest Disclosure

The authors declare that they have no conflict of interests.

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