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Prevalence and factors associated with chemotherapy induced peripheral neuropathy among adult patients with cancer at Mbarara Regional Cancer Centre: a cross-sectional study

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Abstract

Background Chemotherapy is a common modality used for management of cancers but some agents are known to cause peripheral neuropathy. Chemotherapy induced peripheral neuropathy (CIPN) refers to a disorder in structure and functionality of peripheral sensory, motor, and autonomic neurons triggered by the toxic effects of these drugs. CIPN is a common adverse drug reaction (ADR) caused by mainly platinum analogs, vinca alkaloids and taxanes. Severe CIPN can cause paresis, complete immobilization and disability. The objectives of this study were to determine the prevalence, factors associated with and evaluate treatment of CIPN among adult patients with cancer at Mbarara Regional Cancer Centre.

Methods A cross-sectional study was conducted for a period of 2 months among adult patients with cancer receiving chemotherapy at Mbarara Regional Cancer Centre. Consecutive sampling technique was used to enroll 235 participants into the study. Data collection was done through patient interviews and file reviews. Assessment of the clinical features of CIPN was done using EORTC-QLQ-CIPN20 tool. SPSS version 27 was used for data entry and analysis.

Results The prevalence of CIPN was 31.1%. The factors associated with occurrence of CIPN include age greater or equal to 60 years (aOR = 2.04, 95% CI: 1.07–3.91, p-value = 0.031), concurrent administration of non-chemotherapeutic neurotoxic drugs (aOR = 6.50, 95% CI: 1.64–9.36), past resolved neuropathy prior to initiation of chemotherapy (aOR = 6.99, 95% CI: 2.28–9.21). 30.1% of patients with CIPN received treatment and were managed with agents such as pregabalin, gabapentin, cachnerve, Nat B, neuroton, amitriptyline and vitamin B complex. The American Society of Clinical Oncology guideline recommends use of duloxetine for treatment of CIPN.

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Conclusion Nearly one-third of patients at Mbarara Regional Cancer Centre had CIPN. Patient age 60 years and above, past resolved neuropathy and concurrent administration of non-chemotherapeutic neurotoxic drugs are factors associated with occurrence of CIPN. Therefore, such patients require close monitoring for the symptoms of peripheral neuropathy so that appropriate treatment can be initiated promptly.

Keywords Chemotherapy, Adverse drug reaction, Peripheral neuropathy, Prevalence, Cancer, Mbarara

Introduction

Cancer is among the leading diseases that pose a huge health threat to humans [1]. The reported number of new cases in 2022 for all types of cancer globally was about 20 million and this incidence is expected to rise to approximately 35 million by end of 2050 while mortality due to cancer was reported at about 9.7 million deaths in 2022 [2]. In Uganda, 35,968 new cancer cases and 24,629 cancer-related deaths were recorded in 2022 [3]. The most common cancer management modalities include surgery, chemotherapy and radiotherapy [4].

Antineoplastic agents have narrow therapeutic index hence their high likelihood of causing toxicities that can be short-lived or long lasting, acute or chronic and mild or potentially fatal [5]. The common chemotherapy-induced ADRs reported include fatigue, alopecia, neuropathy, nausea, vomiting, anorexia and constipation; Others include myelosuppression, mucositis, cardiac toxicity and electrolyte imbalances [1]. One way to manage a chemotherapy-associated ADR is by lowering the drug dosage for an affected patient. However, use of a lower dose of an antineoplastic drug below its therapeutic level significantly lowers the cure rates of patients with cancer [6].

Chemotherapy-induced peripheral neuropathy is an ADR caused by anticancer drugs with prevalence that ranges from 19% to more than 85% [7]. CIPN is caused by mainly taxanes, platinum analogs and vinca alkaloids [8]. Cumulative exposure to these drugs or their administration at high single doses leads to the occurrence of symptoms of CIPN [9]. Occurrence of symptoms of CIPN can begin a few weeks or months after commencement of treatment with neurotoxic anticancer drugs and may continue for many months or years after treatment cessation [10]. Clinical manifestation of the peripheral neuropathy includes sensory features like numbness and tingling experienced in body extremities; motor features like distal weakness, impaired movement, gait and balance disturbances that pose a risk of falls especially among elderly patients and autonomic symptoms such as decreased urinary function, lowered sexual activity, constipation and orthostatic hypotension [11].

Because of the high prevalence of CIPN as reported in previous studies coupled with the fact that there is no effective regimen for its prevention, the ADR poses a huge health burden for both cancer patients and survivors and is a challenge for health care providers as well

[7]. Furthermore, duloxetine currently has the most consistent evidence supporting its efficacy for treatment of CIPN [12]. Manifestation of symptoms of CIPN warrants a reduction in the dose of the offending antineoplastic drug or even its discontinuation. However, discontinuation affects treatment of the cancer or its prognosis [13]. Clinical features of the peripheral neuropathy especially numbness and tingling in the body extremities and pain usually continue for months or sometimes years after completion of anticancer treatment thus causing immense suffering in cancer survivors [14]. Patients with severe CIPN can have total immobilization, paresis and serious disability [15]. A study conducted by Selvy, Kerckhove [16] reported that sensory and motor chemotherapy induced peripheral neuropathies are linked to depression, worsening quality of life and anxiety in affected individuals.

With the increasing new cases of cancer being registered at Mbarara Regional Cancer Centre, many patients are being initiated on chemotherapy yet most of the drug classes commonly used (taxanes, platinum analogs and vinca alkaloids) are known to cause CIPN. The fact that there is no effective regimen for prevention of CIPN means that a substantial proportion of patients who receive these drugs end up getting the ADR leading to reduced adherence and thus poor treatment outcomes during management of the cancers.

Having knowledge about the burden of CIPN at Mbarara Regional Cancer Centre will improve clinical monitoring of patients for symptoms of the ADR so that it can be promptly and adequately managed by clinicians at the cancer unit. Assessment of the factors associated with occurrence of CIPN will enable clinicians to predict patients with cancer who are more likely to develop the ADR so that use of neurotoxic antineoplastic drugs in such groups can be avoided or close monitoring can be done if the agents are administered. Evaluation of the treatment practices of CIPN that is alignment with guidelines and treatment frequency will offer guidance to the clinicians, hospital and policy makers on development of an algorithm for management of CIPN.

The burden of chemotherapy induced peripheral neuropathy, factors associated with its occurrence and the management practices have not been established in Mbarara Regional Cancer Centre. This study therefore aimed at determining the prevalence of CIPN, assessing factors associated with its occurrence and evaluation of

treatment of the ADR among adult patients with cancer at Mbarara Regional Cancer Centre.

Methods

Study design and setting

A cross-sectional study was conducted among adult patients with cancer receiving chemotherapy at Mbarara Regional Cancer Centre. The study was carried out over a two-month period, from June 2024 to July 2024. Mbarara Regional Cancer Centre is an oncology unit in Mbarara Regional Referral Hospital (MRRH). MRRH is a government health facility that also serves as a teaching hospital for the medical school of Mbarara University of Science and Technology and other health institutions around. The referral hospital is situated in Mbarara city, one of the cities found in Uganda. MRRH serves about 4 million people in 13 districts of South-Western Uganda. Mbarara Regional cancer centre has a total of 45 beds; 18 beds in the adult section, 19 beds in the pediatric section and 8 beds in the infusion room. The unit has 3 specialist oncologists (1 for the adult section and 2 for the pediatric section), 2 Pharmacists and 11 Nurses (5 for the adult section and 6 for the pediatric section). The cancer unit initiates chemotherapy for around 60 new adult patients on a monthly basis, with a total of about 500 patients receiving chemotherapy treatments every month.

Study participants

We included male and female patients aged 18 years and above, with confirmed cancer diagnosis and had received at least one cycle of chemotherapy within the past 3 months. Patients with past resolved neuropathy were included while those with active non-chemotherapy neuropathy due to other conditions such as diabetic neuropathy were excluded. Unconscious patients were excluded from the study.

Sample size

Fisher's formula was used to establish the appropriate sample size for the study [17]. The prevalence of CIPN was estimated at 83.6%, according to a study conducted at Kenyatta National Hospital oncology units in Kenya [18] as no similar studies have been conducted in Uganda. A 95% level of confidence and 5% level of significance were used for sample size calculation and a 10% contingency was added to cater for incomplete data. A total of 235 participants were enrolled into this study. A consecutive sampling method was employed to recruit participants for the study within the stated period.

Data collection tools and procedures

A data abstraction form was used to collect information from patients' files. Such information included patient demographics, anthropometric measurements like

weight and height; information about the cancer, comorbid conditions and drug related information.

A questionnaire was used to conduct patient interviews to obtain subjective information during assessment of symptoms of CIPN that patients experienced in the past one week using the EORTC- QLQ CIPN20 scale [19]. The EORTC-QLQ-CIPN20 scale is a validated patient reported tool designed to assess symptoms of CIPN. It is a 20-question scale where patients are asked to rate how much they experienced sensory, motor and autonomic symptoms of neuropathy during the past week. The scores 1,2,3 or 4 are assigned for each question or symptom depending on the severity; 1 = Not at all, 2 = A little, 3 = Quite a bit, 4 = Very much. Naranjo scale [20] was then used to do causality assessment for patients that had a high score of greater than or equal to 30 on the EORTC-QLQ-CIPN20 scale [21]. Naranjo scale is a validated 10-item ADR probability tool, and was used in this study to rule out other possible causes of peripheral neuropathy. The tool estimates the likelihood that an adverse drug event was caused by the drug which in this case was the chemotherapy agent(s). Additionally, Hartwig's tool [22] was used to assess the severity of CIPN.

The principal investigator (clinical pharmacist) and research assistants (two bachelor nurses) collected data during the study. Training of research assistants was conducted by the clinical pharmacist before the data collection process commenced. The training encompassed information about the research study in general but with particular emphasis on the process of seeking informed consent from potential study participants, the data collection tools and which information was to be collected from patient files or during patient interviews.

The nurses collected information from patient files using the data abstraction forms and then conducted patient interviews to assess clinical features of CIPN using the EORTC-CIPN20 tool. Causality assessment using Naranjo scale and determination of the severity of CIPN using Hartwig's tool was thereafter done by the clinical pharmacist.

Data analysis

SPSS software version 27 was used for data entry and analysis. Patient sociodemographic and clinical characteristics, the prevalence of CIPN, severity of CIPN and evaluation of treatment of CIPN were analyzed using descriptive statistics that is frequencies, percentages, appropriate charts, measures of central tendencies and measures of dispersion. Determination of factors associated with occurrence of CIPN was done using logistic regression. The outcome variable, CIPN, was binary and measured at a single point in time. We thus used univariate logistic regression to estimate crude odds ratios. Variables with $p < 0.05$ at 95% confidence interval were

Table 1 Sociodemographic characteristics of adult patients with cancer receiving chemotherapy at Mbarara Regional Cancer Centre

Variables	Categories	Frequency	Percentage
Gender	Male	144	61.3
	Female	91	38.7
Age in years Mean = 60 SD = 16.65	18–59	104	44.3
	≥ 60	131	55.7
BMI	Normal	125	53.2
	Underweight	56	23.8
	Overweight	39	16.6
	Obese	15	6.4
History of smoking	No	146	62.1
	Yes	89	37.9
History of alcohol drinking	No	98	41.7
	Yes	137	58.3

Table 2 Clinical characteristics of adult patients with cancer receiving chemotherapy at Mbarara Regional Cancer Centre

Variable	Categories	Frequency	Percentage
Stage of tumor	I	8	3.4
	II	12	5.1
	III	59	25.1
	IV	156	66.4
Diabetes	No	219	93.2
	Yes	16	6.8
Chronic kidney disease	No	230	97.9
	Yes	5	2.1
Past resolved neuropathy	No	216	91.9
	Yes	19	8.1
History of surgery done for a cancer	No	189	80.4
	Yes	46	19.6

included in a multivariate logistic regression model to obtain adjusted odds ratios and control for potential confounders. Independent variables with p-values less than 0.05 at multivariate analysis were then considered to have statistically significant association with CIPN.

Results

Sociodemographic characteristics of the participants

A total of 235 participants were included in the final analysis. Majority of the participants were males (61.3%), their mean age was 60 years and most of them (53.2%) had normal BMI. A high proportion (58.3%) of the participants had a history of alcohol drinking while only 37.9% were smokers or had a history of smoking (Table 1).

Clinical characteristics of the participants

Most of the participants (66.4%) had stage IV cancers, only 6.8% and 2.1% had diabetes and chronic kidney disease respectively. Additionally, 8.1% of the patients had neuropathy in the past but resolved before chemotherapy initiation (Table 2).

Table 3 Drug characteristics of adult patients with cancer receiving chemotherapy at Mbarara Regional Cancer Centre

Variables	Categories	Frequency	Percentage
Number of chemotherapeutic agents received	1	99	42.1
	2	94	40.0
	3	37	15.7
	4	5	2.1
Cycle duration	7	20	8.5
	14	17	7.2
	21	181	77.0
Cycles of chemotherapy received	28	17	7.2
	1–3	78	33.2
	4–5	58	24.7
Non-chemotherapeutic neurotoxic drugs*	> 5	99	42.1
	No	221	94.0
Platinum	Yes	14	6.0
	No	140	59.6
Taxane	Yes	95	40.4
	No	106	45.1
Vinca	Yes	129	54.9
	No	217	92.3
	Yes	18	7.7

*Non-chemotherapeutic neurotoxic drugs included; Levofloxacin ($n=7$), ciprofloxacin ($n=3$), metronidazole ($n=3$), nitrofurantoin ($n=3$), thalidomide ($n=1$), bortezomib ($n=1$)

Drug characteristics of the participants

Majority of the patients (77.0%) were receiving their chemotherapy after every 21 days, most of them (42.1%) had received more than 5 cycles of chemotherapy while 6.0% were concurrently receiving non-chemotherapeutic neurotoxic drugs for management of other conditions (Table 3).

Common cancers and comorbid conditions among the participants

The predominant type of cancer identified was prostate cancer (62 patients), followed by breast and esophageal cancers (30 patients with each cancer type) (Fig. 1).

The most common comorbid condition among the participants was hypertension (52 patients) followed by peptic ulcer disease (36 patients), HIV/AIDS (22 patients) (Fig. 2).

Prevalence of chemotherapy induced peripheral neuropathy

Out of 235 participants included in the final analysis, 73 had chemotherapy induced peripheral neuropathy giving an overall prevalence of 31.1% (Fig. 3). Assessment of causality for peripheral neuropathy was performed using Naranjo ADR Probability scale for all the 81 participants whose scores were 30 or more on the EORTC-QLQ-CIPN20 tool. This was done to determine the likelihood that their symptoms of neuropathy were caused by the

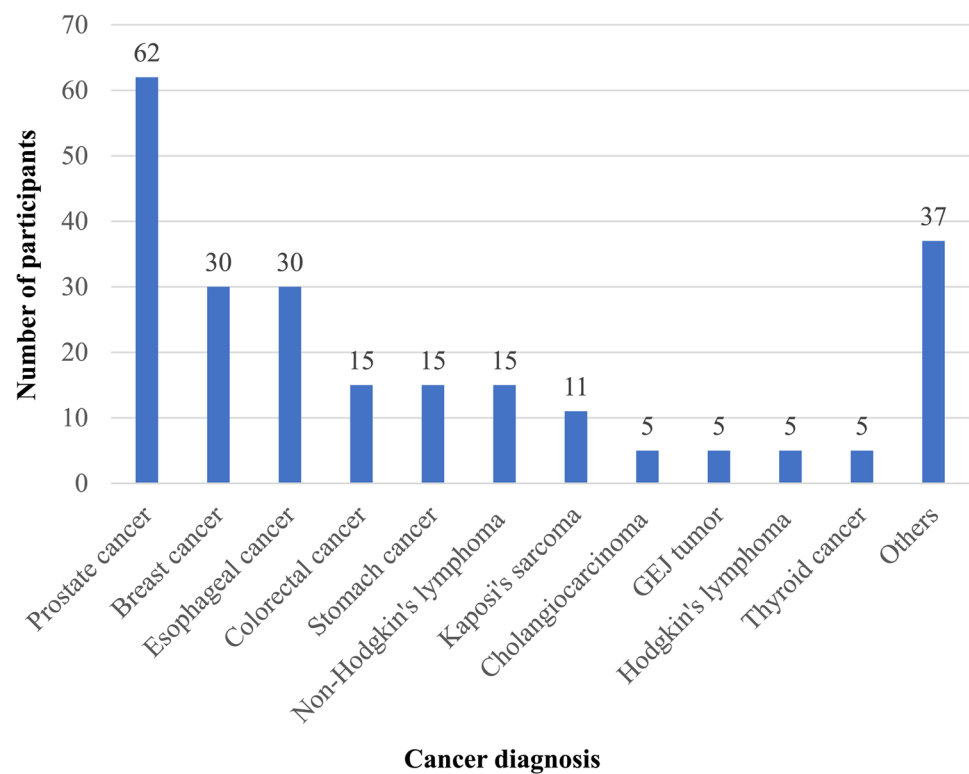


Fig. 1 Common cancers diagnosed among adult patients receiving chemotherapy at Mbarara Regional Cancer Centre

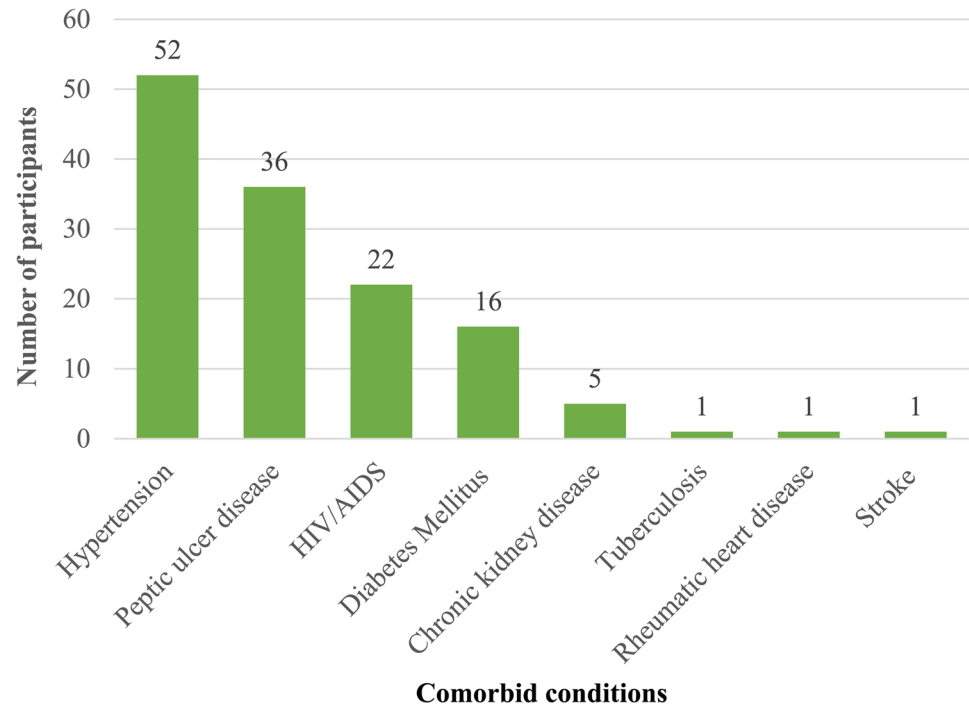


Fig. 2 Common comorbid conditions among adult patients with cancer receiving chemotherapy at Mbarara Regional Cancer Centre

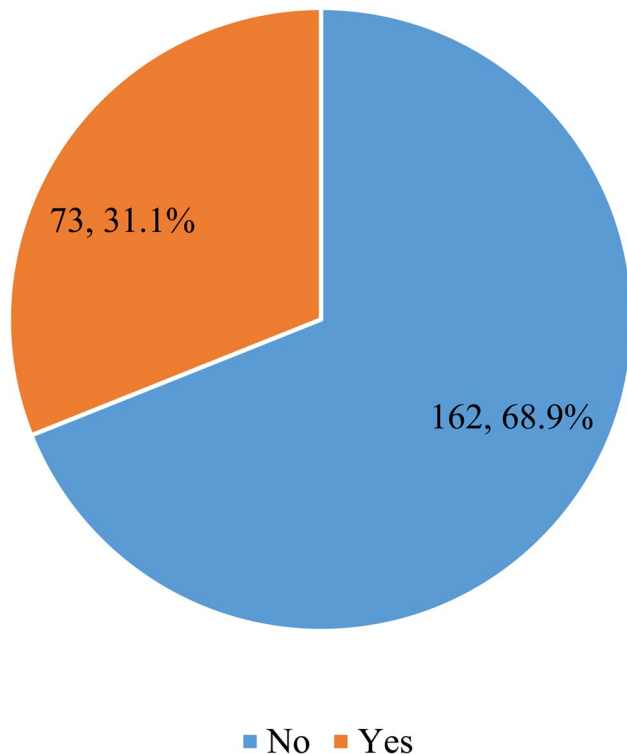


Fig. 3 Prevalence of chemotherapy induced peripheral neuropathy among adult patients with cancer at Mbarara Regional Cancer Centre

chemotherapy agent since similar features occur in other types of neuropathies. 73 had total scores in the categories of “Definite” or “Probable” and were thus concluded to have CIPN. Meanwhile the 8 participants had total scores in the category “Possible” thus their neuropathic symptoms were not caused by the chemotherapy agent. 9.9% of the cases of peripheral neuropathy were possible ADRs, 85.2% were probable ADRs and 4.9% were definite ADRs.

Of the 73 participants with chemotherapy induced peripheral neuropathy, majority (59, 80.8%) had mild neuropathy while the remaining 14 patients (19.2%) had moderate neuropathy.

Factors associated with occurrence of chemotherapy induced peripheral neuropathy

Determination of the factors associated with chemotherapy induced peripheral neuropathy was done using both univariate and multivariate logistic regression techniques. A total of 18 variables were considered for univariate logistic regression analysis but only 9 had p-values less than 0.25; age greater or equal to 60 years (COR=2.85, 95% CI: 1.57–5.20, p-value=<0.001), smoking (COR=2.00, 95% CI: 1.14–3.52, p-value=0.016), overweight/obese (COR=1.57, 95% CI: 0.81–3.08, p-value=0.185), had diabetes (COR=3.11, 95% CI: 1.11–8.72, p-value=0.031), had chronic kidney

disease (COR=9.33, 95% CI: 1.03–13.22, p-value=0.048), received chemotherapy after every 21 days (COR=2.88, 95% CI: 0.81–10.21, p-value=0.101), received a non-chemotherapeutic neurotoxic drug (COR=9.40, 95% CI: 2.54–10.53, p-value=<0.001), had a past resolved neuropathy (COR=7.45, 95% CI: 2.57–9.75, p-value=<0.001), had received 4 or 5 cycles of chemotherapy (COR=1.75, 95% CI: 0.81–3.77, p-value=0.154), had received more than 5 cycles of chemotherapy (COR=2.14, 95% CI: 1.09–4.20, p-value=0.027).

These 9 independent variables were subjected to multivariate logistic regression analysis and 3 retained statistical significance with p-values less than 0.05. These include; age greater or equal to 60 years (aOR=2.04, 95% CI: 1.07–3.91, p-value=0.031) thus older patients have about 2.04 times higher odds of CIPN occurrence compared to those that are in the age range of 18 to 59 years. Patients that concurrently received a non-chemotherapeutic neurotoxic drug had 6.5 times higher odds of CIPN occurrence compared to those that didn't receive these agents (aOR=6.50, 95% CI: 1.64–9.36, p-value=0.008). Patients that had neuropathy in the past but resolved before chemotherapy initiation had about 6.99 times higher odds of CIPN occurrence compared to those without any history of neuropathy (aOR=6.99, 95% CI: 2.28–9.21, p-value=<0.001) (Table 4).

Evaluation of treatment of chemotherapy induced peripheral neuropathy

Only 22 of the 73 patients (30.1%) with chemotherapy induced peripheral neuropathy received treatment for neuropathy while the majority (51, 69.9%) did not receive any treatment.

Of the 22 patients that got treatment for CIPN, none was prescribed duloxetine that is recommended for management of the ADR as per ASCO and ESMO guidelines. Instead the agents prescribed for these patients included amitriptyline, vitamin B complex, cachnerve, neuroton, Nat B, pregabalin and gabapentin (Fig. 4).

Discussion

The prevalence of chemotherapy induced peripheral neuropathy was 31.1%. This was lower than that obtained in a study conducted in Kenya by Ezzi, Othieno-Abinya [18] where the prevalence of peripheral neuropathy among patients receiving cisplatin was found to be 83.6%. The difference can be attributed to the fact that the study in Kenya only assessed the effects of cisplatin which is the most neurotoxic of the platinum analogs hence the high prevalence while in this study, patients on all the different classes of chemotherapeutic agents were recruited. The prevalence of CIPN in this study was also lower than 58.4% obtained in a study conducted in Pennsylvania, United States of America [23]. This difference could

Table 4 Univariate and multivariate logistic regression of the factors associated with chemotherapy induced peripheral neuropathy

Variables	Categories	CIPN		COR (95% CI)	p-value	aOR (95% CI)	p-value
		No n (%)	Yes n (%)				
Age in years	18–59	84 (80.8)	20 (19.2)	1		1	
	≥60	78 (59.5)	53 (40.5)	2.85 (1.57–5.20)	< 0.001*	2.04 (1.07–3.91)	0.031
BMI	Normal	89 (71.2)	36 (28.8)	1		1	
	Underweight	40 (71.4)	16 (28.6)	0.99 (0.49–1.99)	0.975	1.20 (0.54–2.68)	0.652
	Overweight/ Obese	33 (61.1)	21 (38.9)	1.57 (0.81–3.08)	0.185*	1.24 (0.53–2.90)	0.619
History of smoking	No	109 (74.7)	37 (25.3)	1		1	
	Yes	53 (59.6)	36 (40.4)	2.00 (1.14–3.52)	0.016*	1.72 (0.92–3.22)	0.091
Diabetes	No	155 (70.8)	64 (29.2)	1		1	
	Yes	7 (43.8)	9 (56.3)	3.11 (1.11–8.72)	0.031*	2.52 (0.73–8.64)	0.142
Chronic kidney disease	No	161 (70.0)	69 (30.0)	1		1	
	Yes	1 (20.0)	4 (80.0)	9.33 (1.03–13.22)	0.048*	6.49 (0.48–12.04)	0.159
Cycle duration in days	7	17 (85.0)	3 (15.0)	1		1	
	14	13 (76.5)	4 (23.5)	1.74 (0.33–9.19)	0.512	1.82 (0.26–12.74)	0.544
	21	120 (66.3)	61 (33.7)	2.88 (0.81–10.21)	0.101*	3.83 (0.97–15.23)	0.056
	28	12 (70.6)	5 (29.4)	2.36 (0.47–11.82)	0.296	2.69 (0.45–16.12)	0.280
Non- chemotherapeutic neurotoxic drugs	No	159 (71.9)	62 (28.1)	1		1	
	Yes	3 (21.4)	11 (78.6)	9.40 (2.54–10.53)	< 0.001*	6.50 (1.64–9.36)	0.008
History of neuropathy	No	157 (72.7)	59 (27.3)	1		1	
	Yes	5 (26.3)	14 (73.7)	7.45 (2.57–9.75)	< 0.001*	6.99 (2.28–9.21)	< 0.001
Number of chemotherapy cycles received	1–3	61 (78.2)	17 (21.8)	1		1	
	4–5	39 (67.2)	19 (32.8)	1.75 (0.81–3.77)	0.154*	1.12 (0.46–2.77)	0.801
	> 5	62 (62.6)	37 (37.4)	2.14 (1.09–4.20)	0.027*	2.08 (0.98–4.43)	0.057

be explained by the fact that the study in Pennsylvania only involved breast cancer survivors who had received taxane-based chemotherapy and these agents are highly neurotoxic causing clinical features of peripheral neuropathy in most patients whereas in this study only 54.9% of the participants received taxanes and of these 32.6% developed CIPN.

However, the prevalence of CIPN in this study was higher than 17% reported in a previous study in Denmark [21]. This difference can be attributed to the fact that majority of the participants in this study had advanced prostate cancer and were receiving taxanes that are highly neurotoxic hence a higher prevalence.

The current study showed that older patients, 60 years and above, have about 2.04 times higher odds of CIPN occurrence compared to those that are in the age range

of 18 to 59 years. This finding is consistent with that from several previous studies [21, 24–26]. Aging is associated with alterations in structure and biochemical composition of peripheral neurons hence the harmful effect of chemotherapy on these cells is more pronounced in elderly patients compared to younger individuals [27].

Patients that were concurrently receiving non-chemotherapeutic neurotoxic drugs had 6.5 times higher odds of CIPN occurrence compared to those that didn't receive these agents. These drugs included ciprofloxacin, levofloxacin, metronidazole, thalidomide, bortezomib and nitrofurantoin. This association of co-administration of these other neurotoxic drugs with occurrence of CIPN is in line with reports by previous scholars [14, 28]. Thalidomide exerts an antiangiogenic effect that results in secondary ischemia and decreased oxygen levels in

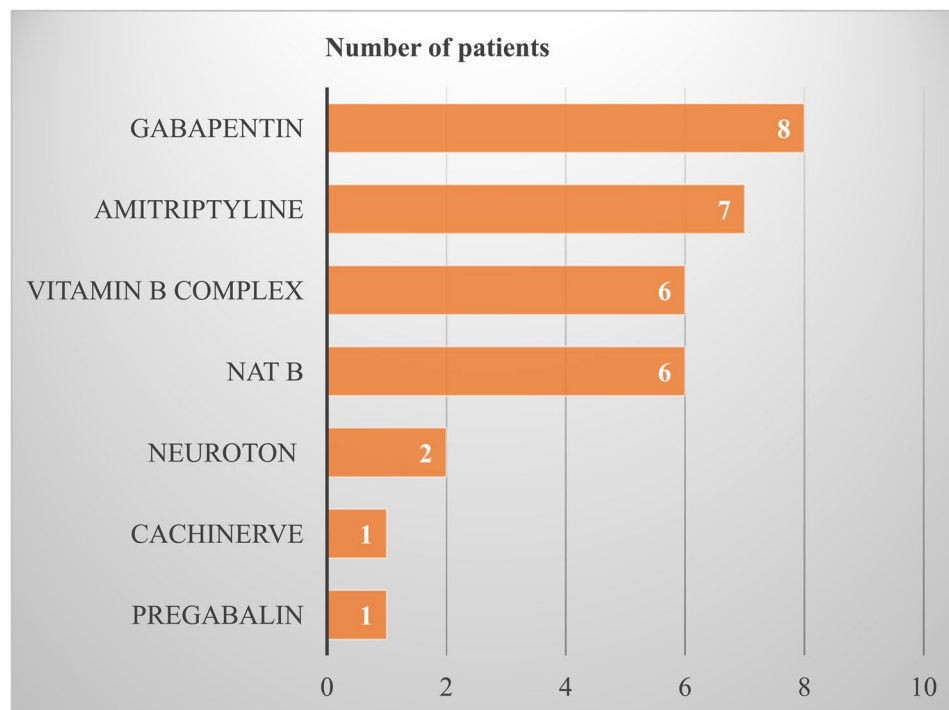


Fig. 4 Drugs prescribed for patients with chemotherapy induced peripheral neuropathy at Mbarara Regional Cancer Centre

neurons, consequently leading to irreversible destruction of sensory nerve fibers [29]. Metronidazole causes axonal degeneration by binding to the RNA of neurons [30]. These mechanisms may contribute to increased neurotoxicity when combined with chemotherapy. Therefore, these non-chemotherapeutic neurotoxic drugs should be avoided and instead safer alternatives given for patients that are receiving neurotoxic chemotherapy.

Patients that had neuropathy in the past but resolved before chemotherapy initiation had about 6.99 times higher odds of CIPN occurrence compared to those without any history of neuropathy. This finding is consistent with that reported by previous scholars [14, 31]. Such patients that had neuropathies in the past but recovered are highly vulnerable to the neurotoxic effects of chemotherapy owing to the fact that complete structural regeneration and gain of functionality of peripheral nerves after damage is a slow process. Therefore, non-neurotoxic chemotherapeutic drugs should be used for patients with history of neuropathy to minimize their risk of developing CIPN.

None of the 22 patients treated for chemotherapy induced peripheral neuropathy was prescribed duloxetine, the recommended drug as per the American Society of Clinical Oncology for management of the ADR. Duloxetine is generally costly and its use for management of CIPN has not yet been adopted into the Uganda Cancer Institute treatment guidelines. The patients were prescribed drugs such as amitriptyline, gabapentin,

pregabalin, cachnerve, neuroton, Nat B and vitamin B complex. The use of these agents for management of CIPN in clinical trials gave inconclusive results [32]. In a randomized, double-blind, placebo-controlled cross-over trial of 231 patients with chemotherapy induced peripheral neuropathic pain, individuals that received a 5-week duloxetine treatment experienced better reduction in pain compared to those that received placebo [mean decrease in average pain of 1.06 (95% CI; 0.72–1.40) vs. 0.34 (95% CI; 0.01–0.66), $p = 0.003$] [32]. A phase III double-blind, placebo-controlled, crossover randomized trial that was conducted among 115 patients with CIPN failed to demonstrate efficacy of gabapentin for treatment of clinical features of CIPN [33]. In a randomized, double-blind, placebo-controlled study that assessed the efficacy of amitriptyline for CIPN, no improvement in the sensory symptoms of neuropathy was demonstrated [34]. Therefore, administration of gabapentin, amitriptyline and other drugs with no proven efficacy for CIPN to patients leads to poor treatment outcomes that include persistence of symptoms of neuropathy and complications of the ADR in affected individuals. Majority of patients with CIPN (51, 69.9%) did not receive treatment for the ADR. This is mainly due to gaps in routine CIPN screening as the cancer unit has few clinicians who have to attend to many patients especially on out-patient clinic days.

Study limitations

The findings of this study should be interpreted in light of the following limitations;

- This was a single center study and therefore its findings may not be generalizable to all cancer units in Uganda.
- Majority of the participants were male and had prostate cancer and this may affect generalizability of the study findings.
- Data on the individual chemotherapy agents and cumulative doses were not captured during the study and this limits interpretability of results since CIPN risk varies depending on the specific drug and exposure levels.
- Some variables such as CKD and non-chemotherapeutic neurotoxic drugs have small sub-group frequencies and this may lead to unstable odds ratios.
- A cross-sectional design was used and this limited determination of the temporal sequence between exposure and outcome.
- Assessment of the symptoms of neuropathy involved asking patients if they experienced those features in the past week and thus recall bias could have led to over estimation.

Conclusions

This study established the prevalence of chemotherapy induced peripheral neuropathy among adult patients with cancer at Mbarara Regional Cancer Centre. Nearly one-third of the patients had symptom-defined CIPN. This high burden of CIPN in our setting necessitates continuous monitoring of patients receiving chemotherapy for clinical features of neuropathy so that treatment can be initiated promptly.

The factors associated with occurrence of CIPN among cancer patients in our setting include older age (greater or equal to 60 years), past resolved neuropathy prior to initiation of chemotherapy and concurrent administration of non-chemotherapeutic neurotoxic drugs. Therefore, neurotoxic chemotherapeutic agents should be avoided in such patients to lower their likelihood of developing CIPN.

The management of patients with CIPN in our setting is not done per ASCO and ESMO guidelines and this can negatively affect treatment outcomes. The recommended drug duloxetine is generally costly and its use for CIPN management has not been incorporated into the national cancer treatment guidelines. We therefore recommend that the Uganda Cancer Institute treatment guidelines should be updated to include management of CIPN in line with evidence from clinical trials. This will offer

guidance to the clinicians so that patients with CIPN are appropriately treated.

Abbreviations

ADR	Adverse Drug Reaction
AIDS	Acquired Immunodeficiency Syndrome
aOR	Adjusted Odds Ratio
ASCO	American Society of Clinical Oncology
BMI	Body Mass Index
CI	Confidence interval
CIPN	Chemotherapy Induced Peripheral Neuropathy
COR	Crude Odds Ratio
DNA	Deoxyribonucleic acid
EORTC	European Organization for Research and Treatment of Cancer
ESMO	European Society of Medical Oncology
GLOBOCAN	Global Cancer Observatory
HIV	Human Immunodeficiency Virus
MRRH	Mbarara Regional Referral Hospital
MUST	Mbarara University of Science and Technology
NCI	National Cancer Institute
QLQ	Quality of Life Questionnaire
REC	Research Ethics Committee
RNA	Ribonucleic acid
SD	Standard Deviation
SPSS	Statistical Package for the Social Sciences
WHO	World Health Organization

Acknowledgements

The authors extend their heartfelt gratitude to the administration of Mbarara Regional Referral Hospital and the cancer unit for allowing them to conduct the study at the facility. We would also like to thank the research assistants: Ms. Tukundane Brendah and Ms. Byiringiro Mary Grace for their dedication and great team work exhibited during the data collection period. We also extend our sincere thanks to the study participants and their caretakers for their cooperation.

Authors' contributions

All authors listed in this manuscript have made significant contributions to the work and fulfill the criteria for authorship. SA, JI, RT and TMY were involved in conceptualization of the research, data collection, data analysis and interpretation, as well as writing and revision of the manuscript. JK, DA, CN, SNN, IKK and LB participated in data analysis, interpretation and manuscript writing/revision.

Funding

Not applicable.

Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Mbarara University of Science and Technology Research Ethics Committee (MUST REC) with reference number MUST-2024-1484. Additionally, administrative clearance was provided by the hospital director of MRRH before the study commenced. Informed consent was sought from patients who fulfilled the criteria for inclusion before they were enrolled into the study. The informed consent form was translated into Runyankole, the local language, to assist participants who had limited literacy skills. For those who couldn't read, the translated form was read aloud, and participants expressed their consent by using their thumbprints. To enhance the integrity of the process, literate family members or caregivers served as witnesses, ensuring that the content was accurately conveyed and confirmed to the participants.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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Received: 4 November 2024 / Accepted: 13 June 2026

Published online: 23 June 2026

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