

**PREVALENCE, SEVERITY AND FACTORS ASSOCIATED
WITH PERIPHERAL NEUROPATHY AMONG CANCER
PATIENTS ON CHEMOTHERAPY AT MOI TEACHING AND
REFERRAL HOSPITAL, ELDORET KENYA.**

BY

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**A THESIS SUBMITTED TO THE SCHOOL OF MEDICINE IN
PARTIAL FULFILLMENT FOR AN AWARD OF THE DEGREE
MASTER OF MEDICINE (INTERNAL MEDICINE) OF MOI
UNIVERSITY.**

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DECLARATION

Student's Declaration:

This thesis is submitted to the School of Medicine as part of the fulfillment of the requirements of the Masters of Medicine degree in Internal Medicine, Moi University.

I declare that this is my original thesis and that it has never been presented for a degree in any other university.

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Supervisors' Declaration:

We submit this thesis for review with our approval as university supervisors.

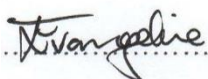
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DEDICATION

First and foremost, I dedicate this work to Allah, the Almighty, whose mercy, guidance, and protection have enabled me to reach this important milestone. Every step of this journey has been through His will.

To my family—my children, my parents, and my siblings—your love, prayers, and unwavering support have been my greatest source of strength. Thank you for your patience, encouragement, and belief in me throughout this journey.

To my extended family and close friends,

Your kindness, motivation, and continuous support have been deeply appreciated.

This work is dedicated to all of you, with sincere gratitude.

ABSTRACT

Background: Peripheral neuropathy among cancer participants on chemotherapy is a disabling condition. It is majorly associated with drugs such as platinum compounds, taxane, vinca alkaloids among others. Severe peripheral neuropathy may require reduction of the chemotherapy dose or complete cessation. The prevalence, severity and associated factors of peripheral neuropathy among cancer participants on chemotherapy in our set up has not been clearly defined.

Objectives: The purpose of the study was therefore to determine the prevalence, severity and factors associated with peripheral neuropathy among participants receiving chemotherapy at Moi Teaching and referral hospital (MTRH).

Methods: This was a descriptive cross-sectional study investigating peripheral neuropathy among cancer participants on chemotherapy at MTRH. Systematic sampling was used to recruit 211 cancer participants on chemotherapy. The first patient was selected randomly using the sampling randomizer software thereafter every fourth patient was recruited into the study. A structured questionnaire was used to collect demographic, clinical and disease characteristics data. The Total Neuropathy Score (TNS) was used to measure peripheral neuropathy among the study participants. Data was analyzed using both descriptive and inferential statistics. The prevalence of peripheral neuropathy among patient on chemotherapy was calculated as those with peripheral neuropathy as proportion of the study sample and expressed as a percentage. Bivariate analysis was used to calculate the severity of PN and results are presented as frequencies, percentages and P Values. Factors associated with PN were analysed using multivariate logistic regression. Results are presented as odds ratios and confidence intervals.

Results: The study found that 70.1% of participants at MTRH had peripheral neuropathy, of which 49.3% had mild symptoms, 42.6% had moderate symptoms, and 8.1% had severe symptoms. Autonomic symptoms were the most common at 84.8% followed by sensory symptoms at 57.8%. Amongst the factors associated with CIPN, age was found to be a significant factor, with older participants at a higher risk of getting CIPN. Participants with comorbidities such as HIV, diabetes mellitus, and hypertension also had increased risk of CIPN although not statistically significant with a P value of 0.212.

Conclusion: The prevalence of CIPN was high among patient on chemotherapy at MTRH though most patient had mild symptoms.

Recommendations: We highly recommend for the introduction of routine screening protocol for peripheral neuropathy among patients receiving chemotherapy at MTRH as this can help mitigate the severity of symptoms and improve patient quality of life and outcomes.

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ABBREVIATIONS OF TERMS

CIPN	Chemotherapy Induced Peripheral Neuropathy
CKD	Chronic Kidney Disease
DNA	Deoxyribonucleic Acid
ECOG	Eastern Cooperative Oncology Group
HIV	Human Immunodeficiency Virus
IL 6	Interleukin 6
IL 8	Interleukin 8
KNH	Kenyatta National Hospital
NCI-CTAE	National Cancer Institute Common Terminology for Adverse Events
MTRH	Moi Teaching and Referral Hospital
NRTI	Nucleoside Reverse Transcriptase Inhibitors
OXAIPN	Oxaliplatin Induced Peripheral Neuropathy
SPSS 28.0	Statistical Package for the Social Sciences version 28
TNS	Total Neuropathy Score
PN	Peripheral Neuropathy
UoN	University of Nairobi
WHO	World Health Organization

DEFINITION OF TERMS

Peripheral Neuropathy: refers to a disease that affects the nerves outside the brain or spinal cord, resulting in pain, tingling, numbness, or muscle weakness.

Typically starts in the hands and feet, it gradually worsens.

Chemotherapy and other cancer treatments may result in peripheral neuropathy. In addition, it could be caused on by other factors such an infection, physical trauma, poisoning, or illnesses including diabetes, kidney failure, or a B12 deficiency.

Chemotherapeutic agents: also referred to as antineoplastic agents, are used to directly or indirectly inhibit the uncontrolled growth and proliferation of cancer cells.

Chemotherapy-induced neuropathy: Refers to somatic or autonomic signs or symptoms resulting from damage to the peripheral nervous system (PNS) or autonomic nervous system (ANS) caused by chemotherapeutic agents. It is a serious clinical problem caused by a substantial number of cytotoxic drugs, including taxanes, platinum, vinca alkaloids, epothilones, eribulin, and bortezomib which havebeen shown to cause different pathologic insults to neurons.

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background

Chemotherapy-induced peripheral neuropathy (CIPN) is a complex and often debilitating condition characterized by the dysfunction of peripheral nerves resulting from exposure to one or more chemotherapeutic agents (Desforges et al., 2022). This form of neurotoxicity arises when certain drugs used in cancer treatment adversely affect the integrity and function of the peripheral nervous system, leading to a range of sensory, motor, and autonomic symptoms. The prevalence of CIPN among cancer patients and survivors can be remarkably high, with estimates approaching over 90%, depending on various factors such as the specific patient population, the types of chemotherapeutic agents employed, the cumulative dose administered over time, and the diagnostic criteria used to identify CIPN (Kandula et al., 2016). This high prevalence underscores the significant clinical challenge posed by CIPN in oncology care.

The pathophysiology of CIPN involves the disruption of normal nerve function, which can impair sensory perception, motor coordination, and autonomic regulation. Different classes of chemotherapeutic drugs induce neurotoxicity through distinct molecular mechanisms, although their clinical manifestations often overlap. For example, platinum compounds like cisplatin and oxaliplatin primarily cause DNA damage and mitochondrial dysfunction in neurons, whereas taxanes such as paclitaxel interfere with microtubule dynamics essential for axonal transport (Starobova & Vetter, 2017). Despite these differences at the molecular level, the end result is damage to nerve fibers that manifests as a range of symptoms affecting patients' quality of life.

Symptoms of CIPN are particularly concerning because they can be severe, persistent,

and sometimes untreatable. Patients often experience a "stocking and glove" distribution of sensory deficits—meaning symptoms primarily affect the distal extremities, such as the hands and feet. These symptoms include numbness, tingling sensations, burning pain, paresthesia, and in some cases, motor weakness or autonomic dysfunction. Such symptoms can significantly impair daily activities, reduce mobility, and diminish overall quality of life. Notably, CIPN symptoms can persist long after the conclusion of chemotherapy, sometimes lasting months or even years, which highlights the need for effective management strategies and supportive care interventions (Starobova & Vetter, 2017).

In recent years, the global burden of cancer has grown significantly. The latest estimates indicate that approximately 18.1 million new cancer cases are diagnosed annually worldwide (Desforbes et al., 2022). Advances in targeted therapies, immunotherapies, and early detection have contributed to increased survival rates, particularly in high-income countries. For instance, in the United States, there has been a 27% decline in overall cancer mortality between 1991 and 2016, reflecting improvements in treatment and early diagnosis (Desforbes et al., 2022). However, this increased survival has led to a rising number of cancer survivors living with long-term treatment-related complications, including CIPN.

Peripheral neuropathy (PN), as a manifestation of CIPN, remains a common and particularly challenging complication associated with several widely used chemotherapeutic agents, such as platinum compounds, taxanes, vinca alkaloids, and bortezomib (Knoerl et al., 2020). The development of PN can adversely influence treatment outcomes by necessitating longer infusion times, dose reductions, or even premature discontinuation of chemotherapy. These modifications, while sometimes

necessary, can compromise the overall efficacy of cancer treatment and negatively impact patient survival and quality of life. Meta-analyses of randomized controlled trials and cohort studies suggest that approximately 50% of patients undergoing chemotherapy develop some degree of CIPN during treatment (Seretny et al., 2014). Severe cases may lead healthcare providers to halt or reduce chemotherapy doses to prevent further nerve damage, which could compromise cancer control.

The clinical presentation of CIPN primarily involves the peripheral nervous system, with symptoms often following a characteristic "stocking and glove" distribution. Sensory deficits include numbness, tingling, burning pain, and hypersensitivity to stimuli, which can severely impair daily functioning. Patients may also experience motor impairments such as weakness or loss of coordination, and autonomic symptoms like blood pressure fluctuations or gastrointestinal disturbances. The impact of PN on patients' quality of life is profound, affecting their physical well-being, emotional health, and social functioning (Kanbayashi et al., 2017). Moreover, the presence and severity of PN frequently lead to reductions in chemotherapy dose intensity or complete discontinuation, thereby potentially affecting treatment outcomes. Notably, PN symptoms can develop during active chemotherapy or manifest several months after treatment completion, often persisting for extended periods and posing long-term health challenges.

Recent studies in Kenya have highlighted the magnitude of this issue in local settings. For example, a study conducted at Kenyatta National Hospital reported that 83.6% of participants receiving cisplatin-based chemotherapy exhibited signs of peripheral neuropathy (Ezzi et al., 2019). This high prevalence underscores the importance of understanding CIPN within the context of resource-limited settings, where screening,

management, and supportive care may face additional barriers.

In conclusion, CIPN remains a significant and multifaceted complication of cancer therapy worldwide. Its high prevalence, impact on treatment adherence, and long-lasting effects on patients' quality of life necessitate ongoing research into its mechanisms, risk factors, prevention, and management strategies. Addressing CIPN effectively requires a multidisciplinary approach that integrates clinical care, patient education, and the development of targeted interventions to mitigate its burden on cancer survivors.

1.2 Statement of the Problem

The prevalence of peripheral neuropathy has been found to be high among participants on chemotherapy. Most of these chemotherapy drugs are neurotoxic. This may have adverse effect on the patient quality of life. In addition, peripheral neuropathy among patient on chemotherapy has also been associated with increased comorbidities as well as higher economic cost.

Despite the fact that peripheral neuropathy is a significant complication of chemotherapy, there is paucity of data on its overall impact, prevalence, severity and risk factors in our setting and this study was set out to attempt to fill this gap.

1.3 Justification

Despite the fact that PN is a significant complication of chemotherapy, there is no data on the prevalence, associated factors and severity of CIPN in our setting. This is despite using drugs that are known to be neurotoxic and have adverse implication on the wellbeing of patients in the long run. Understanding the impact of CIPN in our setting would help in coming up with protocols for both preventive and therapeutic management that will help in the better management of patients in our setting and

the whole country in general thus improving the quality of life of patients.

Furthermore, it is anticipated that information generated from this study may form a basis for further studies.

Once we have a better understanding of the impact that CIPN has in our environment, we will be better able to devise guidelines for the therapeutic and preventative management of the condition.

1.4 Research Question

What is the prevalence, severity and factors associated with peripheral neuropathy among patients on chemotherapy at Moi Teaching and Referral Hospital?

1.5 Objectives

1.5.1 Broad objectives

To determine the prevalence, severity and factors associated with peripheral neuropathy among patients on chemotherapy at Moi Teaching and Referral Hospital.

1.5.2 Specific Objectives

- 1 To determine the prevalence of peripheral neuropathy among patients on chemotherapy at Moi Teaching and referral hospital.
- 2 To determine the severity of peripheral neuropathy among participants on chemotherapy at Moi Teaching and referral hospital.
- 3 To determine factors associated with peripheral neuropathy among participants on chemotherapy at Moi Teaching and referral hospital.

1.6 Conceptual Framework

Independent variables

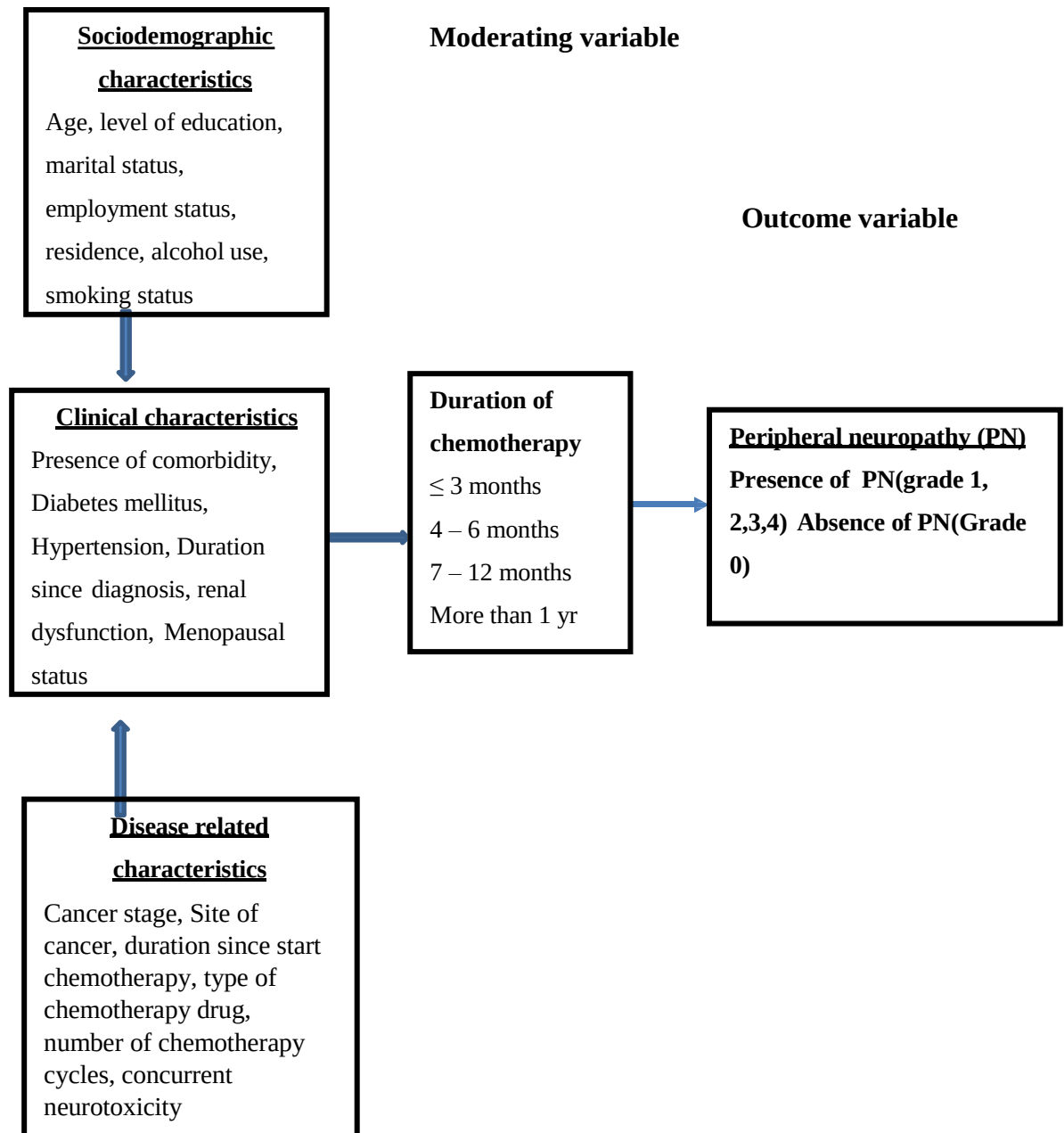


Figure 1: Conceptual Framework

In the conceptual framework above, the socio demographic and disease related characteristics directly affect the clinical characteristics which in turn affect the duration of chemotherapy hence affecting the dependent variable which is the study outcomes.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 Introduction

Chemotherapy-induced peripheral neuropathy (CIPN) is an increasingly recognized complication of cancer treatment that significantly contributes to patient morbidity and compromised treatment adherence. As global oncology practice evolves toward aggressive treatment of both early-stage and advanced malignancies, the use of neurotoxic chemotherapeutic agents such as platinum compounds, taxanes, vinca alkaloids, and proteasome inhibitors has become widespread (Seretny et al., 2014). However, this progress has been paralleled by a corresponding rise in the incidence and burden of peripheral neuropathies, often manifesting as chronic, disabling conditions long after cessation of chemotherapy (Cavaletti & Marmiroli, 2015).

CIPN typically presents as a symmetrical, length-dependent sensory neuropathy affecting the hands and feet. It manifests clinically with symptoms such as numbness, tingling, burning sensations, and in severe cases, neuropathic pain and functional impairment. In addition to sensory manifestations, motor and autonomic involvement may occur depending on the neurotoxic agent and cumulative exposure (Windebank & Grisold, 2008). Despite its prevalence, the pathogenesis of CIPN remains incompletely understood, and there is a dearth of effective prophylactic and therapeutic options.

Importantly, CIPN is not only a dose-limiting side effect it is a determinant of treatment outcomes and patient well-being. Severe neuropathy may necessitate chemotherapy dose reductions or premature discontinuation, potentially undermining oncologic efficacy (Ocean & Vahdat, 2004). Furthermore, the persistence of symptoms in cancer survivors has profound implications for health-related quality of life (HRQoL), daily functioning, and employment (Smith et al., 2013). The chronic nature of CIPN

underscores its relevance not only during active treatment but also throughout survivorship.

Historically, the emergence of CIPN as a clinical entity coincided with the widespread adoption of neurotoxic chemotherapeutic agents such as vincristine and cisplatin in the 1960s and 1970s (Windebank & Grisold, 2008). Initially underrecognized due to the overriding focus on tumor eradication, attention gradually shifted towards survivorship issues as long-term cancer survival rates improved. Studies in the early 2000s, such as those by Park et al. (2003), highlighted that neurological toxicity often persisted for years post-treatment, prompting calls for routine monitoring and intervention protocols.

In Africa, research into CIPN remains limited compared to Western countries. Nonetheless, a few studies conducted in South Africa and Nigeria indicate similar prevalence patterns, albeit compounded by challenges such as late cancer presentation, comorbid HIV infection, and limited access to supportive care (Adesina et al., 2018).

In the context of low- and middle-income countries (LMICs), including Kenya, the burden of CIPN is likely underestimated due to limited routine screening, lack of standardized assessment tools, and underreporting. To add on that, there exists a paucity of local data on the epidemiology, clinical profile, and management of CIPN despite increasing chemotherapy utilization in tertiary referral hospitals such as Moi Teaching and Referral Hospital (MTRH), Eldoret.

2.2 Epidemiology of peripheral neuropathy among patients on chemotherapy.

Peripheral neuropathy among cancer patients has been a major dose limiting adverse effects of various cancer chemotherapeutic drugs (Balayssac et al., 2011). Platinum anticancer drugs (cisplatin, oxaliplatin, carboplatin), taxanes (paclitaxel, docetaxel), vinca alkaloids (vincristine, vinblastine, vinorelbine), proteasome inhibitors

(bortezomib) and angiogenesis inhibitors (thalidomide) are mostly associated with CIPN (Kerckhove et al., 2017).

Previous literature has established that the prevalence of peripheral neuropathy among chemotherapy patients has been high. A population based cross sectional study conducted in Denmark assessed peripheral neuropathy among cancer patients. The study utilized CIPN 20 tool. A summary score was calculated based on the 1 – 18 items of CIPN20. Based on the tool, a total score of 30 points or more on the CIPN20 score was used to group patients with and those without peripheral neuropathy. Those who had a score of more than 30 were considered to have peripheral neuropathy. Thus, based on this scoring the findings established that the prevalence of peripheral neuropathy was 17% ranging between 6 – 33 percent between diagnosis groups (Nielsen et al., 2022).

A cross-sectional study conducted in Minnesota in United States assessing the burden of peripheral neuropathy among cancer patients on neurotoxic chemotherapy. The findings established that out of 509 patients, 52.7% of the patients had peripheral neuropathy. The findings further established that the median time from incident exposure to first document symptoms was 71 days. Patients with CIPN received a neuropathy ICD-9 diagnosis in only 37 instances. Pain symptoms and use of pain medications were observed more often in patients with CIPN (Shah et al., 2018).

A prospective cohort study conducted in Thailand investigating the prevalence of peripheral neuropathy among breast cancer patients on chemotherapy revealed that 89% of the patients had peripheral neuropathy based on the European Organization for Research and Treatment of Cancer CIPN specific self-report questionnaire (EORTC QOL-CIPN20) (Rattanakrong et al., 2022).

In the Netherlands, Oortgiesen et al. (2022) investigated the burden of peripheral neuropathy among cancer patients. The ICPNQ questionnaire was employed to help investigate different types of peripheral neuropathy (grade 0,1,2,3,4) The severity of the different items on the ICPNQ was assessed by using the Visual Analog Scale (VAS). The findings established that 69% of the participants had peripheral neuropathy.

An observational cross-sectional uncontrolled study conducted in Brazil investigating clinical prevalence of peripheral neuropathy in chemotherapy participants utilized the DN4 questionnaire. Out of the 23 participants who were included in the study, 47.6% had neuropathy. This was however lower compared to other previous studies which found higher prevalence of peripheral neuropathy (Frigotto et al., 2022).

A cross sectional study conducted at Kenyatta National Hospital in Kenya assessing the prevalence of peripheral neuropathy among cancer patients on chemotherapy. The findings established that the prevalence of peripheral neuropathy among patients on chemotherapy was 83.6% (Ezzi et al., 2019).

2.3 Pathophysiology of Chemotherapy-Induced Peripheral Neuropathy

CIPN is a heterogeneous condition arising from the interaction between chemotherapeutic agents and the peripheral nervous system. Although the exact pathophysiological processes vary depending on the drug class, common themes include axonal degeneration, microtubule disruption, mitochondrial dysfunction, oxidative stress, and neuroinflammatory responses. These mechanisms converge to produce structural and functional damage to peripheral nerves, particularly sensory neurons located in the dorsal root ganglia (DRG), which lack a protective blood-nerve barrier and are therefore especially vulnerable (Starobova & Vetter, 2017).

2.3.1 Mechanisms of Neurotoxicity by Chemotherapeutic Agents

Different chemotherapeutic agents induce neuropathy through distinct neurotoxic mechanisms. Platinum compounds such as cisplatin and oxaliplatin accumulate in the DRG and cause DNA adduct formation, leading to apoptosis of sensory neurons. Taxanes, including paclitaxel and docetaxel, stabilize microtubules excessively, thereby interfering with axonal transport and inducing Wallerian-type degeneration (Park et al., 2013). Vinca alkaloids inhibit microtubule polymerization, resulting in both sensory and motor dysfunction, whereas proteasome inhibitors like bortezomib disrupt protein degradation pathways, promoting cellular stress and apoptosis in neurons (Richardson et al., 2012).

2.3.2 Oxidative Stress and Mitochondrial Dysfunction

Oxidative stress is a central element in the pathogenesis of CIPN. Many chemotherapeutic agents increase the generation of reactive oxygen species (ROS) within neuronal cells, leading to oxidative damage of lipids, proteins, and nucleic acids (Areti et al., 2014). The role of mitochondrial dysfunction is particularly well documented in platinum and taxane-induced neuropathies. Damaged mitochondria exhibit impaired respiratory chain activity, reduced ATP production, and increased membrane permeability, culminating in energy failure and apoptosis of neuronal cells. The presence of swollen mitochondria and vacuolated axons has been observed in animal models following administration of paclitaxel and cisplatin, reinforcing the role of mitochondrial pathology in CIPN (Podratz et al., 2011).

2.3.3 Calcium Dysregulation and Ion Channelopathy

Alterations in calcium homeostasis contribute significantly to CIPN pathogenesis. Chemotherapeutic agents such as oxaliplatin modulate calcium channel activity, particularly by enhancing the expression of voltage-gated calcium channels and disrupting calcium buffering systems within neurons (Grolleau et al., 2001). These changes lead to hyperexcitability of sensory neurons and the development of cold-induced paresthesias and dysesthesias, which are characteristic of oxaliplatin-induced acute neuropathy. In addition, sodium and potassium channels may also be affected, leading to abnormal neuronal firing and the generation of neuropathic pain (Flatters & Bennett, 2006).

2.3.4 Axonal Degeneration and Microtubule Disruption

Disruption of the axonal transport system is another hallmark of CIPN. Microtubules are essential for the movement of organelles, proteins, and neurotransmitters along axons. Agents such as taxanes and vinca alkaloids interfere with microtubule dynamics, resulting in defective axonal transport and accumulation of neurotoxic substances (Jamieson et al., 2007). This leads to axonal swelling, distal degeneration, and ultimately neuronal cell death. The resulting pathology is characterized by loss of large myelinated fibers, reduced intraepidermal nerve fiber density, and demyelination.

2.3.5 Neuroinflammation and Immune-Mediated Injury

Emerging research highlights the role of immune-mediated processes in CIPN. Chemotherapy has been shown to activate glial cells and macrophages in the peripheral and central nervous systems, triggering the release of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF- α), interleukin-6 (IL-6), and interleukin-1 β (IL-1 β) (Krukowski et al., 2016). These cytokines contribute to neuronal sensitization, demyelination, and recruitment of additional inflammatory cells, thereby amplifying nerve injury. The involvement of Toll-like receptors and the nuclear factor-kappa B

(NF- κ B) pathway further supports the inflammatory basis of CIPN, particularly in bortezomib- and paclitaxel-induced neuropathies.

2.4 Chemotherapeutic Agents Implicated in Peripheral Neuropathy

The risk, severity, and clinical pattern of CIPN vary substantially according to the chemotherapeutic agent used. A detailed understanding of agent-specific neuropathy profiles is essential for optimizing clinical management.

2.4.1 Platinum-Based Agents

Platinum-based chemotherapeutic agents, particularly cisplatin and oxaliplatin, are among the most effective and widely used drugs in the treatment of various solid tumors. Cisplatin is used extensively in testicular, ovarian, bladder, head and neck, and lung cancers, while oxaliplatin is a cornerstone in the management of colorectal and gastrointestinal malignancies. Despite their substantial clinical utility, both agents are well recognized for their neurotoxicity, which often manifests as chemotherapy-induced peripheral neuropathy (CIPN). Among all drug classes implicated in CIPN, platinum compounds are considered some of the most potent inducers of persistent, and in some cases, irreversible peripheral nerve damage.

Cisplatin-induced peripheral neuropathy (CIPN) is typically a dose-dependent, cumulative toxicity. It predominantly affects large, myelinated sensory neurons within the dorsal root ganglia (DRG). Cisplatin exerts its neurotoxic effect by forming intrastrand and interstrand DNA adducts within these sensory neurons, which ultimately trigger mitochondrial dysfunction, oxidative stress, and apoptosis. The dorsal root ganglia are especially vulnerable to these effects due to the absence of a protective blood-brain barrier, permitting direct exposure to systemic chemotherapeutic agents (Park et al., 2013). Clinically, patients experience numbness, tingling, and proprioceptive deficits that often start in the feet and progress proximally in a length-

dependent manner. Reflexes may be diminished, and severe cases can lead to ataxia or difficulty in ambulation.

Cisplatin-induced neuropathy often appears at cumulative doses exceeding 300 mg/m², although individual susceptibility varies. A particularly challenging feature of cisplatin neurotoxicity is the "coasting phenomenon," wherein neuropathic symptoms not only persist but may worsen after discontinuation of therapy. This delayed progression is thought to result from ongoing neuronal degeneration initiated during treatment but not clinically apparent until weeks later (Cavaletti & Marmiroli, 2010). Unlike other chemotherapy side effects that may abate soon after cessation, cisplatin-induced neuropathy often shows minimal recovery and may become a permanent disability, especially if early signs are not identified and addressed.

Oxaliplatin, though structurally related to cisplatin, presents a distinct neurotoxicity profile. It causes two well-characterized forms of neuropathy: acute and chronic. The acute form occurs within hours to days after infusion and is often triggered or exacerbated by cold exposure. Patients report perioral tingling, pharyngolaryngeal dysesthesia (sensation of throat tightening), and distal paresthesias. This acute syndrome is believed to result from sensory neuron hyperexcitability, mediated by alterations in voltage-gated sodium channels, which are more reactive under lower temperatures (Gamelin et al., 2002). Fortunately, the acute symptoms are typically transient and resolve within 72 hours without long-term consequences.

In contrast, chronic oxaliplatin-induced neuropathy closely resembles cisplatin neuropathy in its pathophysiology and presentation. It is cumulative in nature, dose-dependent, and primarily affects sensory neurons. Chronic symptoms include persistent numbness, tingling, and difficulty with fine motor tasks. Unlike cisplatin, however,

oxaliplatin-induced neuropathy may show partial recovery over time typically months to years following treatment cessation although this recovery is highly variable across patients and may be incomplete.

Given the high incidence and impact of platinum-induced neuropathy, there has been considerable interest in the development of neuroprotective agents. Amifostine, a cytoprotective thiol compound, has shown some ability to reduce cisplatin-induced nephrotoxicity and neurotoxicity in small studies. It is thought to act by scavenging free radicals and protecting DNA from adduct formation. Similarly, glutathione, an endogenous antioxidant, has been investigated for its potential to prevent mitochondrial dysfunction and limit neuronal injury (Albers et al., 2011). However, while early-phase clinical trials have demonstrated some promise, the evidence remains limited and inconclusive, largely due to small sample sizes, heterogeneous study designs, and short follow-up durations. As such, no neuroprotective agent has gained widespread acceptance or been incorporated into standard treatment guidelines for CIPN prevention.

Furthermore, clinical strategies to mitigate platinum-induced neurotoxicity often involve dose reduction, increased infusion times, or switching to less neurotoxic agents, but these adjustments carry the risk of reduced therapeutic efficacy. The absence of reliable biomarkers to predict neuropathy risk complicates early intervention. Research into pharmacogenomics and biomarkers may offer future avenues for identifying patients at greatest risk and customizing treatment plans accordingly.

In conclusion, platinum-based agents like cisplatin and oxaliplatin play an indispensable role in cancer therapy but are frequently complicated by peripheral neuropathy. While the acute and chronic manifestations differ between agents, the functional burden on patients can be profound, and current management remains largely preventive and supportive. There is a pressing need for large-scale, high-quality studies to explore effective neuroprotective interventions and to develop standardized protocols for early detection and mitigation of this disabling side effect

2.4.2 Taxanes

Paclitaxel and docetaxel, both belonging to the taxane class of chemotherapeutic agents, are among the most commonly used drugs in the treatment of various malignancies, including breast, ovarian, prostate, and lung cancers. Their mechanism of action involves binding to and stabilizing microtubules, thereby preventing their depolymerization. While this disruption is beneficial in arresting mitosis in cancer cells, it also interferes with the normal function of microtubules in neurons particularly in axonal transport which is crucial for maintaining neuronal integrity and communication. As a result, taxanes are known to induce a form of peripheral neuropathy, predominantly affecting sensory neurons.

Taxane-induced peripheral neuropathy (TIPN) is characterized by a dose-dependent pattern of sensory dysfunction. Clinical symptoms typically emerge after cumulative paclitaxel doses of around 1000 mg/m². Patients commonly report symmetrical paresthesias (tingling or prickling sensations), dysesthesias (unpleasant abnormal sensations), numbness, and burning pain, predominantly in the hands and feet. While sensory symptoms are most prominent, motor dysfunction may also occur in more severe or prolonged cases, manifesting as muscle weakness or impaired coordination (Scripture et al., 2006). TIPN can significantly impact a patient's quality of life, limit

physical functioning, and even result in chemotherapy dose reductions or discontinuation, potentially compromising cancer control and survival outcomes.

A unique feature of taxane-induced neuropathy is the so-called “coasting” phenomenon, where symptoms not only persist but may actually worsen after the cessation of chemotherapy. This delayed progression is also observed in platinum-induced neuropathies and is believed to be related to continued degeneration of neurons already damaged during chemotherapy exposure. The coasting effect adds complexity to the clinical management of TIPN, as patients may report the onset or intensification of symptoms weeks after treatment ends, requiring prolonged follow-up and supportive care (Kruse F. L. et al. 2025)

Pharmacokinetics also play a critical role in TIPN development. The duration of taxane infusion significantly influences the severity of neurotoxicity. Shorter infusion times, such as 1-hour infusions, result in higher peak plasma concentrations of the drug, which are associated with greater neurotoxic effects. In contrast, longer infusion durations—such as 3- or 24-hour infusions are associated with more gradual drug exposure, potentially lowering the risk of neuropathy (Smith et al., 2020). This observation has led to modifications in clinical practice, with some protocols preferring longer infusion times to reduce TIPN incidence without compromising therapeutic efficacy.

Despite the substantial burden TIPN places on patients, effective preventive strategies remain elusive. Numerous pharmacologic and non-pharmacologic agents have been studied for their potential to protect against taxane-induced neurotoxicity. Among these, compounds such as glutamine, amifostine, vitamin E, Acetyl-L-carnitine, and omega-3 fatty acids have received attention. However, clinical trials assessing these agents have yielded inconsistent or inconclusive results. Many of these studies are

limited by small sample sizes, lack of standardized outcome measures, heterogeneity in study design, and short follow-up periods (Hershman et al., 2014). Furthermore, none of these agents have demonstrated sufficient efficacy to be recommended for routine clinical use by major oncology guidelines such as those from ASCO or ESMO.

Current clinical management of TIPN is therefore primarily supportive and symptomatic. Patients are often advised on lifestyle modifications, such as avoiding cold exposure (which can exacerbate symptoms), engaging in physical therapy, and using assistive devices when necessary. Pharmacologic interventions, particularly duloxetine, have shown modest benefits in alleviating neuropathic pain associated with TIPN. Other agents such as gabapentin and pregabalin are commonly used off-label, although robust evidence for their effectiveness in TIPN remains limited. (ASCO et al., 2014; Starobova & Vetter, 2022;).

Paclitaxel and docetaxel are invaluable in cancer treatment but carry a significant risk of peripheral neuropathy, predominantly sensory in nature. The neurotoxicity is influenced by cumulative dose, infusion duration, and individual susceptibility. While several agents have been tested for TIPN prevention, no intervention has consistently demonstrated efficacy. Further large-scale, methodologically rigorous clinical trials are needed to develop evidence-based preventive and therapeutic strategies for TIPN. (Starobova et al. (2022).

2.4.3 Vinca Alkaloids

Vincristine is a chemotherapeutic agent belonging to the class of vinca alkaloids, a group of cytotoxic compounds derived from the periwinkle plant (*Catharanthus roseus*). It is widely used in the treatment of various hematologic and solid malignancies, including acute lymphoblastic leukemia (ALL), non-Hodgkin's lymphoma, Hodgkin's lymphoma, and pediatric tumors such as Wilms' tumor and

rhabdomyosarcoma. The antineoplastic effect of vincristine arises from its ability to bind to tubulin, thereby inhibiting the polymerization of microtubules. Microtubules are essential structural components of the mitotic spindle, as well as crucial mediators of intracellular transport within neurons. By disrupting microtubule formation, vincristine impedes mitosis and halts cell division. However, this same mechanism also disrupts axonal transport in peripheral neurons, ultimately contributing to the development of neurotoxicity.

Vincristine-induced peripheral neuropathy (VIPN) is a well-recognized, dose-limiting toxicity that significantly impacts treatment outcomes and quality of life. VIPN presents as a mixed neuropathy involving sensory, motor, and autonomic nerve fibers. Sensory symptoms are typically the earliest and most prominent, with patients reporting numbness, tingling, burning sensations, and pain, particularly in a stocking-glove distribution. Motor involvement may manifest as distal muscle weakness, reduced deep tendon reflexes, and difficulties with coordination and mobility. Autonomic dysfunction, though less common, can result in symptoms such as constipation, orthostatic hypotension, urinary retention, and erectile dysfunction (Ocean & Vahdat, 2004). In severe cases, VIPN can be profoundly disabling, necessitating dose reduction or discontinuation of vincristine therapy and, consequently, compromising oncologic efficacy.

Certain populations are particularly vulnerable to VIPN. Pediatric patients, especially those undergoing long-term chemotherapy for ALL or lymphoma, exhibit heightened susceptibility. This may be due to the ongoing development of the nervous system, making it more prone to injury. Additionally, individuals with pre-existing peripheral neuropathies, such as those resulting from diabetes mellitus, HIV infection, or previous

exposure to neurotoxic agents, are at greater risk of developing severe VIPN. The presence of comorbid conditions, nutritional deficiencies (e.g., vitamin B12), or renal and hepatic dysfunction may further exacerbate the neurotoxic effects.

Strategies to mitigate the risk of VIPN have been implemented in clinical practice. One such strategy involves capping the maximum single dose of vincristine at 2 mg, regardless of body surface area. This practice, widely adopted in pediatric oncology protocols, has been shown to reduce the incidence and severity of neurotoxicity without compromising therapeutic outcomes. Another preventive measure includes altering the frequency of administration; administering vincristine weekly rather than biweekly has been associated with a lower risk of neurotoxic complications (Gilchrist et al., 2009).

Despite these measures, predicting which patients will develop VIPN remains challenging. One of the major contributors to interindividual variability in VIPN risk is genetic polymorphism, particularly involving the **CYP3A5** gene. This gene encodes a cytochrome P450 enzyme responsible for metabolizing vincristine. Variants of **CYP3A5**, particularly the *CYP3A5* *3/*3 genotype, are associated with reduced enzyme activity and decreased clearance of vincristine, resulting in higher plasma and tissue concentrations and, consequently, increased neurotoxicity (Egbelakin et al., 2011). Pharmacogenetic screening may offer a future avenue for individualized dosing to reduce toxicity while maintaining efficacy.

Vincristine-induced peripheral neuropathy is a complex, multifactorial condition that arises from the drug's disruption of microtubule dynamics. While preventive strategies have mitigated its severity in some settings, the variability in clinical presentation and underlying genetic predisposition underscores the need for more personalized approaches to therapy.

2.4.4 Other Agents

Bortezomib, a reversible inhibitor of the 26S proteasome, is a cornerstone in the treatment of multiple myeloma and certain subtypes of non-Hodgkin lymphoma. It exerts its antineoplastic effects by disrupting the ubiquitin-proteasome pathway, a critical system for degrading misfolded or damaged proteins within cells. By inhibiting this pathway, bortezomib induces the accumulation of defective proteins, leading to endoplasmic reticulum stress and apoptosis of malignant plasma cells. However, this same mechanism can inadvertently affect healthy peripheral neurons, leading to bortezomib-induced peripheral neuropathy (BIPN).

BIPN is typically characterized by a predominantly sensory neuropathy, with patients reporting numbness, tingling, burning pain, and heightened sensitivity to tactile stimuli, especially in the hands and feet. In most cases, the neuropathy presents in a length-dependent, symmetrical pattern consistent with a distal axonopathy. Although less common, motor symptoms such as weakness or gait instability can occur in more severe or prolonged cases (Flatters et al., 2019)

One of the defining features of BIPN, which differentiates it from neuropathies induced by other chemotherapeutic agents such as cisplatin or paclitaxel, is its potential reversibility. Clinical studies have shown that dose reduction, increased dosing intervals, or complete drug discontinuation can often lead to symptom stabilization or even significant improvement (Richardson et al., 2005). This reversibility makes early detection and prompt dose adjustment particularly important in preventing long-term disability.

The route and frequency of administration influence the risk of neuropathy. Evidence suggests that subcutaneous administration, as opposed to intravenous infusion, and once-weekly dosing schedules reduce the incidence and severity of BIPN without

compromising therapeutic efficacy (Moreau et al., 2011). These findings have informed current clinical guidelines and highlight the importance of tailored treatment approaches to optimize outcomes while minimizing toxicity

Thalidomide, originally developed as a sedative and later infamously withdrawn due to its teratogenic effects, has re-emerged in modern oncology as an immunomodulatory agent, particularly in the management of multiple myeloma and other hematologic malignancies. It is often used in combination with dexamethasone and other chemotherapeutic agents as part of first-line or maintenance therapy in both transplant-eligible and transplant-ineligible patients. While thalidomide has proven efficacy in improving survival outcomes in multiple myeloma, its clinical utility is frequently complicated by the development of peripheral neuropathy, a well-recognized dose- and duration-dependent adverse effect.

Thalidomide-induced peripheral neuropathy (TiPN) is typically sensory in nature, manifesting as numbness, tingling, burning sensations, and occasionally shooting pains, primarily in the hands and feet. Motor and autonomic involvement are rare but may occur in advanced cases. The underlying pathophysiological mechanisms of TiPN are not fully elucidated; however, anti-angiogenic activity has been proposed as a central factor. Thalidomide inhibits vascular endothelial growth factor (VEGF) and other pro-angiogenic cytokines, leading to capillary rarefaction and ischemia within peripheral nerves. This ischemic injury contributes to axonal degeneration and impaired neuronal function (Shen et al., 2012).

The risk of neuropathy increases with cumulative exposure. Studies indicate that neuropathic symptoms commonly begin after several months of therapy, and the severity often correlates with the total dose received. Unlike bortezomib-induced

neuropathy, which is often reversible with dose adjustments, TiPN tends to be slowly progressive and less reversible, even after discontinuation of therapy. As a result, thalidomide neuropathy presents a growing challenge in oncology, particularly in low- and middle-income countries where thalidomide is widely used due to its relative affordability compared to newer immunomodulatory drugs like lenalidomide.

Early recognition and regular monitoring of neuropathic symptoms are essential in minimizing irreversible nerve damage. Dose limitation strategies and substitution with less neurotoxic agents should be considered when symptoms progress.

Chemotherapeutic agents differ markedly in their neuropathogenic mechanisms, clinical patterns, reversibility, and management implications, necessitating individualized risk assessment and monitoring. Although thalidomide dose reductions and treatment interruptions can mitigate neuropathy progression, no proven preventive interventions currently exist (Richardson et al., 2005).

Additionally, newer agents such as eribulin, ixabepilone, and carfilzomib have been associated with varying degrees of peripheral neuropathy. Eribulin, a microtubule dynamics inhibitor used in metastatic breast cancer, causes mild to moderate neuropathy in approximately 25% of treated patients (Cortes et al., 2011). Carfilzomib, while offering reduced neuropathic toxicity compared to bortezomib, still poses risks particularly in heavily pretreated populations (Brighen et al., 2010).

As newer chemotherapeutic agents enter clinical practice, vigilance regarding their neurotoxic profiles remains essential. Post-marketing surveillance studies and robust phase IV trials are necessary to capture real-world incidences and guide mitigation strategies.

2.4.5 Severity of peripheral neuropathy among patients on chemotherapy

The severity of CIPN varies widely among patients and depends on several factors, including the type and dose of chemotherapy, predisposing conditions, and individual susceptibility. Accurate assessment of severity is critical for guiding clinical decisions, particularly in determining whether to reduce chemotherapy dose, change regimens, or implement supportive measures.

2.4.6 Clinical Spectrum: Sensory, Motor, and Autonomic Features

CIPN is predominantly a **sensory neuropathy**, characterized by symptoms such as:

- Paresthesia (tingling)
- Dysesthesia (unpleasant abnormal sensation)
- Burning pain
- Numbness in a stocking-glove distribution

Motor symptoms include distal muscle weakness, decreased deep tendon reflexes, and gait instability. **Autonomic involvement**, though less frequent, can present as orthostatic hypotension, urinary retention, and constipation—features more commonly seen with vincristine and bortezomib (Windebank & Grisold, 2008).

Grading Tools

Several standardized instruments are available for grading the severity of CIPN. These include:

a) National Cancer Institute – Common Terminology Criteria for Adverse Events (NCI-CTCAE)

This is the most widely used clinician-reported grading scale. In version 5.0, sensory neuropathy is graded from:

- Grade 1 (asymptomatic, loss of deep tendon reflexes)
- To Grade 4 (life-threatening disability)

However, NCI-CTCAE is limited by its reliance on clinician judgment, leading to underestimation of patient-reported symptoms (Cavaletti & Marmiroli, 2010).

b) Total Neuropathy Score (TNS)

The TNS combines symptoms, clinical signs, and nerve conduction studies into a single score. While comprehensive, its reliance on electrodiagnostic testing limits feasibility in low-resource settings.

c) FACT/GOG-Ntx and EORTC QLQ-CIPN20

These are validated **patient-reported outcome measures (PROMs)**. They assess both symptom severity and functional impact on activities of daily living. These tools have demonstrated greater sensitivity to changes over time compared to clinician-based grading alone (Lavoie Smith et al., 2019).

2.5 Prevalence and Severity of Chemotherapy-Induced Peripheral Neuropathy

Estimating the true prevalence of CIPN is complicated by heterogeneity in diagnostic criteria, assessment tools, chemotherapy regimens, and follow-up durations. Nonetheless, meta-analyses provide valuable insights.

Seretny et al. (2014) conducted a landmark meta-analysis comprising 31 studies and reported CIPN prevalence rates of 68.1% immediately post-chemotherapy, 60.0% at three months, and 30.0% at six months. These findings highlight the persistent nature of neuropathic symptoms in a substantial proportion of patients long after treatment completion.

Prevalence estimates vary markedly by agent. For instance, oxaliplatin-induced neuropathy rates exceed 80% in some studies, with approximately 15–20% of patients developing severe, disabling neuropathy (Gamelin et al., 2002). Similarly, taxane-induced neuropathy affects nearly 60% of treated individuals, with about 25%

experiencing grade 2 or higher symptoms (Park et al., 2013).

Prevalence declines over time but remains substantial: around 30% of survivors still report neuropathic symptoms six months after treatment cessation (Seretny et al., 2014).

Factors influencing prevalence include:

- Type of chemotherapeutic agent
- Cumulative dose
- Pre-existing neuropathy
- Diabetes mellitus
- Age

Studies from Africa are limited, but existing data suggest similarly high rates of CIPN among patients receiving neurotoxic agents (Kisa et al., 2018).

Impact of Severity on Treatment and Quality of Life

Severity grading has important implications for clinical management. For example, the occurrence of Grade 2 or higher neuropathy often prompts dose reduction or treatment delay to prevent irreversible damage. Additionally, higher severity scores are associated with substantial impairments in physical functioning, emotional well-being, and overall quality of life (Molassiotis et al., 2019).

Majority of patients with chemotherapy induced peripheral neuropathy have had mild peripheral neuropathy (grade 2 and grade 3). A study conducted in Brazil by Frigotto revealed that severity of peripheral neuropathy was based on the classification of the Brazilian National Cancer Institute (INCA), which found that 23.85% of the participants had no signs of peripheral neuropathy on physical examination, 19.1% participants were classified as grade 1, 33.3% were classified as grade 2, 19.1% grade 3 and 5% of the participants were grade 4 (Frigotto et al., 2022).

A cross sectional study in Netherlands investigating the burden of peripheral

neuropathy among cancer participants on chemotherapy established that out of the 69% of participants with peripheral neuropathy, 26% had grade 1, 38% had grade 2 while 5% experienced grade 3 peripheral neuropathy. Numbness, a tingling sensation, pain, alterations in the perception of temperature, and loss of muscle strength were the symptoms of peripheral neuropathy that were mentioned the most frequently by people who had the condition. Alterations in the patient's perception of temperature, together with discomfort in the patient's fingers, toes, feet, and lower legs, were the symptoms that received the highest VAS values (Oortgiesen et al., 2022).

Similarly, a cohort study conducted in Australia investigating the severity of peripheral neuropathy among cancer participants revealed that 72.8% of the participants reported neuropathy symptoms at median of eight months since treatment completion. The severity of peripheral neuropathy was measured based Common Terminology Criteria for Adverse Events (CTCAE) neuropathy sensory subscale version 4.0 to grade CIPN severity. The rating included grade 0 which means no symptoms, grade 1 which involve asymptomatic and not interfering with daily function, grade 2 which include moderate symptoms which limit daily function. Grade 3 which include severe symptoms which limit daily function and self-care while grade 4 which is disabling. The findings from the study revealed that 27.2% of the participants experienced grade 0, 35.8% experienced grade 1, 33.3% experienced grade 2 and 3.7% experienced grade 3 (Trendowski et al., 2021).

Ezzi et al. in a cross sectional study conducted in Kenya revealed that in assessing the severity of peripheral neuropathy among chemotherapy participants, 81% of the participants had mild peripheral neuropathy (grade 1 and grade 2) while 3.6% had severe neuropathy (grade 4) (Ezzi et al., 2019).

2.6 Risk Factors Associated with Chemotherapy-Induced Peripheral Neuropathy

2.6.1 Patient-Related Factors

Age has consistently emerged as a significant predictor of CIPN. Older patients, particularly those above 60 years, exhibit increased susceptibility, possibly due to age-related reductions in neuronal reserve and mitochondrial function (Park et al., 2013). However, some studies have not observed a clear age-related gradient, suggesting that age alone is insufficient as a risk stratifier.

Another cross-sectional study conducted in Italy by Catalano et al. assessed risk factors for peripheral neuropathy among pancreatic cancer participants on paclitaxel and gemcitabine treatment. The findings revealed that age and number of chemotherapy cycles were significantly associated with development of peripheral neuropathy. Older age was associated with increased risk for peripheral neuropathy while in addition increase in the number of chemotherapy cycles were associated with 22% increase in occurrence of peripheral neuropathy (Catalano et al., 2022). Additionally, these findings concur with those from previous studies which have showed that peripheral neuropathy decrease with decreasing duration of treatment (Seretny et al., 2014).

Sex differences in CIPN risk remain contentious. While some studies report higher neuropathy rates among females, potentially due to pharmacokinetic variations and differential pain perception (Hershman et al., 2014), others find no significant sex effect.

Pre-existing conditions such as diabetes mellitus substantially increase CIPN risk, likely via synergistic effects on nerve degeneration (Quasthoff & Hartung, 2002). Diabetic patients receiving neurotoxic chemotherapy should thus be closely monitored, and glycemic control optimized prior to initiation.

A study conducted among African American cancer participants on chemotherapy investigating factors associated with peripheral neuropathy. The findings established that participants with CIPN were more likely to report hypertension (OR =1.28), hypercholesterolemia (OR = 1.32), history of depression (OR = 1.62) and diabetes (OR = 1.33). The findings further identified that after adjusting for age at diagnosis, gender and cancer site, body mass index was also positively associated with CIPN (Trendowski et al., 2021).

Molassiotis et al. (2019) conducted a prospective observational study in three countries, China, Singapore and United Kingdom assessing risk factors for CIPN in participants receiving taxane and platinum-based chemotherapy. The findings revealed that key risk factors included older age (OR =1.08), chemotherapy type with platinum-based chemotherapy showing lower likelihood of CIPN (OR =0.20). Other factors that were associated with increased risk of CIPN were history of neuropathy (OR =8.26), symptom burden (OR =1.06), number of chemotherapy cycles received (1.19) and alcohol intake.

A longitudinal study conducted in Canada investigating factors associated with peripheral neuropathy among breast cancer participants. The findings revealed that receipt of paclitaxel, lower pre-treatment pain catastrophizing and higher post treatment neuropathic pain and sensitivity to cold pain in the hand were significantly associated with peripheral neuropathy (Gauthier et al.)

Other comorbidities, including renal dysfunction, autoimmune diseases, and pre-existing peripheral neuropathies (e.g., from alcohol abuse or HIV infection), also heighten vulnerability to CIPN (Ocean & Vahdat, 2004).

2.6.2 Treatment-Related Factors

Among treatment-related factors contributing to chemotherapy-induced peripheral neuropathy (CIPN), cumulative dose remains the most consistently documented and clinically significant predictor. Numerous studies have established threshold doses beyond which the risk of developing neuropathy increases substantially. For instance, cumulative exposure to cisplatin exceeding 300 mg/m², oxaliplatin over 850 mg/m², and paclitaxel above 1000 mg/m² has been strongly associated with a marked increase in the incidence and severity of peripheral neuropathy (Cavaletti & Marmiroli, 2010). These thresholds reflect the dose-dependent nature of chemotherapy neurotoxicity and underscore the importance of vigilant dose monitoring during treatment.

Despite the existence of these general dose thresholds, interindividual variability in neuropathy susceptibility remains significant. Some patients may develop neuropathic symptoms at doses well below the established limits, while others tolerate higher exposures without noticeable symptoms. This variability is likely influenced by a combination of genetic factors, comorbid conditions, concurrent medications, and individual variations in drug metabolism and clearance.

Treatment schedules also significantly affect neuropathy risk. For example, weekly paclitaxel regimens have been shown to result in higher rates of neuropathy compared to every-three-week dosing schedules (Smith et al., 2020). This difference is attributed to more frequent exposure and potentially higher cumulative toxicity over time. As such, treatment frequency and duration are critical variables in determining neurotoxic burden.

The use of combination chemotherapy regimens can further compound neurotoxicity. A notable example is the FOLFOX regimen, which includes oxaliplatin, 5-fluorouracil (5-FU), and leucovorin. Patients receiving FOLFOX exhibit significantly higher rates

of neuropathy than those receiving oxaliplatin monotherapy, suggesting additive or even synergistic neurotoxic effects (Andre et al., 2004).

Concurrent or prior exposure to other neurotoxic treatments, such as radiation therapy involving peripheral nerve fields, may exacerbate chemotherapy-induced neuropathy. Studies have shown that patients who undergo radiation therapy in regions rich in peripheral nerves may experience heightened neuropathic symptoms when later exposed to neurotoxic chemotherapeutic agents (Vardy et al., 2007). This underscores the importance of comprehensive treatment planning and multidisciplinary evaluation in patients at high risk for CIPN

2.6.3 Genetic and Ethnic Factors

Emerging evidence from pharmacogenomic and neurogenetic research suggests that genetic polymorphisms play a significant role in modulating individual susceptibility to chemotherapy-induced peripheral neuropathy (CIPN). Variability in patient response to neurotoxic agents cannot be explained solely by differences in drug dose or exposure, indicating a genetic basis for differential risk. Studies have identified several single nucleotide polymorphisms (SNPs) in genes involved in key neurobiological pathways as potential contributors to CIPN risk (Flatters et al., 2019).

Polymorphisms in the EPHA5 gene, which encodes a member of the ephrin receptor family involved in axonal guidance and regeneration, have been associated with increased risk of paclitaxel-induced neuropathy. Similarly, POLG, a gene involved in mitochondrial DNA replication and repair, has been implicated in vulnerability to mitochondrial dysfunction under chemotherapeutic stress. Mitochondrial integrity is critical to neuronal survival, and its impairment has been strongly linked to the pathogenesis of CIPN. Additionally, genes related to drug metabolism, such as

CYP2C8 and CYP3A5, have been studied for their role in influencing plasma drug levels and clearance. Variants in these cytochrome P450 enzymes may result in altered metabolism of chemotherapeutic agents like paclitaxel and vincristine, potentially increasing neurotoxicity risk (Beutler et al., 2017).

However, a significant limitation of the current genetic literature on CIPN is its lack of diversity. The vast majority of association studies have been conducted in Caucasian or East Asian cohorts, with African populations grossly underrepresented. This lack of inclusivity is problematic given the high genetic diversity within African genomes, which may harbor unique variants influencing drug response and toxicity.

Extrapolating findings from European or Asian populations to African settings is fraught with challenges and risks misclassification of at-risk individuals. We therefore need local genomic studies urgently to identify population-specific genetic markers relevant to African patients. Such efforts would not only improve the prediction and prevention of CIPN but also represent a critical step toward equitable and personalized oncology care on the continent. The integration of genomics into routine oncology practice could enable tailored dosing, risk stratification, and more effective monitoring strategies, ultimately improving both treatment tolerability and long-term outcomes for patients in Africa (Flatters et al., 2019).

2.7 Diagnosis and Assessment of Chemotherapy-Induced Peripheral Neuropathy

The accurate diagnosis and assessment of CIPN are critical yet challenging aspects of clinical oncology practice. Currently, there is no universally accepted gold standard for CIPN diagnosis, and assessment relies on a combination of patient-reported symptoms, clinical examinations, and, in some cases, objective neurophysiological testing. Chemotherapy-induced peripheral neuropathy (CIPN) presents a significant diagnostic challenge due to its variable clinical manifestations, subjective nature of symptoms, and

the lack of standardized, universally accepted diagnostic criteria. Accurate diagnosis is critical to guide management decisions, prevent irreversible nerve damage, and maintain patients' quality of life during and after chemotherapy (Seretny et al., 2014). Comprehensive assessment involves multiple modalities, including clinical evaluation, patient-reported outcome measures, clinician-graded scales, and objective electrophysiological studies

2.7.1 Clinical Assessment

Clinical evaluation of CIPN typically involves a thorough history and neurological examination. Key symptoms include:

- Sensory disturbances: numbness, tingling, burning, electric shock-like sensations
- Motor symptoms: weakness, unsteadiness
- Autonomic symptoms: orthostatic hypotension, constipation

Neurological examination findings may include reduced vibration sense, diminished or absent ankle reflexes, impaired pinprick or temperature sensation, and, in severe cases, distal muscle weakness (Quasthoff & Hartung, 2002).

However, clinical examination alone may underestimate the burden of CIPN, particularly early in its course or in milder cases.

2.7.2 Patient-Reported Outcome Measures

Patient-reported outcome (PRO) measures are essential tools in CIPN assessment, capturing the subjective experience of neuropathic symptoms. Commonly used instruments include:

- **The EORTC QLQ-CIPN20:** A 20-item questionnaire evaluating sensory, motor, and autonomic symptoms (Postma et al., 2005).

- **FACT/GOG-NTX (Functional Assessment of Cancer Therapy/Gynecologic Oncology Group–Neurotoxicity):** Assesses the impact of neuropathy on daily functioning (Calhoun et al., 2003).

These tools offer valuable insights but require appropriate cultural and linguistic validation before use in African contexts.

2.7.3 Grading Systems

Clinician-graded scales such as the **Common Terminology Criteria for Adverse Events (CTCAE)** and the **Total Neuropathy Score (TNS)** are widely used in clinical trials to quantify CIPN severity.

- **CTCAE Version 5.0:** Grades neuropathy from 1 (mild) to 5 (death related to neuropathy).
- **TNS:** Incorporates symptoms, clinical signs, and nerve conduction studies for a more comprehensive assessment.

However, clinician-graded scales often underestimate patient symptom severity compared to PROs (Hershman et al., 2014).

2.7.4 Electrophysiological and Other Objective Tests

Nerve conduction studies (NCS) and electromyography (EMG) can objectively document large fiber involvement, aiding in distinguishing CIPN from other neuropathies (e.g., diabetic neuropathy, Guillain-Barré syndrome).

Quantitative sensory testing (QST) and skin biopsy assessing intraepidermal nerve fiber density offer additional diagnostic insights but are rarely available outside specialized centers.

In resource-limited settings such as Kenya, reliance on clinical evaluation and PROs remains the most pragmatic approach.

2.8 Management and Preventive Strategies for Chemotherapy-Induced Peripheral Neuropathy

The management of CIPN poses a significant clinical challenge, as no agent has yet demonstrated consistent efficacy in either prevention or treatment. Management strategies are thus largely symptomatic and supportive.

2.8.1 Preventive Strategies

Numerous pharmacological agents have been investigated for CIPN prevention, including:

- **Calcium and magnesium infusions:** Early trials suggested benefit in oxaliplatin-induced neuropathy, but subsequent studies yielded inconsistent results (Chay et al., 2010).
- **Duloxetine:** Primarily studied for treatment rather than prevention; not proven for prophylaxis.
- **Glutathione, amifostine, vitamin E:** Studied with mixed or inconclusive results (Hershman et al., 2014).

At present, no pharmacological intervention is universally recommended for CIPN prevention. Dose modification of chemotherapy remains the main preventive strategy.

Non-pharmacological approaches such as exercise programs have shown promise in small studies, potentially mitigating neuropathy severity through neuroplastic mechanisms (Morielli et al., 2019).

2.8.2 Symptomatic Treatment

Among available treatments for established CIPN, only duloxetine, a serotonin-norepinephrine reuptake inhibitor (SNRI), has demonstrated moderate efficacy in randomized controlled trials (Smith et al., 2013). It is recommended as the first-line pharmacologic treatment for painful CIPN.

Other agents with less consistent evidence include:

- Tricyclic antidepressants (e.g., amitriptyline)
- Gabapentinoids (e.g., gabapentin, pregabalin)
- Topical agents (e.g., capsaicin, lidocaine patches)

Non-pharmacologic interventions such as acupuncture, physical therapy, and occupational therapy play supportive roles, particularly in improving functional outcomes and coping strategies (Bao et al., 2014).

Patient education regarding symptom recognition, safety modifications to prevent falls, and psychosocial support are integral components of holistic CIPN management.

2.9 Research Gaps and Justification for Current Study

Despite growing recognition of CIPN's impact, several critical research gaps persist:

- **Population-Specific Data:** Most CIPN studies originate from high-income countries with predominantly Caucasian populations. Data on the prevalence, severity, and risk factors for CIPN among African cancer patients, including Kenyans, are severely lacking.
- **Standardized Assessment Tools:** There is an urgent need for validated, culturally adapted PRO measures for CIPN assessment in African settings.
- **Genetic Factors:** Little is known about genetic susceptibilities to CIPN among African populations. Research into pharmacogenomic predictors could enable more individualized chemotherapy approaches.

Interventional Studies: Evidence regarding effective prevention and management strategies for CIPN remains limited, particularly in low-resource contexts

CHAPTER THREE

3.0 METHODOLOGY

3.1 Introduction

This chapter delineates the comprehensive research methodology adopted to explore the prevalence, severity, and factors associated with peripheral neuropathy among adult cancer patients undergoing chemotherapy at Moi Teaching and Referral Hospital (MTRH). The robustness of any scientific study heavily depends on the clarity, appropriateness, and rigor of its methodological framework. Therefore, this section provides an in-depth description of the study setting, design, population, sampling techniques, data collection procedures, tools used, ethical considerations, and data analysis strategies employed throughout the research process.

The importance of selecting an appropriate methodology cannot be overstated, especially in clinical research where the accuracy of findings directly impacts patient care and treatment protocols. This study was situated within MTRH—a leading national referral hospital located in Eldoret, Kenya, which serves as a vital hub for specialized medical services, including oncology. The hospital's Oncology Outpatient Clinic and inpatient wards offer a diverse patient population, providing an ideal environment for gathering relevant data on chemotherapy-related adverse effects such as peripheral neuropathy. The hospital's facilities, patient demographics, and existing clinical workflows were carefully considered to ensure that the study's findings would be representative of the broader patient population in this region.

The research was designed as a descriptive cross-sectional study, which involves collecting data at a single point in time to assess the prevalence and severity of peripheral neuropathy among patients actively receiving chemotherapy. This design was chosen because it allows for efficient estimation of the burden of neuropathy within

the target population, as well as identification of potential associations with various demographic, clinical, and treatment-related factors. The cross-sectional approach is particularly useful for generating hypotheses and informing future longitudinal studies that could explore causal relationships over time.

This chapter further elaborates on the specific inclusion criteria—such as age, treatment status, and consent—and exclusion criteria, including the ability to respond to questionnaires and the severity of illness, to ensure that the selected sample accurately reflects the population of interest. The sampling technique employed was systematic sampling, which helps to minimize bias and ensure an even distribution of participants across the study period. Given the hospital's patient flow—averaging approximately 800 patients on chemotherapy per month—the sampling interval was calculated to achieve the desired sample size, ensuring that the sample was both manageable and representative.

The process of participant recruitment involved detailed steps, including obtaining ethical approval from relevant bodies, securing permissions from hospital administration, and engaging trained research assistants to facilitate data collection. These assistants were carefully selected and trained on the study objectives, ethical considerations, and data collection procedures to uphold quality and consistency. Participants were approached in outpatient clinics or inpatient wards, and informed consent was obtained after thorough explanation of the study's purpose, benefits, and potential risks.

Data collection tools included structured questionnaires, clinical assessments based on the Total Neuropathy Score (TNS), and review of medical records to gather pertinent clinical and laboratory data. The methodology also describes procedures for performing

clinical assessments, capturing patient-reported symptoms, and grading the severity of neuropathy. Ensuring data accuracy and integrity was prioritized through daily checks of completed forms, double data entry, and secure storage of data with appropriate backups.

The chapter concludes with a detailed overview of the data analysis plan, including descriptive statistics, bivariable analyses to test associations, and multivariable logistic regression to identify independent predictors of peripheral neuropathy. Ethical considerations, such as confidentiality, voluntary participation, and adherence to research guidelines, are emphasized to demonstrate the study's commitment to upholding ethical standards.

In sum, this methodology chapter provides a detailed blueprint of the systematic approach taken to investigate chemotherapy-induced peripheral neuropathy in this population. The selected methods are appropriate for achieving the study objectives, ensuring the reliability and validity of the findings, and laying a solid foundation for subsequent interpretation and application of the results. This comprehensive approach aims to generate evidence that can support improved clinical management, inform policy, and guide future research efforts in this critical area of oncology care.

3.2 Study Setting

The study was conducted at MTRH, Oncology Outpatient Clinic and inpatients medical wards. The hospital is located in the city of Eldoret, situated in the Rift Valley region of Kenya with a bed capacity of 1050 with an average of 1300 inpatients at any time and 1500 outpatients per day. It is located along Nandi Road in Eldoret Town, Uasin Gishu County, 310 Kilometers Northwest of Nairobi. It is the second largest level 6 public hospital in the country which serves as a teaching hospital for the School of Medicine and others universities and colleges of

the region. It is a multi-specialty hospital made up of several directorates. The hospital has an active cancer treatment center which handles both inpatient and outpatients.

3.3 Study Design

This was a descriptive cross-sectional study.

3.3.1 Inclusion Criteria

1. Participants aged ≥ 18 years who were on chemotherapy at Chandaria Cancer and chronic disease Centre and those admitted in the inpatient medical wards.
2. All participants must have received their first cycle of chemotherapy about two months before being recruited into the study.
3. Participants who gave informed written consent to participate in the study.

3.3.2 Exclusion Criteria

- 1) Very sick patient who could not respond to questionnaire.
- 2) Participants who had peripheral neuropathy prior to initiation of chemotherapy were excluded from the study.

3.4 Sample Size Determination

For objective one, the sample size to calculate the prevalence of peripheral neuropathy among participants undergoing chemotherapy was calculated using Fischer's formulae (Kholmatova et al., 2016). The formula is as shown:

$$n = \frac{Z^2 x P(1 - P)}{d^2}$$

Where

n = sample population,

z = standard normal at 95% (1.96)

p = is the population with the characteristic

q = is the population without characteristic,

d = is margin of error

A previous prevalence of peripheral neuropathy among participants undergoing chemotherapy was 83.6% in a study conducted at Kenyatta National hospital (Ezzi et al., 2019).

$$n = \frac{Z^2 \times P(1 - P)}{d^2}$$

Where, n = Desired sample size

Z = value from standard normal distribution corresponding to desired confidence level ($Z=1.96$ for 95% CI)

P = expected true proportion (estimated at 83.6%)

d = desired precision (0.05)

$$n_0 = \frac{1.96^2 \times 0.836(0.164)}{0.05^2} = 210.7$$

$$= 211$$

For objective two, on the severity of chemotherapy induced peripheral neuropathy among chemotherapy participants, we referred to a study conducted in United Kingdom by Burgess et al. (2021) which revealed that 84% of chemotherapy participants had severe chemotherapy induced peripheral neuropathy, we achieved our sample size as shown below.

$$n = 1.96^2 \times 0.84 \times 0.16 / (0.05^2)$$

$$0.5163 / 0.0025$$

$$= 206.52$$

$$= 207$$

For objective three, on factors associated with chemotherapy induced peripheral neuropathy. Using Peduzzi formula to calculate the sample size for this objective.

Based on literature the following are associated factors:

1. Age
2. Gender
3. BMI
4. Duration of chemotherapy

5. CKD
6. Tumor stage
7. Concomitant radiotherapy administration
8. HIV
9. DM

Where :- $N = 10k/p$... (where k= number of variables and p= population proportion)

- $n = 10 \times 9 = 90 \quad (90/0.836) = 107.6$

=**108**

Thus, from the sample size calculation, the largest sample size was 211 and this therefore, was our sample size for our study.

3.5 Sampling Technique

A systematic sampling technique was adopted in this study. There were approximately 800 participants per month on chemotherapy at Chandaria cancer and chronic disease center. Thus, using systematic sampling, an interval of $k/n(800/211)$ was calculated. Thus, from a random starting point every fourth patient was approached to be recruited into the study. The first patient was selected using computer software known as the sampling randomizer. After that every fourth patient was included into the study. In the event that a patient did not meet the inclusion criteria or declined to participate in the study, next patient was included until the sample size was achieved. This also applied for participants in the medical ward.

3.6 Recruitment and Consenting

The principal investigator sought approval from IREC, as IREC is mandated to assess ethical aspects of the study. Permission to conduct the study was also sought from Moi Teaching and Referral Hospital. The PI with the help of two research assistants visited the Chandaria cancer and chronic disease center daily. Here

participants were recruited based on the inclusion criteria developed. This was done at the triage to ensure easier access to potential participants. Every day the PI began data collection from a random starting point and select every fourth patient who met the inclusion criteria. An informed consent was sought from each potential participants and only those who met the inclusion criteria were recruited into the study. Prior to consent administration, the PI and the research assistants introduced themselves and explained the purpose of the study, possible benefits and any risks involved. Participation in the study was voluntary and any patient who declined to participate was excluded and the next patient who met the inclusion criteria was considered and recruited if they consented.

3.7 Data Collection Process

After consenting the PI administered a structured questionnaire seeking to document important information regarding disease under management and the treatment modalities the participants were receiving. The structured questionnaire included information on patient demographic characteristics, clinical characteristics, disease characteristics and presence of peripheral neuropathy. The PI led the participants into a secluded area. These helped reducing any interference as well as enhance the level of concentration to obtain better feedback from the participants. The research assistants assisted in the data collection process and ensured smooth and accurate process. The Total Neuropathy Score questionnaire was administered to help in identification of presence and severity of peripheral neuropathy.

3.8 Data Collection Tools

A structured questionnaire was employed as the primary tool for data collection, designed to systematically gather detailed demographic, clinical, and behavioral information from each participant. This questionnaire was carefully developed to ensure clarity, comprehensiveness, and ease of administration, and it included sections covering personal identifiers, medical history, lifestyle factors, and other relevant variables. Alongside this, clinical information was obtained through a thorough review of each participant's medical records, focusing on any pre-existing conditions or factors that could potentially be associated with or influence the development of peripheral neuropathy. This comprehensive chart review aimed to collect data on previous diagnoses, medication history, and other relevant clinical parameters documented during routine care.

A key component of the assessment involved performing a focused neurologic examination on each participant, following the guidelines outlined in the Total Neuropathy Score (TNS) protocol, as detailed in Appendix IV. This standardized examination included evaluation of sensory, motor, and reflex functions, as well as nerve conduction assessments where applicable. The neurologic examination was critical for identifying signs of neuropathy, determining its severity, and grading its presence accordingly. The grading process involved categorizing the neuropathy as mild, moderate, or severe based on the clinical findings, with specific criteria outlined in the TNS to ensure consistency across examiners.

In addition to the physical examination, chart reviews were conducted to extract baseline laboratory data that provided objective measures of the patient's systemic health. Specifically, laboratory parameters such as hemoglobin levels, serum albumin,

and serum creatinine were retrieved from medical records. These values are important because they can influence or reflect the patient's nutritional status, renal function, and overall health, all of which may impact the risk or severity of peripheral neuropathy. For instance, anemia indicated by low hemoglobin could be associated with fatigue and general decline, whereas hypoalbuminemia might suggest poor nutritional status, which could potentially exacerbate neuropathic symptoms.

In cases where the required laboratory tests were not documented or unavailable in the medical records, additional steps were taken to ensure comprehensive data collection. Blood samples were collected from these participants specifically for the purpose of conducting the necessary laboratory analyses. The testing procedures, as outlined in Appendix I, involved venipuncture performed by trained personnel under aseptic conditions. The collected blood samples were processed in certified laboratories to measure serum levels of hemoglobin, albumin, and creatinine. The costs associated with these tests were covered by the research team to prevent any financial barriers from affecting participation or data completeness. This approach ensured that all participants had complete laboratory data, which was crucial for accurate analysis and interpretation of the study findings.

Furthermore, demographic and clinical parameters were meticulously documented for each participant. These included age, gender, type of cancer (e.g., breast, lung, colorectal), and the stage of cancer at diagnosis, which could influence treatment regimens and the risk of neuropathy. The cumulative dose of chemotherapy administered was recorded to evaluate dose-dependent effects. Information on concurrent radiotherapy was also collected, as radiation exposure could potentially contribute to nerve damage or modify the presentation of neuropathy.

Other health-related variables assessed included nutritional and metabolic status markers, such as hypoalbuminemia, defined as serum albumin levels less than 35.0 g/L, which may indicate malnutrition or systemic inflammation. Hematological status was evaluated through hemoglobin levels, with anemia defined as hemoglobin less than 12.0 g/dL for women and less than 13.0 g/dL for men, reflecting potential blood loss, marrow suppression, or nutritional deficiencies that could influence nerve health. Renal function was assessed through serum creatinine levels, with chronic renal failure identified by a glomerular filtration rate (GFR) of less than 60.0 mL/min/1.73 m², as renal impairment can impact toxin clearance and systemic health, thereby affecting neuropathy risk.

Behavioral factors such as alcohol consumption and smoking history were also documented, given their established roles as risk factors for peripheral nerve damage. Participants were asked about their habits, including frequency and duration of alcohol intake, as well as smoking status (current, former, or never smoker). These variables were included in the analysis to evaluate their potential association with the development or severity of peripheral neuropathy.

Overall, this comprehensive data collection process was designed to capture a multidimensional profile of each participant, integrating clinical, behavioural, and laboratory data. This approach aimed to facilitate a thorough understanding of the factors contributing to peripheral neuropathy in the study population and to identify potential predictors or risk factors that could inform future preventive or therapeutic strategies.

3.9 Recruitment of Research Assistants

To assist in effective data collection, 2 research assistants who are fluent in both English and Swahili were selected and trained to appreciate the aims and objectives of this study. The research assistants were qualified clinical officers. The research assistants received explanation about the research topic and objectives. The researcher also trained the research assistants on key aspects of the study which include; a detailed presentation of the research objectives, a detailed explanation of the data collection tools, sampling procedures ethical issues and code of conduct during data collection. The training concluded with practical sessions focused on accurately extracting data from the participants' charts. The Principal Investigator (PI) oversaw each step of the data collection process to ensure the quality of the data being gathered.

3.10 Total Neuropathy score

The Total Neuropathy Score (TNS) is a clinical tool developed by Johns Hopkins University Hospital. It is used to evaluate and quantify the severity of neuropathy, which is a disorder that affects the nerves and can cause numbness, tingling, pain, and muscle weakness. The TNS is a composite score that considers a variety of clinical measures, including sensory, autonomic, motor, and reflex assessments. The tool is commonly used in clinical trials and research studies to assess the effectiveness of treatments for neuropathy.

The TNS consists of five components namely sensory symptoms, motor symptoms, autonomic symptoms, pin sensibility and vibration sensibility. The strengths of the tool are numerous and include:

3.10.1 Assessment of both symptoms and deficits.

1. Separate measures of sensory, motor and autonomic function.
2. Use of standardized instruments: Neuropen, Rydel-Seiffer calibrated tuning fork.
3. Quantitative measure of sensation bilaterally for both upper and lower limbs.
4. Sensitivity to change along a distal-to-proximal gradient, as most neuropathies begin in the hands and feet and progress to include more proximal sites.
5. Assessment of both large (vibration) and small (pin) fiber sensory function, as these differ in their receptors, pathways, and vulnerabilities to injury.

A TNS score of >2 suggests presence of neuropathy. Furthermore, TNS score can further be graded according to severity from Grade 1 to Grade 4. This grading corresponds to NCI-CTAE grade.

This tool was validated and used at KNH (Ezzi et al 2019)

3.11 Data Analysis and Management

3.11.1 Data Entry

Each day, data collection forms was checked to ensure that all information was properly filled. Errors and omissions detected were discussed and adjusted by the PI and the research assistant. Data was entered into the electronic data entry form using SPSS version 25 and double checked to ensure that data is correctly entered.

3.11.2 Data Management

The process of managing data collected during this study was undertaken with careful attention to accuracy, security, and confidentiality to ensure the integrity of the research findings. To facilitate effective tracking and verification, each participant's data was associated with a unique study identification number (study ID). This ID served as a key reference point, allowing for seamless matching of the collected data with the corresponding entries in the study database during analysis or any necessary cross-

verification procedures. The use of study IDs was instrumental in maintaining participant anonymity and reducing the risk of data mix-ups or misclassification, especially when handling large volumes of information.

The data collection process involved trained research assistants who were responsible for entering the data into a structured electronic data entry form designed specifically for this study. Prior to entry, quality checks were conducted to ensure completeness and correctness of the data collected from paper-based forms or direct interviews. The research assistants worked under the close supervision of the Principal Investigator (PI), who provided guidance, reviewed entries periodically, and ensured adherence to standardized data entry protocols. This oversight was crucial in minimizing errors and discrepancies, thus enhancing data reliability.

Once entered, the datasets were subjected to validation procedures, including double data entry for a subset of forms to identify and rectify inconsistencies or input errors. The electronic data was stored securely on the PI's personal laptop, which was equipped with password protection and encryption features to prevent unauthorized access. Recognizing the importance of data security, access to the laptop was restricted solely to authorized personnel involved in the study.

To further safeguard the data against potential loss or hardware failure, multiple backup copies were created and stored in cloud-based platforms such as Dropbox and Google Drive. These backups were regularly updated to ensure that the most recent data was preserved and could be recovered if necessary. The use of multiple backup locations provided an additional layer of security, protecting the data from risks such as hardware damage, theft, or cyber threats.

Throughout the course of the study, strict confidentiality measures were maintained.

The research team adhered to ethical standards and data protection protocols, ensuring that all personal identifiers were either anonymized or securely stored separately from the main dataset. The data was used exclusively for research purposes, and all team members involved in data handling were bound by confidentiality agreements.

Following the completion of the study, the collected data will be retained for a period of up to five years, in accordance with institutional and ethical guidelines. During this period, the data will be kept in a secure, password-protected environment, accessible only to authorized research personnel. After this retention period, the data will be securely deleted or destroyed to protect participant privacy and comply with data management policies.

In summary, the data management procedures adopted in this study were designed to ensure that data collection, storage, and handling processes upheld the highest standards of accuracy, security, and confidentiality. These measures aimed to facilitate robust data analysis, support the validity of the research findings, and protect the rights and privacy of all study participants throughout the research lifecycle.

3.11.3 Data Analysis

Following data collection, the data was meticulously entered into Statistical Package for Social Sciences (SPSS) software, version 25.0, which facilitated initial data management and preliminary analysis. The process of data analysis began with a comprehensive data cleaning procedure to ensure accuracy, consistency, and completeness of the dataset. This involved checking for any missing values, outliers, or inconsistencies in the data entries, and correcting or addressing these issues as appropriate. Data validation rules and logical checks were applied to identify any discrepancies that could potentially bias the results or undermine the validity of the

analysis.

Once the data cleaning process was completed and verified, the dataset was exported into STATA software, version 15.0, to leverage its advanced analytical capabilities. The decision to use STATA was based on its robust statistical tools, user-friendly interface for complex analyses, and ability to handle large datasets efficiently. The analysis aimed to address the specific objectives outlined in the study protocol, employing both descriptive and inferential statistical methods.

Descriptive Analysis

The first step in data analysis involved summarizing the demographic and clinical characteristics of the study population. For categorical variables such as gender, BMI categories, laboratory results, presence of comorbidities, tumor characteristics, and the specific chemotherapeutic drugs administered, frequencies (counts) and their corresponding proportions (percentages) were calculated. These summaries provided an overview of the distribution of key variables within the sample and helped contextualize subsequent analyses.

For continuous variables such as age, the mean and standard deviation (SD) were computed to describe the central tendency and variability within the population. In cases where the data were skewed or not normally distributed, median and interquartile ranges (IQR) were also considered to provide a more accurate summary. These descriptive statistics served as foundational information to understand the characteristics of the participants and to identify any potential biases or patterns.

Analysis Related to Each Objective

Objective One:

The primary objective was to determine the prevalence of peripheral neuropathy (PN) among patients undergoing chemotherapy. This was calculated by identifying the number of patients who exhibited signs or symptoms of PN and dividing this by the total number of study participants. The resulting proportion was then expressed as a percentage, providing an easily interpretable measure of how common PN was within this patient population.

Objective Two:

To assess the severity of PN, the data was analyzed descriptively. The severity levels, as classified by the study's grading criteria, were summarized using frequency distributions (number of patients in each severity category) and percentages. This approach allowed for a clear visualization of how PN severity was distributed across the sample and facilitated the identification of the proportion of patients experiencing mild, moderate, or severe neuropathy.

Objective Three:

For the analysis of factors associated with PN, the outcome variable was binary—either the patient had PN or did not. To compare the mean age between these two groups, the independent samples t-test was employed. This statistical test assessed whether there was a significant difference in the average age of patients with PN compared to those without. Prior to this, assumptions such as normality of the age distribution within groups and homogeneity of variances were checked to ensure the validity of the t-test.

In addition, the association between PN and various categorical independent variables such as gender, BMI, smoking status, alcohol consumption, and presence of comorbidities was examined using Chi-Square tests. When the expected cell counts

were small (less than 5), Fisher's Exact test was applied instead to obtain more accurate p-values. These tests evaluated whether the distribution of these variables differed significantly between patients with and without PN.

To identify independent predictors of PN, multivariable analysis was conducted using binary logistic regression. Variables that demonstrated statistical significance ($p < 0.05$) at the bivariable level were included in the regression model. This approach allowed for the adjustment of confounding factors and identification of variables independently associated with the likelihood of developing PN. The strength of associations was expressed as odds ratios (OR) with corresponding 95% confidence intervals (CI).

Throughout the analysis, a significance threshold of $p < 0.05$ was set to determine statistical significance. All results, including descriptive statistics, test outcomes, and regression analysis findings, were presented comprehensively in various formats such as detailed text descriptions, organized tables, and graphical charts to facilitate clear interpretation and presentation of the study's findings.

Additional Considerations

To ensure transparency and reproducibility, all analysis steps, assumptions, and decisions were documented thoroughly. Sensitivity analyses were performed where necessary to test the robustness of the findings. The data analysis process aimed to not only answer the research questions but also to uphold the highest standards of statistical rigor and validity.

3.12 Ethical consideration

The study sought ethical approval from MTRH-MU IREC. Approval was also obtained from MTRH administration to ensure that there was compliance with laid down research procedures and access of patient information within the hospital.

Participation in the study was entirely voluntary, and only those who provided consent were recruited. The researcher did not pressure anyone to participate in the study but instead prioritized the respondent's willingness to take part.

The purpose of the study was explained to the respondents including assessment of benefits and potential risks of participation in the study. There were no major risks associated with participation in this study. Only those who met inclusion criteria were recruited to participate in this study.

This study upheld strong emphasis on confidentiality and anonymity which is foundation of ethical research. The researcher maintained anonymity and confidentiality by using none identifiers such as codes that cannot link a participant with the information provided during the study. The information obtained was solely for the purpose of this study and was used in improving care. No personal information was divulged to the public. Recorded data will be under custody of the principal researcher until validation within five years after which the data will be destroyed.

3.13 Study Dissemination

The findings from this study will be disseminated as follows; Firstly, the findings will be presented to the department of Internal medicine and school of Medicine through Thesis defense. Valid and corrected copies will be submitted to the Moi University library. Secondly, the findings of this study will be summarized and published as an original article in an appropriate journal. Lastly the findings of this study will be presented during continuous medical education forums such as seminars and conferences attended by Neurology and Cancer stakeholders in Kenya and throughout the world.

CHAPTER FOUR

4.0 FINDINGS

4.1 INTRODUCTION

This chapter presents a comprehensive analysis of the findings from a cross-sectional study conducted at Moi Teaching and Referral Hospital (MTRH). The primary objective was to assess the prevalence, severity, and factors associated with peripheral neuropathy among adult cancer patients receiving chemotherapy. The study involved 211 participants aged 18 years and above, who were undergoing chemotherapy at Chandaria Cancer and Chronic Disease Centre and admitted in the inpatient wards between June and October 2023. All participants had received at least one cycle of chemotherapy within the two months prior to their interview, ensuring the assessment captured early manifestations of neuropathy related to treatment.

The importance of this investigation stems from the recognition that peripheral neuropathy is a common and often debilitating side effect of many chemotherapeutic agents. It can significantly impair patients' quality of life, interfere with ongoing cancer treatment, and pose challenges for healthcare providers in managing symptoms effectively. Despite its clinical significance, there is limited data on the prevalence and severity of chemotherapy-induced peripheral neuropathy within the local context of MTRH, which is a major referral and oncology center in the region.

This chapter begins with an overview of the sociodemographic and clinical characteristics of the study population, providing context for understanding the distribution of neuropathy and its potential risk factors. It then details the prevalence rates of peripheral neuropathy observed among the participants, including an analysis of sensory, motor, and autonomic symptoms, as well as objective findings from clinical assessments such as vibration and pin sensation tests. The severity of neuropathy is categorized according to established grading systems, allowing for an understanding of

the extent of impairment within this patient group.

Furthermore, the chapter explores the association between various demographic, clinical, and treatment-related factors with the development and severity of peripheral neuropathy. This includes analysis of age, gender, body mass index (BMI), comorbidities such as HIV, diabetes, hypertension, tumor characteristics, and the specific chemotherapeutic agents used. Multivariate analysis is employed to identify independent predictors of neuropathy, which can inform targeted interventions and improve patient management strategies.

In summary, this chapter aims to provide a detailed understanding of chemotherapy-induced peripheral neuropathy in the study population at MTRH, highlighting its prevalence, severity, and associated risk factors. These findings are intended to contribute to the existing body of knowledge, support clinical decision-making, and guide future research efforts aimed at mitigating this adverse effect of cancer treatment.

4.2 SOCIODEMOGRAPHIC AND CLINICAL CHARACTERISTICS

Table 1: Sociodemographic characteristics

	Total N=211
Age	
Mean (SD)	49.8 (14.5)
Range	18 – 82
Gender	
Female	127 (60.2%)
Male	84(39.8)
BMI grouped	
Underweight	38 (18.0%)
Normal	120 (59.9%)
Overweight	33 (15.6%)
Obese	20 (9.5%)
Alcohol intake	
No	199 (94.3%)
Yes	12 (5.7%)
Smoked cigarettes	
No	201 (95.3%)
Yes	10 (4.7%)

The study conducted at MTRH, involved 211 cancer participants undergoing

chemotherapy, and their sociodemographic characteristics were analyzed to provide context for investigating the prevalence, severity, and factors associated with peripheral neuropathy. The participants' ages ranged from 18 to 82 years old, with an average age of 49.8 years and a standard deviation of 14.5 years.

The study population comprised of 127 female participants (60.2%) and 84 male participants (38.6%).

Majority of the participants, 120 (59.9%) had a normal BMI. On the contrary, 38 participants, (18.0%), were classified as underweight, 33 (15.6%) were overweight, and 20 (9.5%), as obese.

With regard to lifestyle factors, few of the participants 12, (5.7%) had reported history of drinking alcohol while only 10 (4.7%) reported history of smoking.

Table 2: Clinical Characteristics

	Total N=211
Underlying comorbidity	
No	164 (77.7%)
Yes	47 (22.3%)
Hypertension	8(17.02%)
Hypertension and DM	20 (42.6%)
HIV	19 (40.4%)
Hemoglobin (g/dL):	
Normal	25 (11.8%)
Low Hb	186 (88.2%)
Potassium Levels (mmol/L):	
Normal	185 (87.7%)
Low	20 (9.5%)
High	6 (2.8%)
eGFR (ml/min):	
Normal (≥ 90)	119 (56.4%)
Abnormal (≤ 89)	92 (43.6%)
Albumin (g/L):	
Normal	99 (46.9%)
Abnormal	112 (53.1%)
Alanine Transaminase (U/L):	
Normal	171(81.0%)
Abnormal	38 (19.0%)
Bilirubin (mg/L):	
Normal	182 (86.3%)

Abnormal	29 (13.7%)
Sodium Levels (mmol/L):	
Normal	166 (78.7%)
Low	36 (17.1%)
High	9 (4.2%)
Creatinine (μmol/mL):	
Normal	147 (69.7%)
Abnormal	64 (30.3%)
Total protein (g/L):	
Normal	90 (42.7%)
Abnormal	121 (57.3%)
Aspartate Transaminase (U/L):	
Normal	190 (90.0%)
Abnormal	21 (10%)
Alkaline Phosphatase (U/L):	
Normal	149 (70.6%)
Low	11 (5.2%)
High	51 (24.2%)
Gamma Glutamyltransferase (U/L):	
Normal	85 (40.3%)
Abnormal	126 (59.7%)
Tumor Site:	
Gynecologic	49 (23.2%)
Bone	38 (18.0%)
Breast	45 (21.3%)
Hematology	18 (8.5%)
GIT	34 (16.1%)
Head and neck	13 (6.2%)
Lung	9 (4.3%)
Skin	5 (2.4%)
Tumor Stage	
1	22 (10.4%)
2	120 (56.9%)
3	57 (27.0%)
4	12 (5.7%)

The clinical characteristics of the 211 cancer patients undergoing chemotherapy at MTRH provide valuable information about their current health status and potential risk factors for peripheral neuropathy. Among them, 47 participants (22.3%) had at least one comorbidity, while the majority, 160 participants (77.7%), had no comorbidities. The most prevalent comorbidities were diabetes and hypertension, affecting 20 participants (42.6%). Additionally, 8 participants had only hypertension, while 19 had HIV. Regarding hemoglobin (Hb) levels, 186 participants (88.2%) had low Hb levels, while 25 (11.8) participants had normal Hb levels. Regarding kidney function, 43.6%

of participants (92 participants) had an abnormal estimated glomerular filtration rate (eGFR) of 89 ml/min or lower, while 56.4% (119 participants) had a normal eGFR of 90 ml/min or higher.

Regarding cancer types, gynecologic tumors(GUT) were the most common, accounting for 28% of the cases (59 participants). Breast cancer ranked second, representing 21.3% of cases(45), followed by bone tumors at 18.0%(38). Gastrointestinal tract (GIT) tumors made up 16.1% (34), while hematological malignancies were found in 1.9% (4) of the participants. Head and neck tumors(ENT) comprised 6.2%, lung cancer contributed 4.3% (9 cases), and skin cancer had the prevalence at 2.4% (5 cases), as shown in the figure below.

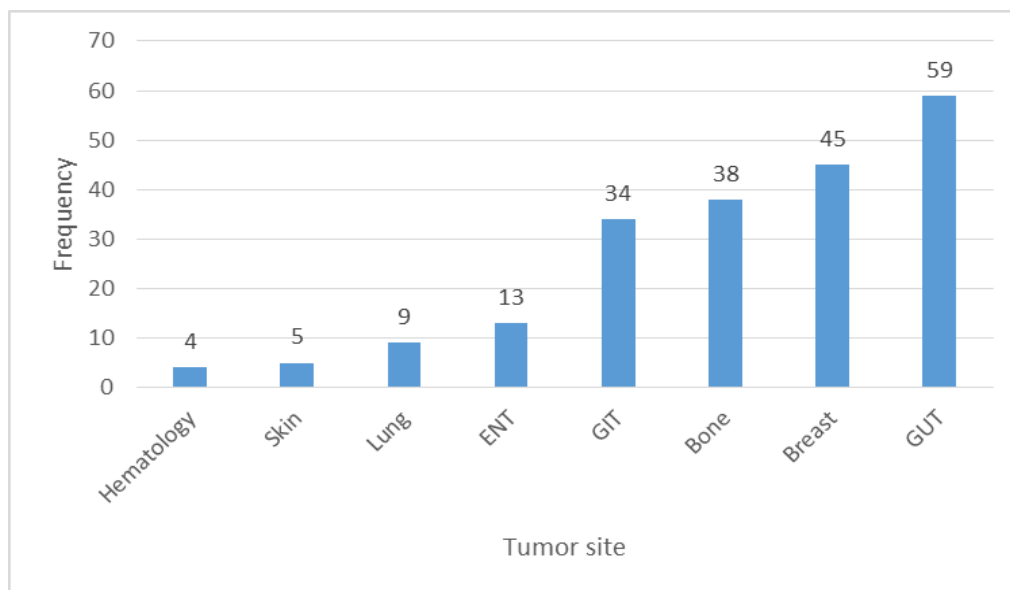


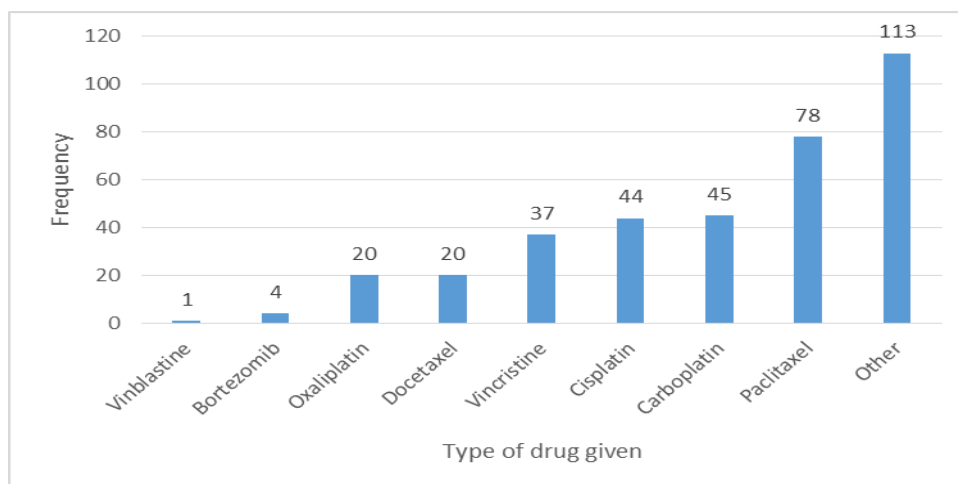
Figure 2: Regarding cancer types

The participants' cancer stages varied, with stage 2 being the most common, affecting 56.9% (120 participants), followed by stage 3 at 27.0% (57 participants), stage 1 at 10.4% (22 participants), and stage 4 at 5.7% (12 participants). This reflects the diverse progression of the disease within the group.

Table 3: Treatment

	Total N=211
Type of Drug Given	
Cisplatin	44 (20.9%)
Oxaliplatin	20 (9.5%)
Carboplatin	45 (21.3%)
Paclitaxel	78 (37.0%)
Docetaxel	20 (9.5%)
Vincristine	37 (17.5%)
Vinblastine	5 (2.4%)
Bortezomib	4 (1.9%)
Other	113 (53.6%)

Among the 211 cancer patients receiving chemotherapy, paclitaxel was the most commonly prescribed drug, given to 37.0% of participants (78 patients). It was closely followed by carboplatin, administered to 21.3% (45 patients), and cisplatin, given to 20.9% (44 patients). Additionally, 9.5% of participants (20 patients) received either docetaxel or oxaliplatin. Vinblastine was used less frequently, given to 2.4% (5 patients), while bortezomib was administered to 1.9% (4 patients). Vincristine was prescribed to 17.5% (37 patients). Furthermore, 53.6% (113 participants) received chemotherapy treatments typically not associated with peripheral neuropathy.

**Figure 3: Types of drug given**

This diverse array of medications reflects tailored treatment plans designed to meet each patient's unique needs, aiming to maximize effectiveness while minimizing side effects.

The prevalence of peripheral neuropathy among participants on chemotherapy at Moi Teaching and referral hospital.

4.3 PREVALENCE OF PERIPHERAL NEUROPATHY

Table 4: Prevalence of neuropathy

Variable	Total N=211 Frequency
Sensory symptoms	
Normal	89 (42.2%)
Abnormal	122 (57.8%)
Sensory symptoms grade	
Mild	50 (41%)
Moderate	41 (33.6%)
Severe	31(25.4%)
Motor symptoms	
Normal	114 (54.0%)
Abnormal	97 (46.0%)
Motor symptoms grade	
Mild	32 (19.6%)
Moderate	39 (53.6%)
Severe	26 (26.8%)
Autonomic symptoms	
Normal	32 (15.2%)
Abnormal	179 (84.8%)
Autonomic symptoms grade	
Mild	104 (58.1%)
Moderate	52 (29.1%)
Severe	23 (12.8%)
The results for pin sensation testing	
Normal	159 (75.4%)
Abnormal	52 (24.6%)
Grade of abnormal pin sensation	
Mild	28 (53.8%)
Moderate	20 (38.5%)
Severe	4 (7.7%)
The results for vibration sensation testing	
Normal	166 (78.7%)
Abnormal	45 (21.3%)
Grade of abnormal vibration sensation testing	
Mild	23 (51.1%)
Moderate	19 (42.2%)
Severe	3 (6.7%)
Presence of neuropathy	
No	63(29.9%)
Yes	148 (70.1%)

Key findings regarding the prevalence of peripheral neuropathy among the 211 cancer patients receiving chemotherapy at MTRH revealed that 70.1% of participants experienced peripheral neuropathy.

The most common type of symptoms were autonomic; a staggering 84.8% of participants (179) had abnormal symptoms. Of them, 58.1 %, (104 participants) reported mild symptoms, 29.1%(52 participants) had moderate symptoms, and 12.8% (23 participants) had severe symptoms. Given the high frequency of autonomic symptoms, the majority of chemotherapy participants have a serious concern regarding autonomic neuropathy.

The majority of the participants had sensory symptoms, with 57.8% (122 participants) reporting abnormal sensory symptoms. Among those reporting symptoms, the severity varied: 41% had mild symptoms, 33.6% (41 participants) had moderate symptoms, and 25.4% (31 participants) had severe sensory symptoms. Motor symptoms were notable, though less common than sensory symptoms: 46.0% (97 participants) had abnormal motor symptoms. The distribution of motor symptom severity was as follows: 26.8% (26 participants) had severe symptoms, 53.6% (52 participants) had moderate symptoms, and 19.6% (19 participants) had mild symptoms. These results imply that motor neuropathy is a widespread problem, with a significant fraction of participants experiencing moderate to severe motor impairment.

Pain sensation test showed abnormal results in 24.6% of the participants (52 participants) of which 53.8% (28 participants) had mild symptoms, 38.5% (20 participants) had moderate symptoms, and 7.7% (4 participants) had severe symptoms among those with abnormal pain sensation. Comparably, vibration sensation testing revealed that 21.3% (45 participants) had abnormal results, with mild symptoms affecting 51.1% (23 participants), moderate symptoms affecting 42.2% (19 participants), and severe symptoms affecting 6.7% (3 participants)..

Objective two: To determine the severity of peripheral neuropathy among participants on chemotherapy at Moi Teaching and referral hospital.

4.4 SEVERITY OF PERIPHERAL NEUROPATHY

Table 5: Severity of neuropathy

	Total N=148
Severity of neuropathy	
Grade 1	73 (49.3%)
Grade 2	42 (28.4%)
Grade 3	21 (14.2%)
Grade 4	12 (8.1%)
Severity of neuropathy	
Mild	73 (49.3%)
Moderate	63 (42.6%)
Severe	12 (8.1%)

At MTRH, in our study, 148 out of 211 cancer participants showed signs of peripheral neuropathy. These participants' neuropathy ranges in severity across grades and levels. The data showed that 73 participants, or nearly half of the participants (49.3%) had Grade 1 neuropathy, which denotes mild symptoms. 28.4% of participants had grade 2 neuropathies while 14.2% of the participants had Grade 3 neuropathy, which is characterized by moderate symptoms (63 participants). Less frequently occurring were more severe cases, which were categorized as Grade 4 neuropathy, which accounted for 8.1% (12 participants).

In terms of overall severity, 49.3% of the participants (73 participants) had mild neuropathy, 42.6% had moderate neuropathy (63 participants), and 8.1% had severe neuropathy (12 participants). A smaller proportion of the participants had severe neuropathy.

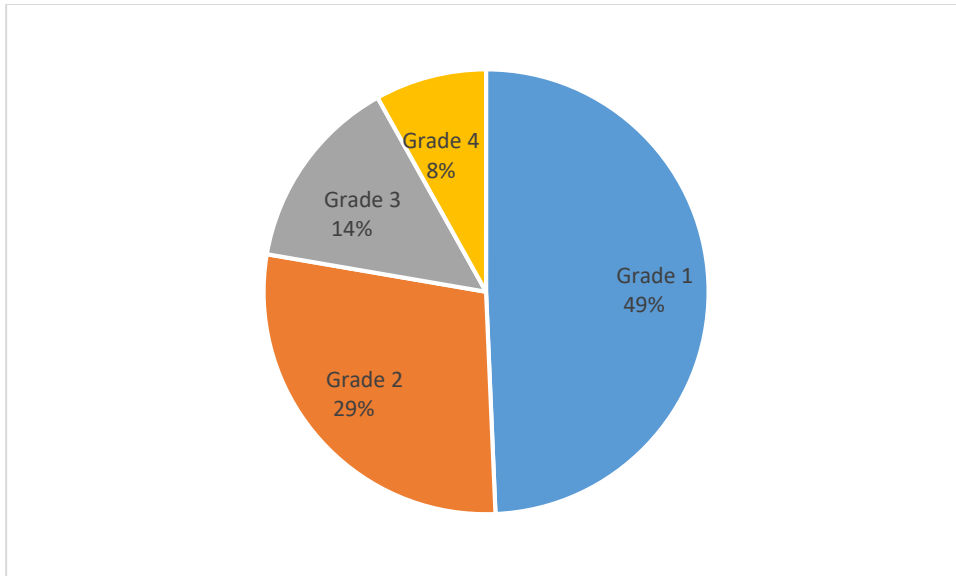
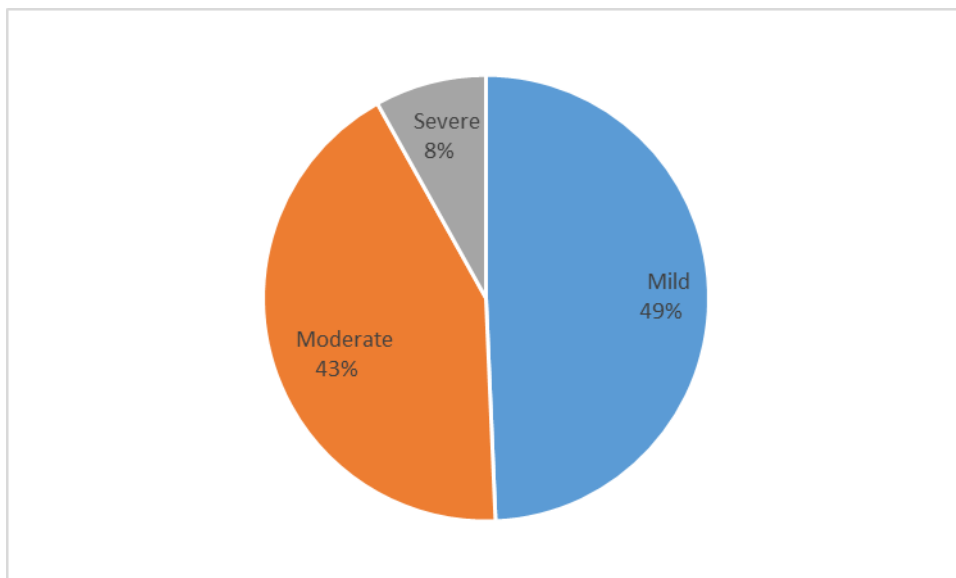


Figure 4: Grading



Objective three: To determine factors associated with peripheral neuropathy among participants on chemotherapy at Moi Teaching and referral hospital.

4.5 FACTORS ASSOCIATED WITH PERIPHERAL NEUROPATHY

Table 6: Bivariate analysis of Demographic and clinical characteristics by neuropathy

	No N=63	Yes N=148	p-value
Age			0.005 ^t
Mean (SD)	45.4 (15.0)	51.6 (13.9)	
Range	18 – 76	18 – 82	
Gender			0.950 ^c
Female	38 (29.5%)	91 (70.5%)	
Male	25 (30.5%)	57 (69.5%)	
BMI			0.468 ^c
Underweight	8 (21.1%)	30 (78.9%)	
Normal	42 (34.4%)	80 (65.6%)	
Overweight	9 (29.0%)	22 (71.0%)	
Obese	4 (20.0%)	16 (80.0%)	
Alcohol consumption			0.728 ^f
No	57 (28.9%)	140 (71.1%)	
Yes	2 (20.0%)	8 (80.0%)	
Smoker			0.444 ^f
No	62 (30.5%)	141 (69.5%)	
Yes	1 (12.5%)	7 (87.5%)	
Presence of comorbidity (HIV,DM,HTN)			0.212 ^c
No	53 (32.3%)	111 (67.7%)	
Yes	10 (21.3%)	37 (78.7%)	
eGFR grouped			0.945 ^c
Normal (>=90)	37 (31.1%)	82 (68.9%)	
Abnormal (<=89)	26 (28.3%)	66 (71.7%)	
Tumor Stage:			0.960 ^f
1	7 (31.8%)	15 (68.2%)	
2	35 (29.2%)	85 (70.8%)	
3	15 (26.3%)	42 (73.7%)	
4	6 (50.0%)	6 (50.0%)	
Drugs used			
Platinum-based chemo	27 (26.5%)	75 (73.5%)	0.523 ^c
Taxanes	22 (24.7%)	67 (75.3%)	0.395 ^c
Vinca alkaloids	4(44.4)	5 (55.6%)	0.324 ^f
Bortezomib	0	4 (100.0%)	0.580 ^f
Other	33 (29.2%)	80 (70.8%)	0.806 ^c

Age and the existence of neuropathy are statistically significantly correlated ($p=0.005$).

Compared to participants without neuropathy (45.4 years), those with neuropathy had a mean age of 51.6 years.

With regards to gender, there was no significant correlation between gender and the presence of neuropathy with p value of 0.950. The prevalence rates of neuropathy were

similar in males (71.3%) and females (71.7%), suggesting that gender may not contribute significantly to the development of peripheral neuropathy in our setup.

Concerning, BMI and neuropathy, no statistical significance was noted, ($p=0.468$). Similar rates of neuropathy were seen in participants in the four BMI categories—underweight, normal, overweight, and obese.

Smoking and alcohol consumption were associated with peripheral neuropathy though it was not statistically significant with values of $p=0.444$ and $p=0.728$ respectively. However, it's important to note that the number participants who had history of consumption of the above were few, that is, a total of 18.

There was no statistically significant correlation between neuropathy and comorbidities such as HIV, diabetes mellitus (DM), and hypertension (HTN) ($p=0.212$). However, it was observed that neuropathy was more common among participants with any of these comorbidities, with a prevalence of 78.7% compared to 69.4% among participants without comorbidities, although this difference was not statistically significant.

In relation to the Glomerular Filtration Rate Estimated (eGFR): no association was noted with neuropathy ($p=0.945$) though most participant with abnormal kidney function were in stage 2 CKD.

Pertaining the tumor stage, there was no discernible correlation between the tumor stage and neuropathy ($p=0.960$). In each of the four tumor stages—68.2% in stage 1, 70.8% in stage 2, 73.7% in stage 3, and 75.0% in stage 4—the prevalence of neuropathy was similar.

On the subject of class of chemotherapy drugs, there was no statistically significant correlation found between the type of chemotherapy drug administered and neuropathy. In particular, the rates of neuropathy among participants were comparable for taxanes ($p=0.395$), vinca alkaloids ($p=0.324$), bortezomib ($p=0.580$), platinum-based

chemotherapies ($p=0.523$), and other medications ($p=0.806$). Notably, neuropathy developed in 100% of participants treated with vinca alkaloids and 100% of participants treated with bortezomib; however, these results were not statistically significant.

Table 7: Multivariate analysis of Factors associated with neuropathy

Variables	aOR	p	[95% CI.]
Age	1.029	0.010	1.007 - 1.052
Presence of comorbidity (HIV,DM,HTN)			
No	Ref		
Yes	1.342	0.471	0.603 – 2.985

Important insight is revealed by the multivariate analysis of peripheral neuropathy-related factors among cancer participants receiving chemotherapy at MTRH. This includes information on age and the presence of comorbidities like HIV, diabetes mellitus (DM), and hypertension (HTN).

Age has been found to be a significant factor in the presence of neuropathy. Age has an adjusted odd ratio (aOR) of 1.029, a 95% confidence interval (CI) of 1.007 to 1.052, a p-value of 0.010. This means that the likelihood of developing neuropathy rises by about 2.9% for every year of age. Older participants are therefore more likely to experience neuropathy during chemotherapy treatment.

Comorbidities (HIV, diabetes, and hypertension) were also assessed, but this multivariate analysis did not reveal a statistically significant correlation between them and neuropathy. An adjusted odd ratio (aOR) of 1.342, with a 95% confidence interval of 0.603 to 2.985 and a p-value of 0.471, was observed in participants with comorbidities. Given that the p-value is higher than the standard cutoff of 0.05 and the confidence interval encompasses 1, it can be concluded that the presence of these comorbidities does not substantially raise the risk of neuropathy development in the study population.

CHAPTER FIVE

5.0 DISCUSSION

5.1 Introduction

This section provides a detailed overview of the key findings from the study focused on peripheral neuropathy among cancer patients receiving chemotherapy at Moi Teaching and Referral Hospital (MTRH). It begins with an examination of the socio-demographic characteristics of the participants, including age, gender, body mass index (BMI), and lifestyle factors such as smoking and alcohol consumption. These demographic details are important because they can influence an individual's susceptibility to developing peripheral neuropathy, as well as the severity and progression of the condition.

The analysis then explores the clinical features observed within the study population. This includes the prevalence of comorbid conditions such as hypertension, HIV infection, and diabetes mellitus, which are known to potentially complicate or exacerbate peripheral neuropathy. The section discusses how these underlying health issues might contribute to nerve damage or affect the patient's response to chemotherapy. Additionally, laboratory findings related to hematological parameters, biochemical markers, kidney function, and liver function are evaluated, providing a comprehensive picture of the participants' overall health status. These laboratory results are crucial because abnormalities in these areas can influence both the risk of developing neuropathy and the patient's ability to tolerate chemotherapy.

Attention is also given to the chemotherapy regimens administered to the patients, with particular focus on the commonly used agents such as paclitaxel, cisplatin, and carboplatin. The study findings reveal that these drugs are significantly associated with the development of peripheral neuropathy, which aligns with existing literature on their

neurotoxic effects. The severity of neuropathy experienced by patients varies, with most cases classified as mild or moderate, although some individuals reported severe symptoms that impacted their daily functioning. The section discusses how different chemotherapeutic agents contribute to nerve damage and underscores the importance of monitoring patients closely during treatment.

Further analysis highlights that age is a significant factor associated with increased risk of developing peripheral neuropathy. Older patients tend to be more vulnerable, possibly due to age-related nerve degeneration or decreased regenerative capacity. Conversely, other factors such as gender, BMI, and the presence of comorbidities like hypertension or HIV did not show statistically significant associations with neuropathy in this study. This suggests that while these factors may influence individual experiences, they are not strong predictors of neuropathy development within this specific patient population.

The discussion emphasizes the importance of early detection and routine screening for peripheral neuropathy in cancer patients undergoing chemotherapy. It suggests that implementing proactive assessment protocols can help identify neuropathy at an early stage, allowing for timely interventions that may prevent progression and improve patient quality of life. The chapter also advocates for a multidisciplinary approach involving oncologists, neurologists, nurses, and physiotherapists to effectively manage symptoms and provide supportive care.

This section also encompasses an overview of the strengths and limitations of the study, highlighting its methodological robustness as well as areas where interpretative caution is warranted.

In conclusion, the findings underscore the need for heightened awareness of peripheral neuropathy as a common and potentially debilitating side effect of certain chemotherapeutic agents. By understanding the factors that contribute to its development and severity, healthcare providers can better tailor treatment plans, optimize supportive care, and ultimately enhance treatment outcomes for patients. This comprehensive approach is essential in ensuring that cancer therapy remains effective while minimizing adverse effects and preserving the patient's functional ability and overall well-being.

5.2 Socio-Demographic Characteristics

A number of significant trends that could influence the frequency and severity of peripheral neuropathy in chemotherapy participants are revealed by the study population's demographic analysis.

The wide age range of 18 to 82 years provides a comprehensive representation of the population receiving chemotherapy, with an average age of 49.8 years. This is comparable with the local cancer registry that states that 60% of Kenyans affected with cancer are younger than 70 years old and 70-80% of cancer stages are diagnosed at late stages(<https://kenyacancernetwork.wordpress.com/kenya-cancer-facts/>). Furthermore, significant number of cancer patients are lost to follow-up for a variety of reasons, including financial difficulties or psychological problems like depression, which prevents them from being recruited or monitored to the end, others default due to the side effects of chemotherapy medication. In addition, the natural life expectancy in our nation is approximately 64 years old, which contributes to the lower mean age.

The female gender made up the majority of participants at 61.4%, this was due to high number of cervical and breast cancer in our setting and globally. Cervical cancer is a major health burden and the second most common cancer after breast cancer among

women in Kenya (E. Mwaliko et.al 2023). Additionally, numerous studies conducted globally, including one in Kibera, Kenya by Muriithi et al in 2009, have extensively documented that women exhibit better health-seeking behaviors compared to men. The study conducted in Kibera observed a significant proportion of female participants seeking health care services, irrespective of the type of illness.

Although most participants (57.0%) have normal BMIs, a sizable fraction of the population is underweight (18.4%), overweight (15.0%), or obese (9.7%), according to the BMI data. According to data on alcohol and cigarette consumption, most participants (95.2% of non-drinkers and 96.1% of non-smokers) do not participate in these specific risk behaviors.

The results of this study about the lifestyle and demographic factors influencing peripheral neuropathy in chemotherapy participants are supported by multiple studies. For example, studies have repeatedly demonstrated that body mass index (BMI) has a substantial effect on the course of chemotherapy and the likelihood of adverse effects, such as peripheral neuropathy. According to Jesse et al (2019) participants with an obesity-related BMI were more likely than those with a normal BMI to experience chemotherapy-induced neuropathy.

Similar to this, Aikeland et al., (2021) describes lifestyle choices like drinking alcohol and smoking being linked to an increase in neuropathic symptoms; however, due to low prevalence of these habits in the participants in this study there was no significant increase in peripheral neuropathy among this group. In contrast, some research indicates that populations with distinct demographic profiles may have a higher prevalence of peripheral neuropathy. As an illustration of the variability of risk factors across different patient groups, Selvy et al. (2020) found that older populations and those with higher incidences of smoking and alcohol consumption had higher rates of neuropathy.

The distribution on BMI is important because it affects not only the participants' overall health outcomes but also the metabolism and effectiveness of chemotherapy drugs. Participants who are overweight or obese may respond to chemotherapy differently pharmacologically, which could raise their risk of peripheral neuropathy. In contrast, participants who are underweight may be more susceptible to the harmful effects of chemotherapy because of their smaller body mass and malnutrition.

5.3 Clinical Characteristics

There is an interplay of comorbidities, hematological abnormalities, biochemical imbalances, and liver function issues that significantly impact cancer management and patient outcomes. Comorbidities such as diabetes mellitus, hypertension, and HIV can significantly influence the development and severity of CIPN. Diabetes, known for causing peripheral neuropathy independently, may predispose patients to more severe neurotoxic effects when combined with chemotherapy (Smith et al., 2018). Hypertension and HIV can also impair nerve health and immune function, potentially exacerbating neuropathic symptoms and complicating management. Addressing these comorbidities proactively is crucial to minimize their additive impact on CIPN and improve overall patient outcomes. Hypertension can exacerbate side effects of chemotherapy and necessitate careful management to avoid additional cardiovascular complications.

The clinical characteristics of 211 cancer participants undergoing chemotherapy reveal a complex interplay of comorbidities, hematological, biochemical, and liver function abnormalities, as well as varied cancer types and stages. The combination of hypertension and diabetes was the most frequently observed comorbidity, impacting 42.6% (20) of participants with comorbid conditions. The second most common comorbidity was HIV, which affected 40.4% (19), while hypertension alone was

present in 14.9% (8) of the participants. There was increased prevalence of peripheral neuropathy among patient with these comobidites though it was not statistically significant. This is because the number of participants with comorbidities were small in number compared to the sample size (47 out of 211) . These comorbidities can complicate cancer management and increase the risk of chemotherapy-related side effects, including peripheral neuropathy.

One of the notable outcomes of this study was the high prevalence of anemia among the participants, with 89% exhibiting anemia during their chemotherapy treatment. This significant prevalence aligns with existing literature that identifies anemia as a common hematologic toxicity associated with chemotherapeutic agents, particularly those used in the treatment of solid tumors and hematologic malignancies (Bohlius et al., 2016). Anemia in cancer patients can result from multiple factors, including marrow suppression by chemotherapy, nutritional deficiencies, and the disease process itself. The high rate of anemia observed in this cohort underscores its clinical relevance as a potential contributor to the overall morbidity experienced by patients with CIPN. This result is in line with a study conducted in 2020 by Anand et al. that discovered anemia is prevalent in cancer participants (79.8%) and can negatively impact treatment outcomes and quality of life.

Anemia may exacerbate symptoms such as fatigue, weakness, and reduced functional capacity, which can further impair patients' quality of life and interfere with ongoing cancer treatment (Aapro et al., 2019).

Despite this very high prevalence, anemia did not demonstrate a statistically significant association with the development of chemotherapy-induced peripheral neuropathy (CIPN). This finding highlights an important clinical distinction: although anemia is common in oncology populations, it may not independently influence neuropathy risk.

The absence of a significant correlation in our study aligns with several reports in the existing literature. For instance, Jiwpanya et al. (2021) found that anemia was *not* a significant predictor of CIPN among breast cancer patients receiving neurotoxic chemotherapy. Similarly, Zhi et al. (2023) demonstrated that while BMI predicted paclitaxel-induced neuropathy in early-stage breast cancer patients, baseline hemoglobin showed no significant relationship with CIPN severity. Another large retrospective analysis by Hiramoto et al. (2021) reported that cumulative paclitaxel dose and BMI—but not anemia—were the dominant predictors of neuropathy. Recent observational findings by Li et al. (2024) further support this pattern, showing no consistent laboratory predictors, including hemoglobin, for CIPN across their cohort. Together, these studies strengthen the interpretation that laboratory hematologic parameters such as hemoglobin may have limited predictive value for CIPN, especially when neurotoxicity is primarily driven by the specific chemotherapy agent and cumulative dosing.

From a biological perspective, CIPN arises mainly from direct neurotoxic mechanisms including axonal degeneration, mitochondrial injury, microtubule disruption, and dorsal root ganglion toxicity—rather than from systemic hypoxia or hematologic status. This mechanistic independence helps explain why even severe anemia may not correlate with neuropathy in some populations. Additionally, in our cohort, the overwhelmingly high anemia prevalence created limited variability between CIPN and non-CIPN groups, reducing the statistical power to detect subtle differences. It is also possible that other factors—such as chemotherapy regimen type, cumulative dose, genetic predisposition, comorbidities, and renal function—play more dominant roles in CIPN development than hemoglobin levels.

Overall, our findings contribute to the growing body of evidence suggesting that while anemia remains a critical clinical issue in cancer care, its role in predicting CIPN is inconsistent and likely minimal. Clinically, this reinforces the need for CIPN prevention and monitoring strategies to focus more on chemotherapy-specific risk factors rather than hematologic indices. However, given the profound impact of anemia on fatigue, functional status, and treatment tolerance, its management remains essential for optimizing the overall well-being of patients undergoing chemotherapy, even if it does not modify neuropathy risk.

Renal function assessments indicated that 44.4% of the study participants exhibited abnormal estimated glomerular filtration rate (eGFR) levels, reflecting different stages of renal impairment. This finding highlights the substantial prevalence of compromised kidney function within the cohort. Participants with renal impairment tended to experience a slightly higher incidence of peripheral neuropathy compared to those with normal renal function. However, this observed difference did not reach statistical significance, suggesting that renal impairment alone may not be a strong independent predictor of neuropathy in this population.

Most individuals with renal impairment were classified as having stage 2 chronic kidney disease (CKD), characterized by mild to moderate reductions in kidney function. Stage 2 CKD is often asymptomatic but can contribute to metabolic disturbances that potentially influence nerve health. The subtle increase in neuropathy among those with renal impairment may be related to factors such as the accumulation of neurotoxic waste products or electrolyte imbalances associated with decreased kidney clearance.

This is in line with studies like Santos et al. (2020), which highlight the prevalence of renal impairment in cancer participants and its implications for chemotherapy dosing and toxicity where it was reported 80% of the participants having renal insufficiency.

Most of the chemotherapeutic agents are nephrotoxic. These nephrotoxic agents can directly damage renal tubules, leading to acute kidney injury (AKI) and diminished renal function. The risk of renal impairment is further exacerbated by common side effects of chemotherapy, including nausea, vomiting, and diarrhea. These gastrointestinal issues can lead to dehydration and electrolyte imbalances, which compound the risk of renal damage.

Additionally, chemotherapy-induced complications, such as tumor lysis syndrome, can contribute to acute renal insufficiency, especially in patients with rapidly proliferating tumors. The release of intracellular components (like potassium and uric acid) into the bloodstream may overwhelm the kidneys' ability to process these substances, leading to further renal dysfunction.

Nonetheless, the lack of statistical significance indicates that further research with larger sample sizes or more precise measures may be necessary to fully elucidate the relationship between renal function decline and peripheral neuropathy.

Liver function tests indicated that 58.5% of participants exhibited abnormalities in various hepatic parameters, including albumin levels, alanine transaminase (ALT), bilirubin, gamma-glutamyltransferase (GGT), and total protein. These alterations suggest potential underlying issues such as liver dysfunction or malnutrition. Elevated or decreased levels of these markers can reflect hepatocellular injury, impaired liver synthetic capacity, or cholestasis. For instance, abnormal albumin and total protein levels may indicate compromised hepatic protein synthesis, often seen in chronic liver conditions or malnutrition. Elevated ALT and GGT levels can point towards hepatocellular damage or biliary tract involvement. Elevated bilirubin levels may signify impaired bilirubin metabolism or excretion, further supporting the presence of liver dysfunction.

The high prevalence of these abnormalities suggests that a significant proportion of participants may be experiencing liver-related issues, which could be due to underlying liver disease, malnutrition, or other systemic illnesses affecting liver function. These findings underscore the importance of comprehensive nutritional assessment and liver health monitoring in this population, particularly when managing conditions that may impact hepatic function or require hepatotoxic medications.

Regarding cancer staging among the participants, the majority were diagnosed at stage 2, accounting for 56.9% (120 individuals) of the cohort. This was followed by stage 3, representing 27% (57 individuals), while stage 1 comprised 10.4% (22 individuals), and stage 4 included 5.7% (12 individuals). The predominance of diagnoses at stage 2 and 3 reflects a pattern of delayed detection, primarily attributable to limited access to healthcare facilities among these patients, many of whom originate from rural settings. Several factors contribute to this delay, including geographical barriers, insufficient healthcare infrastructure, and financial constraints that hinder timely medical consultation and screening. Most health facilities within the counties and sub-counties lack the specialized capacity to accurately diagnose and stage cancer early, often resulting in patients presenting with more advanced disease stages. These systemic challenges highlight the need for improved healthcare access, early detection programs, and enhanced diagnostic capabilities to facilitate earlier diagnosis and potentially improve treatment outcomes for this population.

In this study, the prevalence of chemotherapy-induced peripheral neuropathy (CIPN) remained consistently high across tumour stages 1 to 3, with between two-thirds and three-quarters of patients in each group experiencing neuropathy. This pattern suggests that the development of CIPN is influenced more by the neurotoxic potential of the chemotherapy regimens used than by the extent of the underlying malignancy. Many

patients across the early and locally advanced stages receive standard first-line regimens containing taxanes, platinum compounds, or vinca alkaloids, all of which are well-documented causes of sensory neuropathy. The progressively increasing proportions of CIPN from stage 1 (68.2%) to stage 3 (73.7%) may also reflect the intensification of treatment as tumour burden increases, including higher cumulative doses, combination regimens, and more cycles administered.

Interestingly, stage 4 disease demonstrated a markedly different pattern, with an equal proportion of patients with and without CIPN (50.0%). This deviation is likely attributable to the small sample size in this subgroup, which limits the stability of percentage-based comparisons. Additionally, patients with advanced disease often receive modified or less intensive chemotherapy—either palliative regimens with lower neurotoxicity profiles or early dose reductions due to frailty, comorbidities, and performance status considerations. These treatment adjustments may mitigate the cumulative neurotoxic exposure, resulting in a lower observed prevalence of CIPN compared to earlier stages.

Overall, these findings underscore that CIPN is a common and significant complication across all tumour stages, with its occurrence appearing to be driven predominantly by chemotherapy-related factors rather than disease stage alone. The high burden of neuropathy even among early-stage patients highlights the need for routine screening, patient education, and early intervention strategies regardless of tumour extent. Future studies with larger stage-specific sample sizes and chemotherapy-specific stratification may provide clearer insight into the interaction between cancer stage, treatment intensity, and the risk of developing CIPN.

Potential liver dysfunction or malnourishment is indicated by abnormal levels of ALT, bilirubin, GGT, and protein, as well as abnormal liver function test results (abnormal albumin levels) in 58.5% of participants. Certain chemotherapy agents, such as methotrexate, doxorubicin, and cisplatin, can cause direct damage to liver cells, leading to elevated liver enzymes and impaired liver function. The liver is primarily responsible for drug metabolism. Chemotherapy can alter liver enzyme activity, potentially affecting how drugs are metabolized, leading to toxicity and liver dysfunction. The presence of tumors, particularly liver metastases, can directly disrupt liver architecture and function, leading to hepatic dysfunction.

This result is consistent with Calistri et al., (2020), who highlight the frequency of liver abnormalities in cancer participants because of liver pre-existing conditions, chemotherapy toxicity, or metastasis.

Regional differences in cancer epidemiology are reflected in the distribution of cancer types in this cohort, with gynecological tumors being the most common (28.5%). This prevalence aligns with results from the ME et al., (2024) reports, which show that certain populations have higher than average incidences of gynecological cancers. With a prevalence of 21.7%, breast cancer and lung cancer is among the most common cancers worldwide, in line with global trends.

5.4 Treatment

The data demonstrates the wide variety of chemotherapy medication regimens used, demonstrating the customized strategy used to maximize treatment effectiveness while reducing side effects. 37.0%(78) of participants receiving chemotherapy, with paclitaxel being the most commonly administered medication, followed by carboplatin 21.3%(45) and cisplatin 20.9%(44). Other noteworthy medications included vincristine, which was used in 17.5%(37) of cases, and docetaxel and

oxaliplatin, which were each given to 9.5%(20) of participants. Vinblastine 2.4%(5) and bortezomib 1.9%(4) were the less commonly used medications, with 54.6% of participants receiving other chemotherapy treatments that are not known to cause peripheral neuropathy. Using multiple drugs, or combination therapy, in cancer treatment is a common approach to improve therapeutic outcomes and manage the disease more effectively. Different drugs may target various pathways or mechanisms involved in cancer growth and survival. Combining drugs with different modes of action can lead to a synergistic effect, enhancing the overall effectiveness of treatment. Additionally, Cancer cells can develop resistance to single-agent therapies. By using multiple drugs, the likelihood of cancer cells developing resistance to all agents is reduced, as they have to adapt to multiple mechanisms of action simultaneously.

Combination therapies can help to achieve a better overall response rate. This can be particularly important in aggressive cancers where rapid tumor reduction is needed to control disease progression. When using lower doses of multiple agents, it may be possible to minimize the side effects associated with high doses of a single drug. This is particularly relevant as some cancer treatments can have significant toxicities that limit their use (Aikeland et al., (2021)

This individualized approach to chemotherapy aligns with research results from other studies. For example, paclitaxel was found to be widely used in treating various cancers due to its efficacy in a study by Nawara et al. (2021), which is comparable to the high usage seen in the MTRH cohort. Corresponding to the substantial usage observed in the MTRH data, Tsvetkova and Ivanova (2022) stated that carboplatin and cisplatin are frequently used in the treatment of cancers such as ovarian, lung, and head and neck cancers.

On the other hand, Xue et al.'s study from Southeast Asia in 2022 revealed that immunotherapies and targeted therapies were used more frequently than conventional chemotherapeutic drugs like carboplatin and cisplatin. This distinction draws attention to the different approaches depending on local drug availability, infrastructure in various healthcare systems and existing protocols.

5.5 The Prevalence of Peripheral Neuropathy Among Participants on Chemotherapy at Moi Teaching and Referral Hospital

According to this study, 70.1% of the 211 participants had neuropathy, this is lower than study done at KNH which showed 83.6% (Ezzi et al., 2019). This because the study done was looking at peripheral neuropathy induced by one agent(Cisplatin) compared to our study that was looking at all chemotherapeutic in general. Additional the sample size was small compared to our study. However this study was in agreement with a study done In the Netherlands, Oortgiesen et al. (2022) investigated the burden of peripheral neuropathy among cancer patients. The findings established that 69% of the participants had peripheral neuropathy.

Autonomic and sensory symptoms were prevalent among the participants, accounting for 86.5% and 58.9% of cases, respectively. Among those reporting sensory symptoms, 58.2% experienced severe symptoms, whereas 40.2% reported moderate sensory impairment. Regarding motor symptoms, 46.9% of participants were affected, with 53.6% exhibiting moderate impairments and 26.8% experiencing severe impairments. Additionally, a substantial proportion (86.5%) of participants reported autonomic symptoms, with 58.1% experiencing mild symptoms, 29.1% moderate, and 12.8% severe.

Further assessments revealed that 25.1% of participants exhibited abnormalities in vibration perception, while 21.7% demonstrated abnormal pain perception.

In contrast to these findings, Selvy et al. (2021b) reported that only 26.9% of participants exhibited sensory chemotherapy-induced peripheral neuropathy (CIPN). Interestingly, they found that participants with and without sensory CIPN had similar histories of neuropathic pain, suggesting that neuropathic pain may occur independently of sensory CIPN. Similarly, Hsieh et al. (2023) observed that 16.0% to 17.3% of participants reported neuropathic pain, while sensory and motor CIPN were reported in 34.7% to 54.7% of cases, respectively.

Supporting these variations, Smith et al. (2021) highlighted that the reported prevalence of CIPN varies significantly depending on the measurement methods used. They found that Grade 2 sensory or motor CIPN was observed in 2.8% to 29% of cases, whereas grades ≥ 3 were less common, affecting 1% to 12%. They also noted that the absence of standardized cut-points for mild, moderate, or severe neuropathy contributed to a wide range of prevalence estimates—ranging from 26.7% to 78% for scores ≥ 1 , and 17% to 86.6% for scores ≥ 5 —underscoring the variability in assessment techniques and reporting.

According to seven studies, neuropathic pain associated with CIPN was present in 1.3–60.6% of participants.

Peripheral neuropathy is highly prevalent among cancer participants at MTRH, indicating the substantial impact of CIPN. The prevalence of autonomic and sensory symptoms highlights the need for comprehensive management approaches to deal with these crippling side effects. The intensity of the motor and sensory symptoms points to a significant impairment that may have an impact on the participants' quality of life

and ability to receive further treatment.

The increased frequency of autonomic symptoms is especially concerning because of the possible consequences, which include unpredictable cardiovascular disease and gastrointestinal disorders. These results imply that early intervention and routine screening are necessary for the effective management of CIPN.

Variations among studies could be caused by a number of things, such as patient demographics, types of chemotherapy, and methods of assessment. The high rates of neuropathy in these participants may be related to the particular chemotherapy regimens administered at MTRH, which include paclitaxel, cisplatin, and carboplatin, all of which have a history of neurotoxicity.

5.6 The Severity of Peripheral Neuropathy Among Participants On Chemotherapy at Moi Teaching and Referral Hospital

Approximately half (49.3%) of the 148 cancer participants who developed peripheral neuropathy had Grade 1 neuropathy, which denotes mild symptoms. While more severe cases, categorized as Grade 4 neuropathy, were less common, affecting 8.1% of participants. moderate symptoms (Grade 2 and 3) were present in 42.6% of participants. Regarding the total severity, mild neuropathy accounted for 49.3% of cases, moderate neuropathy for 42.6%, and severe neuropathy for 8.1% of cases. This distribution suggests that a smaller percentage of participants have severe neuropathy, but a significant number have mild to moderate neuropathy.

According to Sreeram et al. (2023), 68% of participants had CIPN, with 53% having persistent CIPN and 52% having current CIPN. Prevalent CIPN had a severity distribution of 32.2% mild, 30.8% moderate, and 36.9% severe cases.

According to Chen et al. (2022), there was a greater finding of sensory than motor CIPN (mean = 10.8, ranged [-3.3, 52.1] for CIPNS; mean = 3.5, ranged [-7.5, 35.0] for

CIPNM). No CIPN, Mixed CIPN, and Sensory-dominant CIPN were found to be the three groups (maximum CIPNS: mean = 12.7 vs. 40.9 vs. 74.3, $p < 0.001$; maximum CIPNM: mean = 5.4 vs. 25.5 vs. 36.1, $p < 0.001$; average CIPNS–CIPNM: mean = 2.8 vs. 5.8 vs. 24.9, $p < 0.001$). Biomarkers of motor CIPN shared characteristics with those of sensory CIPN that had been previously discovered, such as decreased serum histidine levels ($p = 0.029$)

Li et al. (2020) reported that a total of forty-three full text articles that looked at twenty-three phase III trials ($N = 8218$) met the criteria. The range of neuropathy incidence was found to be 8.4% to 80.5% (median = 37.8%), with 1% to 33.2% (median = 8%) corresponding to severe neuropathy (grade 3-4). Both the recently diagnosed and relapsed cohorts reported similar cases of neuropathy of any grade and severe neuropathy.

In contrast, Selvy et al.'s study from 2021 revealed a lower prevalence and severity of CIPN overall, with only 26.9% of participants reporting motor symptoms and sensory CIPN. Differences in patient demographics, the kinds of chemotherapy medications used, or the methods of assessment could be the cause of this disparity. The variability in CIPN prevalence and severity across different populations and treatment regimens is highlighted by Hsieh et al. (2023) reporting a lower prevalence of severe neuropathy.

Peripheral neuropathy is highly prevalent among cancer participants at MTRH, which highlights the substantial impact of CIPN in this population. The majority of participants have mild to moderate neuropathy, which suggests that while many people are impacted, severe cases are less common but still noteworthy. These results highlight the urgent need for early intervention, systematic management approaches, and routine screening to address the various degrees of neuropathy severity and lessen its effects on participants' quality of life and adherence to treatment.

5.7 Factors Associated with Peripheral Neuropathy Among Participants On Chemotherapy at Moi Teaching and Referral Hospital

Assessment methods, chemotherapy schedules, and patient demographics could all have an impact on the observed differences between studies. The high rates of neuropathy in this group may be explained by the particular chemotherapy medications used at MTRH, such as paclitaxel, cisplatin, and carboplatin, which are known to have neurotoxic potential. This emphasizes the value of individualized treatment programs and continuing research to comprehend and treat CIPN in a range of patient populations. The research identifies a number of significant variables that are linked to the incidence of chemotherapy-induced peripheral neuropathy (CIPN) in cancer participants. Compared to younger participants (mean age 45.4 years), the majority of participants (mean age 51.6 years) had a statistically significant increased risk of developing neuropathy. This finding is in line with the findings of Burgess et al. (2021), who found that CIPN is typically more prevalent in older adults. Similarly, Lixian et al. (2024) conducted a prospective cohort study on 350 participants with breast cancer and found a strong correlation between paclitaxel-induced CIPN and advancing age, especially in those 45 years of age and above.

Kleckner et al. (2021), yielded conflicting results, indicating that age was not a major contributing factor to the development of CIPN. These disparities might result from variations in the study populations, kinds of chemotherapy administered, or approaches to assessing neuropathy. Gender had no significant factor in determining the risk of developing neuropathy from chemotherapy, as evidenced by the lack of significant correlation ($p=0.950$) between gender and the presence of neuropathy. While Nielsen et al. (2022) reported that females were more likely to have higher neuropathy scores (19% vs. 14%, $p=.008$). The study concluded that there is no significant association between neuropathy and BMI ($p=0.468$) is consistent with findings by Kleckner et al.

(2021).

In line with research by Kleckner et al. (2021), the study found no significant correlation ($p=0.328$) between BMI and neuropathy, suggesting that neuropathy risk is largely unaffected by BMI. However, other research, including that conducted by Lixian et al. (2024), has discovered a possible link between a higher BMI and a higher risk of neuropathy. There was no statistically significant association ($p=0.444$ and $p=0.728$, respectively) between alcohol or smoking and neuropathy. This could be due reduced number of participants who are exposed to this risk factors in this population. This result is also consistent with the findings of Selvy et al.'s research from 2021, which did not find a significant correlation between these lifestyle factors and CIPN. On the other hand, smoking may make neuropathy worse because of its vascular effects, according to Lixian et al. (2024).

Although there was a slight, non-significant trend suggesting more neuropathy in participants with comorbidities, the study did not find a statistically significant correlation ($p=0.212$) between having comorbidities (HIV, diabetes mellitus, and hypertension) and neuropathy. This lack of significance might also be due to the small number of participants with comorbidities. This aligns with Zhang's et al (2021) findings, which indicate that although conditions like diabetes may worsen the clinical symptoms, they do not independently predict the onset of CIPN. . Augusta N. et al (2012) observed trends, but not statistically significant relationships, between diabetes and modifiable variables (hypertension, smoking, or statin use) and severity and incidence of neuropathy.

In this study, no clear relationship was found between peripheral neuropathy and renal function (eGFR), likely because most patients with abnormal GFR were at stage 2 CKD. However, Salat et al (2020) suggests that renal function could be a risk factor for neuropathy, indicating that renal impairment may contribute to the occurrence of chemotherapy-induced peripheral neuropathy (CIPN).

Furthermore, neuropathy was prevalent in all four tumor stages at similar rates. In this study there were 68.2% in stage 1, 70.8% in stage 2, 73.7% in stage 3, and 75.0% in stage 4. This implies that CIPN can affect participants regardless of the course of their cancer and that the type and dosage of chemotherapy have a greater bearing on CIPN prevalence than the tumor's stage.

It's noteworthy that, although some chemotherapy drugs are known for their neurotoxic effects, this study did not find a significant correlation between the use of these drugs and the prevalence of neuropathy. However, neuropathy was observed in 100% of participants treated with bortezomib and vinca alkaloids. Despite the lack of statistical significance due to small sample sizes, this observation underscores the high risk of neuropathy associated with these medications, as previously reported by Selvy et al. (2021).

The prevalence of chemotherapy induced peripheral neuropathy (CIPN) is influenced by the type and dosage of chemotherapy, rather than the stage of cancer progression. Common drugs like Paclitaxel, cisplatin, and carboplatin are linked to high rates of neuropathy at MTRH, emphasizing their neurotoxic potential. The high prevalence and varying severity of PN in cancer participants at MTRH highlight the significant impact of CIPN on this population. The predominance of mild to moderate neuropathy suggests that while severe cases are less common, the overall burden on participants is significant. Therefore, prompt identification and management of neuropathy symptoms

are crucial. A multidisciplinary approach, including pharmacological and non-pharmacological interventions, can help address the various degrees of neuropathy severity. Educating participants about the signs and symptoms of neuropathy and providing psychological and social support can help them manage their condition effectively and improve treatment adherence.

In multivariate analysis, the study reveals that age is a significant factor in the development of peripheral neuropathy (PN) in cancer participants receiving chemotherapy at MTRH. The likelihood of developing PN increases by 2.9% per year of age, with a confidence interval of 1.007 to 1.052. However, the presence of comorbidities like HIV, diabetes mellitus, and hypertension does not significantly correlate with neuropathy. The findings suggest that older participants are at higher risk for PN, but comorbidities do not significantly increase this risk. Therefore, the focus should be on age and chemotherapeutic agents when assessing and managing neuropathy risk.

5.8 Strength and Limitations

5.8.1 Study Strength

This study's cross-sectional design offers several notable strengths that enhance the reliability and applicability of its findings. First, because it was conducted at a single point in time, it effectively minimized issues commonly associated with longitudinal studies, such as loss to follow-up, participant attrition, and missing data, which can compromise data integrity and introduce bias. This approach allowed for a comprehensive snapshot of the prevalence and clinical features of peripheral neuropathy among cancer patients receiving chemotherapy at MTRH. Additionally, the use of the Total Neuropathy Score (TNS), a well-validated and widely accepted tool, strengthened the accuracy and consistency of neuropathy assessment. The TNS

combines clinical examination and patient-reported symptoms, providing a standardized measure of severity that enhances comparability across different studies and settings. Conducting the study at Moi Teaching and Referral Hospital (MTRH), which functions as a major referral center for the western region and the North Rift, further broadens the generalizability of the findings. The diverse patient population served by MTRH, including various socio-economic backgrounds and comorbid conditions, reflects the broader demographic of cancer patients receiving chemotherapy in this region. This setting thus increases the external validity of the results, making them relevant for similar healthcare contexts within Kenya and potentially other sub-Saharan African settings. Overall, the methodological rigor, validated assessment tools, and strategic location of the study contribute significantly to the robustness and applicability of the findings.

5.8.2 Study limitation

Despite these strengths, the study also has certain limitations inherent to its design and scope. Being a cross-sectional study, it provides a snapshot of clinical features of peripheral neuropathy at a single point in time but cannot capture the dynamic nature of the condition. Peripheral neuropathy, especially chemotherapy-induced peripheral neuropathy (CIPN), often fluctuates in severity and progression over time, influenced by factors such as cumulative dose, treatment cycles, and individual patient responses. Consequently, this design does not allow for assessment of the progression, development, or long-term outcomes of neuropathy, which are critical for understanding its full impact and for developing effective management strategies. Furthermore, the study was unable to evaluate the impact of CIPN on patients' quality of life, daily functioning, or mental health, which are essential aspects of the overall burden of the condition. The assessment of symptom severity was also limited, as

symptoms of peripheral neuropathy can fluctuate depending on several factors, including recent chemotherapy doses, timing of assessment relative to treatment cycles, and individual variability. This variability means that a single assessment may not accurately reflect the true severity or the patient's experience over time. Additionally, certain confounding variables may not have been fully accounted for, such as concurrent medications (e.g., other neurotoxic drugs) or pre-existing neurological conditions (e.g., diabetic neuropathy), which could influence the observed associations between chemotherapy and neuropathy. These unmeasured factors may introduce bias or confound the results, limiting the ability to establish definitive causal relationships. Lastly, reliance on patient-reported symptoms and clinical examinations, while valuable, may be subject to recall bias or subjective interpretation, further affecting accuracy. Recognizing these limitations underscores the need for future longitudinal studies that can track neuropathy over time, incorporate quality-of-life assessments, and control for additional confounding factors to deepen our understanding of CIPN and improve patient management.

CHAPTER SIX

6.0 CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

The prevalence of peripheral neuropathy was high (70.1%) among participants receiving chemotherapy at MTRH.

Majority of the participants were noted to have mild symptoms of peripheral neuropathy (49.3%)

Age was the only factor significantly associated with CIPN, with participants above 60 years showing a higher likelihood of developing neuropathy.

6.2 Recommendations

We highly recommend for the introduction of routine screening protocol for peripheral neuropathy among patients receiving chemotherapy at MTRH as this can help mitigate the severity of symptoms and improve patient outcomes.

Individualized plan of management is crucial for older participants, as they are more susceptible to chemotherapy induced peripheral neurotherapy.

Further research is recommended to explore the long-term impact of chemotherapy-induced peripheral neuropathy (CIPN) on patients' quality of life.

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APPENDICES

Appendix I: Informed consent

Study Title: PREVALENCE, SEVERITY AND FACTORS ASSOCIATED WITH PERIPHERAL NEUROPATHY AMONG CANCER PATIENT ON CHEMOTHERAPY AT MOI TEACHING AND REFERRAL HOSPITAL, ELDORET KENYA.

Name of Principal Investigator(s): Dr. Hassan Abdi Mohamed

Name of Sponsor/Funding Agency: Self-funded by the principal investigator

Informed Consent Form for:

Adult participants on chemotherapy seeking care at Chandaria Cancer and chronic disease centre.

This Informed Consent Form has two parts:

- Part I: Information Sheet [to share information about the study with you]
- Part II: Certificate of Consent [for signatures if you choose to participate]

PART I: INFORMATION SHEET

Introduction: You are being asked to take part in a research study. This information is provided to tell you about the study. Please read this form carefully. You will be given a chance to ask questions.

Taking part in this research study is voluntary. Decline to participate in the study will not affect your rights to health care or any other services. Your treatment/payment or enrollment in any health plans or eligibility for benefits will not be affected if you decide not to take part. You are also free to withdraw from this study at any time. If after data collection you choose to quit, you can request that information provided by you be destroyed under supervision. This would be before data is de-identified and aggregated. You will be notified if new information becomes available about the risks or benefits of this research. You will receive a copy of this form after it is signed

Purpose of the study: To determine the prevalence, severity and factors associated with peripheral neuropathy among participants on chemotherapy at Moi Teaching and referral hospital.

Study site: The study will be conducted at MTRH, Oncology Outpatient Clinic and in participants.

Study population: The study will include adult participants on chemotherapy seeking care at Chandaria Cancer and chronic disease centre.

Study procedures: The principal investigator will seek approval from IREC which will assess ethical aspects of the study. Permission to conduct the study will also be sought from Moi Teaching and Referral Hospital. This will allow access to participants on chemotherapy treatment at the facility. The PI with the help of two research assistants will approach the Chandaria cancer and chronic disease center where participants will be sampled based on the inclusion criteria developed. This will be done at the triage to ensure that its easier access to participants. Every day the PI will begin data collection from a random starting point and select every fourth patient who meet the inclusion criteria. An informed consent will be administered and only those who meet the inclusion criteria will be recruited into the study. Prior to consent administration, the PI and the research assistants will introduce themselves, the purpose of the study, possible benefits and any risks involved. Participation in the study will be voluntary and any patient who refuse to participate will be excluded and the next patient who meet the inclusion criteria will be considered.

After consenting the PI will administer a structured questionnaire seeking to understand on important information regarding disease development and management. The structured questionnaire will include information on patient

demographic characteristics, clinical characteristics, disease characteristics and presence of peripheral neuropathy. The PI will lead the participants into a secluded area to reduce any disturbance as well as enhancing the level of concentration to attain better feedback. The research assistants will assist in the data collection process to ensure smooth and accurate process. The Total Neuropathy Score will also be administered to help in identification of presence of peripheral neuropathy. All participants will be informed their PN Score at the end

The presence of neuropathy will be graded accordingly. Chart review will be performed to extract baseline laboratory blood values such as haemoglobin, albumin, and creatinine levels. For participants who do not have the required laboratory tests, we shall obtain blood samples to run the tests. Demographic and clinical parameters will be documented include age, sex, type and stage of cancer, cumulative dose, concurrent radiotherapy, hypoalbuminemia (serum albumin levels less than 35.0 g/L), anemia (hemoglobin levels less than 12.0 g/dL in women and less than 13.0 g/dL in men), chronic renal failure (glomerular filtration rate less than 60.0 mL/min/1.73 m²), habit of alcohol consumption, and smoking history.

If you agree you will do the following: You will be required to answer some structured questions in form of questionnaires that will ask personal and sometimes emotional questions that you will be required to answer, should you wish not to answer some of the questions you can skip a particular section and you may or may not provide a reason. I will be asking you questions on demographics and assess your clinical and laboratory information. I will do this by checking your medical file. In addition, I might need to collect blood samples from a visible vein on your arm, which will be analysed at the lab to find out your Creatinine levels, liver function and HbA1C. A sterile 10cc capacity syringe and an 18gauge needle will be used to draw sample from a cleaned and

sterilized anterior cubital vein on your body. A tourniquet will be used to facilitate the collection of blood samples, and this may be associated with some feeling of pain. You may also experience some pain when your skin is punctured and blood samples are drawn; which we do not expect to last for long. Approximately 4 cc of whole blood will be drawn.

Benefits: This is a research project and the findings may be used by the MTRH management, Government's policy makers and health providers to design appropriate policies and plans to provide better health services for CIPN management. This will also help quantify the burden of CIPN and integrate favorable approaches.

Risks/Discomforts: I am aware of the fact that some of the questions regarding research participation are not convenient to you. Everything you will tell me will be kept confidential. Under no circumstance will we link your name to the data during analysis and dissemination of the study findings.

Payments and Reimbursements: There is no payment or reimbursement for participating in the study

Confidentiality: All reasonable efforts will be made to keep your protected information (private and confidential). Using or sharing ("disclosure") of such information will follow National privacy guidelines. By signing the consent document for this study, you are giving permission ("authorization") for the use and disclosure of your study information. We may need to share your protected information with the community advisory board, MTRH/MU-IREC, NACOSTI or the healthcare team. We will retain your research records for at least six years after the study is completed. At that time, the research information is destroyed [Inform the participant how the records will be destroyed]. If you decide to withdraw your permission for use of your personal data, contact the [PI] in writing and let them know your decision.

At that time, we will stop further collection of any information about you. However, the health information collected before this withdrawal may continue to be used for the purposes of reporting and research quality.

Compensation for injury: There will be no expected injuries during the study

PART II: CONSENT OF PATICIPANT:

I have read or have had someone read to me the description of the research study. The investigator or his/her representative has explained the study to me and has answered all the questions I have at this time. I have been told of the potential risks, discomfort, and possible benefits (if any) of the study. I freely volunteer to take part in this study.

[This section must be written in the first person. If the participant is illiterate, or for some reason is unable to write, they should provide a thumbprint and a competent witness must be engaged during the consent process]

_____	_____	_____
Name of Participant	Signature of participant/Thumbprint	Date & Time

_____	_____	_____
Name of Witness [Optional]	Signature of Witness	Date & Time

_____	_____	_____
Name of the person obtaining consent	Signature of person obtaining consent	Date & Time

_____	_____	_____
Printed name of the investigator	Signature of Investigator	Date

Contacts for questions about the study

Questions about the study: I Contact Information

[Dr. **Hassan Abdi Mohamed**, 0722 828 263, hassanabdimohamed607@gmail.com]

Questions about your rights as a participant: You may contact the Institutional Ethics and Research Committee (MTRH//MU-IREC) 0787723677 or email irec@mtrh.go.ke or irecoffice@gmail.com. The MTRH//MU-IREC is a group of people that review studies for safety and to protect the rights of participants.

Kiambatisho II: Ridhaa ya taarifa

Kichwa cha Utafiti: MAAMBUKIZI, UKALI NA MAMBO YANAYOHUSIANA NA NEUROPATHY YA PEMBENI KATI YA MGONJWA WA SARATANI KWENYE CHEMOTHERAPY KATIKA HOSPITALI YA MAFUNDISHO NA RUFAA YA MOI, ELDORET KENYA.

Jina la Mpelelezi Mkuu(s): Dkt. Hassan Abdi Mohamed Mpelelezi Mwenza(s): Dkt. Evangeline Wawira

Jina la Shirika: CHUO KIKUU CHA MOI Anwani: PO BOX 4606 - 30100 ELDORET

Jina la Mdhamini / Wakala wa Ufadhili: Kujifadhili na mpelelezi mkuu Fomu ya Idhini ya Taarifa kwa:

Wagonjwa watu wazima kwenye chemotherapy wanaotafuta huduma katika Saratani ya Chandaria na kituo cha magonjwa sugu.

Fomu hii ya Ridhaa ya Taarifa ina sehemu mbili:

Sehemu ya I: Karatasi ya habari [kushiriki habari kuhusu utafiti na wewe]

Sehemu ya II: Cheti cha Idhini [kwa saina ikiwa utachagua kushiriki]

SEHEMU YA I: KARATASI YA HABARI

Utangulizi: Unaombwa kushiriki katika utafiti wa utafiti. Taarifa hii hutolewa ili kukueleza kuhusu utafiti. Tafadhali soma fomu hii kwa makini. Utapewa nafasi ya kuuliza maswali. Kushiriki katika utafiti huu wa utafiti ni hiari. Kukataa kushiriki katika utafiti hakutaathiri haki zako za huduma za afya au huduma nyingine yoyote. Matibabu yako / malipo au uandikishaji katika mipango yoyote ya afya au ustahiki wa faida hautaathirika ikiwa utaamua kutoshiriki. Pia uko huru kujiondoa katika utafiti huu wakati wowote. Ikiwa baada ya ukusanyaji wa data unachagua kuacha, unaweza kuomba habari hiyo iliyotolewa na wewe kuharibiwa chini ya uangalizi. Hii itakuwa kabla ya data kutambuliwa na kujumuishwa. Utaarifiwa ikiwa habari mpya itapatikana kuhusu hatari au faida za utafiti huu. Utapokea nakala ya fomu hii baada ya kusainiwa

Madhumuni ya utafiti: Ili kubaini maambukizi, ukali na mambo yanayohusiana na neuropathy ya pembeni kati ya wagonjwa kwenye chemotherapy katika Moi Teaching na hospitali ya rufaa.

Sehemu ya utafiti: Utafiti utafanywa katika MTRH, Kliniki ya Wagonjwa wa Nje ya Oncology na wagonjwa.

Idadi ya utafiti: Utafiti huu utajumuisha wagonjwa watu wazima walio kwenye tiba ya chemotherapy wanaotafuta huduma katika kituo cha saratani ya Chandaria na kituo cha magonjwa sugu.

Taratibu za utafiti: Mchunguzi mkuu atatafuta idhini kutoka IREC ambayo itatathmini masuala ya maadili ya utafiti. Ruhusa ya kufanya utafiti huo pia itatafutwa kutoka Hospitali ya Ualimu na Rufaa ya Moi. Hii itawezesha upatikanaji wa wagonjwa kwenye matibabu ya chemotherapy katika kituo hicho. PI kwa msaada wa wasaidizi wawili wa utafiti watakaribia saratani ya Chandaria na kituo cha magonjwa sugu ambapo wagonjwa watachukuliwa sampuli kulingana na vigezo vya ujumuishaji vilivyotengenezwa. Hii itafanyika katika triage ili kuhakikisha kuwa upatikanaji wake rahisi kwa wagonjwa. Kila siku PI itaanza ukusanyaji wa data kutoka hatua ya kuanzia bila mpangilio na kuchagua kila mgonjwa wa nne ambaye anakidhi vigezo vya kuingizwa. Idhini ya habari itasimamiwa na wale tu ambao wanakidhi vigezo vya kuingizwa wataajiriwa katika utafiti. Kabla ya utawala wa idhini, PI na wasaidizi wa utafiti watajitambulisha, madhumuni ya utafiti, faida zinazowezekana na hatari yoyote inayohusika. Ushiriki katika utafiti huo utakuwa wa hiari na mgonjwa yeyote atakayekataa kushiriki atatengwa na mgonjwa atakayekidhi vigezo vya ujumuishaji atazingatiwa. Baada ya kukubali PI itasimamia dodoso lililoundwa linalotaka kuelewa juu ya habari muhimu kuhusu maendeleo na usimamizi wa magonjwa. Dodoso lililoundwa litajumuisha habari juu ya sifa za idadi ya wagonjwa, sifa za kliniki, sifa za ugonjwa na uwepo wa neuropathy ya pembeni. PI itaongoza washiriki katika eneo lililotengwa ili kupunguza usumbufu wowote pamoja na kuimarisha kiwango cha mkusanyiko ili kupata maoni bora. Wasaidizi wa utafiti watasaidia katika mchakato wa ukusanyaji wa data ili kuhakikisha mchakato laini na sahihi. Alama ya Jumla ya Neuropathy pia itasimamiwa kusaaidia katika utambuzi wa uwepo wa neuropathy ya pembeni.

Uwepo wa ugonjwa wa neuropathy utawekwa alama ipasavyo. Uhakiki wa chati utafanywa ili kutoa viwango vya msingi vya damu vya maabara kama vile hemoglobini, albin na viwango vya kreatini. Kwa wagonjwa ambao hawana vipimo vinavyohitajika vya kimaabara, tutapata sampuli za damu ili kufanya vipimo. Vigezo vya demografia na kiafya vitarekodiwa ni pamoja na umri, jinsia, aina na hatua ya saratani, dozi ya ziada, tiba ya mionzi kwa wakati mmoja, hypoalbuminemia (viwango vya albin katika seramu ya damu. chini ya 35.0 g/L), anemia (kiwango cha hemoglobin chini ya 12.0 g/dL kwa wanawake na chini ya 13.0 g/dL kwa wanaume), kushindwa kwa figo sugu (kiwango cha kuchujwa kwa glomerular chini ya 60.0 mL/min/1.73 m²), tabia historia ya unywaji pombe na uvutaji sigara.

Ukikubali utafanya yafuatayo:

Utatakiwa kujibu baadhi ya maswali yaliyoundwa kwa njia ya dodoso ambazo zitaauliza maswali binafsi na wakati mwingine ya kihisia ambayo utatakiwa kujibu, ikiwa unataka kutojibu baadhi ya maswali ambayo unaweza kuruka sehemu fulani na unaweza au usitoe sababu. Ili kuwezesha kipimo cha maabara kuweza kutendeka, Tunaweza hitaji damu itatolewa kotoka kwa mshipa wa damu ambao unaonekana kwa rahisi. Mara nyingi mshipa wa damu ambao hutumika kutolea damu ni mshipa unaopatikana sehemu ya ungo wa kikukuu. Sindano yenye ukubwa wa kipimo cha 18, na yenye uwezo wa kubeba damu kiwango cha 4mls ndio itakayo tumika wakati wa kutoa damu kwa ajili ya vipimo vya maabara. Nina tarajia yakuwa huenda uka hisi maumivu kiwango ndogo, ambayo sidhanii itakaa kwa muda mrefu, pindi damu itakapotolewa kwenye mshipa wa damu. Kifaa cha kusahilisha utowaji wa damu pia itatumika, na hii huenda itakufanya kuhisi mbano kwenye sehemu ya mwili ambayo kifaa hichi kilitumika. Huenda ukahisi maumivu pindi kifaa hichi kitatumika, lakini natumai maumivu haitaendelea kwa muda mrefu.

Faida kujiuhisha na huu utafiti: Huu ni mradi wa utafiti na matokeo yanaweza kutumiwa na usimamizi wa MTRH, watunga sera wa Serikali na watoa huduma za afya kubuni sera na mipango sahihi ya kutoa huduma bora za afya kwa usimamizi wa CICN. Hii pia itasaidia kupima mzigo wa CIPN na kuunganisha njia nzuri.

Hatari / Usumbufu: Ninafahamu ukweli kwamba baadhi ya maswali kuhusu ushiriki wa utafiti sio rahisi kwako. Kila kitu utakachoniambia kitawekwa siri. Katika hali yoyote hatutaunganisha jina lako na data wakati wa uchambuzi na usambazaji wa matokeo ya utafiti.

Malipo na Malipo: Hakuna malipo au malipo ya kushiriki katika utafiti

Usiri: Jitihada zote za busara zitafanywa kuweka taarifa zako zilizolindwa (binafsi na siri). Kutumia au kushiriki ("disclosure") ya taarifa hizo itafuata miongozo ya faragha ya Taifa. Kwa kusaini hati ya idhini ya utafiti huu, unatoa ruhusa ("idhini") kwa matumizi na ufichuzi wa maelezo yako ya utafiti. Tunaweza kuhitaji kushiriki habari zako zilizolindwa na bodi ya ushauri wa jamii, MTRH / / MU-IREC, NACOSTI au timu ya huduma ya afya. Tutahifadhi rekodi zako za utafiti kwa angalau miaka sita baada ya utafiti kukamilika. Wakati huo, taarifa za utafiti huharibiwa [Mjulisha mshiriki jinsi kumbukumbu zitakavyoharibiwa]. Ikiwa unaamua kuondoa ruhusa yako ya matumizi ya data yako ya kibinafsi, wasiliana na [PI] kwa maandishi na uwajulishe uamuzi wako. Wakati huo, tutaacha ukusanyaji zaidi wa habari yoyote kuhusu wewe. Hata hivyo, taarifa za afya zilizokusanywa kabla ya uondoaji huu zinaweza kuendelea kutumika kwa madhumuni ya kuripoti na ubora wa utafiti.

Fidia ya majeraha: Iwapo kutatokea jeraha litakalotokana na kushiriki katika utafiti huu, gharama za matibabu zitafunikwa kwa matibabu ya jeraha hilo.

SEHEMU YA II: IDHINI YA MHUSIKA:

Nimesoma au nimepata mtu aliyenisomea maelezo ya utafiti wa utafiti. Mpelelezi au mwakilishi wake amenieleza utafiti huo na amejibu maswali yote niliyonayo kwa wakati huo. Nimeambiwa juu ya hatari zinazoweza kutokea, usumbufu, na faida zinazowezezekana (ikiwa zipo) za utafiti. Ninajitolea kwa uhuru kushiriki katika utafiti huu.

[Sehemu hii lazima iandikwe kwa mtu wa kwanza. Ikiwa mshiriki hajui kusoma na kuandika, au kwa sababu fulani hawezi kuandika, anapaswa kutoa kidole gumba na shahidi mwenye uwezo lazima ashiriki wakati wa mchakato wa idhini]

Saini ya Mshiriki

Tarehe

Saini ya Shahidi

Tarehe

Saini ya Mtafiti

Tarehe

Mawasiliano kwa maswali kuhusu utafiti Maswali kuhusu utafiti:

Ninawasiliana na habari [Dkt. Hassan Abdi Mohamed, 0722 828 263, hassanabdimohamed607@gmail.com]

Maswali kuhusu haki zako kama mshiriki:

Unaweza kuwasiliana na Kamati ya Maadili na Utafiti wa Taasisi (MTRH//MU-IREC) 0787723677 au barua pepe irec@mtrh.go.ke au irecoffice@gmail.com. MTRH//MU-IREC ni kundi la watu wanaokagua masomo kwa ajili ya usalama na kulinda haki za washiriki.

Appendix III: Study Questionnaire

Section A: Patient characteristics

1. What is your age? (Years).....
2. What is your gender? Male [☐]
Female [☐]
3. What is your height?.....
4. What is your weight?.....
5. What is your body mass index?
6. Do you drink alcohol? Yes [☐] No [☐]
7. If Yes, do you drink ≥ 5 glasses (men) or ≥ 4 glasses (women) in a single occasion, usually
within 2 hours? Yes [☐] No [☐]
8. Do you or have you ever smoked cigarettes? Yes [☐] No [☐]
9. If Yes, Did you smoke in the last month? Yes [☐] No [☐]
10. How many cigarettes do you smoke in a week?.....
11. Do you have any underlying comorbidity? Yes [☐] No [☐]
12. If yes, which of the following
13. Diabetes mellitus Yes [☐] No [☐]
14. Hypertension Yes [☐] No [☐]
15. HIV Yes [☐] No [☐]

Laboratory Results

Hemoglobin (g/dL):	Sodium Levels (mmol/L):
Potassium Levels (mmol/L):	Creatinine (μ mol/mL):
eGFR (ml/min):	Total protein (g/L):
Albumin (g/L):	Aspartate Transaminase (U/L):
Alanine Transaminase (U/L):	Alkaline Phosphatase (U/L):
Bilirubin (mg/L):	Gamma Glutamyltransferase (U/L):

Tumor Characteristics

Tumor Site:	
Tumor Type:	
Tumor Stage:	☐ 1 ☐ 2 ☐ 3 ☐ 4

Chemotherapy Details:

Type of Drug Given (check all that applies):

☐ Cisplatin	☐ Paclitaxel	☐ Vincristine
☐ Oxaliplatin	☐ Docetaxel	☐ Vinblastine
☐ Carboplatin	☐ Thalidomide	☐ Bortezomib

Drug :- Details:

DRUG NAME

Dose (mg/m²per session:

Frequency drug given:

Cumulative dose(mg/m²)

Appendix IV: Total neuropath score assessment**TNS Supplementary Instruction Manual SENSORY SYMPTOMS:**

READ THE FOLLOWING TO THE SUBJECT: I want to ask about your sensory symptoms. I want to concentrate on any change in the past week and any change that is present on multiple occasions or for days at a time. I do not want to ask about sensory symptoms that are longstanding or due to a known disease.

Have you had tingling in your limbs over the past week? Yes or No? If no, stop.

If yes, is it on multiple occasions or for days at a time? If no, stop.

If yes, is it in your lower limbs?

If no, continue to upper limbs questions.

If yes, is it on both the right and left sides or just one side?

Is it in your toes, and if so, how high does it go? SCORE form.

If yes, is it in your upper limbs?

If no, stop.

If yes, is it on both the right and left sides or just one side?

Is it in your fingers, and if so, how high does it go? SCORE form.

Are there other reasons for these symptoms? This might include pain due to osteoarthritis, pain due to an injury, pain due to another medical condition, etc.

If the subject has symptoms that are not distal predominant or occur in other distributions or proximally, do not score, but capture as Sensory AE.

MOTOR SYMPTOMS:

READ THE FOLLOWING TO THE SUBJECT: I want to ask about your strength and how well you function. I want to concentrate on any change in the past week and any change that is on multiple occasions or for days at a time. I do not want to ask about difficulties that are longstanding or due to known disease such as osteoarthritis pain, low back pain, or prior injuries.

Do you have any new or worsening symptoms in the feet such as difficulty walking on tiptoes or heels, difficulty clearing your foot over a curb or a step, or operating pedals in the car?

If no, stop.

If yes, are these in the right foot, the left foot, or both feet? If yes, are these new in the last week and have they occurred on multiple occasions or for days at a time? If yes, for each foot, rate the level of difficulty as slight, moderate, requiring help or assistive device, or unable to do at all.

Do you have any new or worsening symptoms in the legs such as difficulty climbing steps or difficulty standing from a sitting position?

If no, stop.

If yes, are these in the right leg, left leg or both legs? If yes, are these new in the last week and have they occurred on multiple occasions or for days at a time? If yes, for each leg, rate the level of difficulty as slight, moderate, requiring help or assistive device, or unable to do at all.

Do you have any new or worsening symptoms in the hands such as difficulty with buttoning, writing, tying shoe laces, opening jars or turning a key in a lock?

If no, stop.

If yes, are these in the right hand, left hand or both hands? If yes, are these new in the last week and have they occurred on multiple occasions or for days at a time? If yes, for each hand, rate the level of difficulty as slight, moderate, requiring help or assistive device, or unable to do at all.

Do you have any new or worsening symptoms in the arms such as difficulty combing hair, using a hair dryer or reaching to a high shelf?

If no, stop.

If yes, all are these in the right arm, left arm or both arms? If yes, are these new in the last week and have they occurred on multiple occasions or for days at a time? If yes, for each arm, rate the level of difficulty as slight, moderate, requiring help or assistive device, or unable to do at all.

AUTONOMIC SYMPTOMS:

READ THE FOLLOWING TO THE SUBJECT: I want to ask about the following symptoms. I want to concentrate on any change in the past week and on any change that has occurred on multiple occasions or for days at a time. I do not want to ask about symptoms that are longstanding or due to another medical condition.

1. Do you have lightheadedness or dizziness when getting up from a lying position? If yes, is this new in the last week and has this occurred on multiple occasions or for days at a time? If yes, SCORE.
2. Do you have difficulty eating a meal because you get full too quickly or get bloated? If yes, is this new in the last week and has this occurred on multiple occasions or for days at a time? If yes, SCORE.

3. Do you have diarrhea that awakens you at night? If yes, is this new in the last week and has this occurred on multiple occasions or for days at a time? If yes, SCORE.
4. Do you have constipation that cannot be attributed to your medications? If yes, is this new in the last week and has this occurred on multiple occasions or for days at a time? If yes, SCORE.
5. Do you have problems controlling your bladder such as needing to go urgently or wetting yourself? If yes, is this new in the last week and has this occurred on multiple occasions or for days at a time? If yes, SCORE.
6. For men only, do you have difficulty with erections that cannot be due to another illness or medication? If yes, is this new in the last week and has this occurred on multiple occasions or for days at a time? If yes, SCORE.

PIN SENSIBILITY

INSTRUCTIONS TO TESTER: Prior to testing, please gain familiarity with the Neuropen (see Manual). This instrument has a sharp point on one end and a cap on the other end. You will show the subject how the testing is done by testing a site with the subject's eyes open. This is most easily done by testing on the face.

READ THE FOLLOWING TO THE SUBJECT: I am going to test how well you can tell a sharp point from a dull point. This is similar to tests a doctor would do in the office. We will start with a practice test on the face so you can learn about the test and then we will test your legs and arms. We will do the practice test with your eyes open so that you can see the difference between the sharp and the dull sensation. During the actual test, your eyes will be closed, and I will touch you 10 times. Each time I touch

you, I will ask you whether the touch is sharp or dull. We will start by testing the face with the eyes open.

INSTRUCTIONS TO TESTER: Test the sharp side three times and then test the dull side three times. If the subject gets those correct and seems to understand the test, ask the subject to close their eyes. Test 6 more times: three sharp and three dull in random order. If the subject gets those correct, begin the real testing. If the subject does not get this correct, repeat until they do the test correctly.

READ THE FOLLOWING TO THE SUBJECT: We are now going to begin the actual testing. We are going to start by testing the toe. During testing, I will touch you at a site with one of the stimuli and ask you whether the touch feels sharp or dull. I will present 10 stimuli with a random order of five sharp and five dull. You must get 8 correct to pass. If you do not get 8 correct, we will test another site. Even if you do not feel the touch, please say sharp or dull.

INSTRUCTIONS TO TESTER: Hold the Neuropen perpendicular to the site of stimulation and press until the gauge reaches the 40 g marker for the sharp stimuli. For the dull stimuli, you should also press until the gauge reaches the 40 g marker. Hold each stimulus for 1 to 2 seconds. If the subject correctly identifies eight or more of the stimuli of 10, check the normal box and stop testing that limb. If the subject makes more than two errors in the 10 presentations, check the abnormal box and test the next most proximal location.

Each side is tested separately.

Once you have finished with the lower limbs, repeat starting at the fingertips testing each side. Locations:

great toe: top surface of the great toe immediately proximal to the nail bed
 ankle: top surface of the ankle, midway between the lateral and medial malleolus

knee: overlying the medial epicondyle of the femur

mid-thigh: anterior surface of quadriceps muscle midway between the knee and hip

Finger: top surface of the index finger immediately proximal to the nail bed

Wrist: top surface of the wrist at the midline, approximately 1 cm proximal to the wrist crease
 Elbow: overlying the medial epicondyle

Mid-upper arm: anterior surface over biceps muscle

VIBRATION TESTING

INSTRUCTIONS TO TESTER: Prior to testing, please gain familiarity with the Rydel-Seiffer graduated tuning fork. This device will measure vibration sensation and give a number. You will show the subject how the testing is done by testing a site with the subject's eyes open. This is most easily done by testing on the head.

The test is started by strongly pinching the top of the tuning fork using two fingers. Never bang the tuning fork against a hard object. Place the metal bulb at the base of the stem of the tuning fork against the skin at the test site and hold the fork with moderate pressure perpendicular to the test surface. Throughout testing, maintain an unobstructed view of the triangles on each prong. As the vibration intensity diminishes, an optical illusion will cause the appearance of two merging triangles on each prong, with the point of their intersection gradually ascending. Record the vibration intensity on the 0-8 scale at the time the subject reports that he/she can no

longer feel the vibration, and enter the intensity to the nearest 0.5 units. If the subject reports that he/she does not feel the vibration at the initial contact, enter a score of 0.

READ THE FOLLOWING TO THE SUBJECT: I am going to test how well you can feel vibration. This is similar to tests a doctor would do in the office. We will start with a practice test on your head, so you can learn about the test, and then we will test your legs and arms. We will do the practice test with your eyes open. During the actual test, your eyes will be closed. Each time I put the tuning fork on you, I will ask you whether you feel it at all and then if you feel it, when you stop feeling the vibration. I know you will still feel the tuning fork itself, a pressure sensation, but I am interested in the vibration feeling. We will start by testing on your head with the eyes open.

INSTRUCTIONS TO TESTER: Start the test as above by placing the vibrating tuning fork on the subject's head. Ask if they can feel the vibration and when it ends. Almost all subjects should score 8. If the subject scores 7 or above and seems to understand the test, ask the subject to close their eyes. Test again. If the subject scores 7 or above, you can begin the real testing. If the subject does not get this correct, repeat until they do the test correctly.

READ THE FOLLOWING TO THE SUBJECT: We are now going to begin the actual testing. We are going to start by testing the toe. During testing, the vibrating tuning fork will be placed on you like we did with your head. Please let me know if you feel the vibration and then when it ends.

INSTRUCTIONS TO TESTER: Start the test as above by placing the vibrating tuning fork on the subject's toe. Ask if they can feel the vibration and when it ends. Record the vibration intensity on the 0-8 scale at the time the subject reports that he/she can

no longer feel the vibration and enter the intensity to the nearest 0.5 units. If the subject reports that he/she does not feel the vibration at the initial contact, enter a score of 0.

If the subject scores normally (see normal values below), do stop testing in that limb and go to the opposite side. If the subject scores in the abnormal range, move proximally.

Locations:

Great Toe: top surface of great toe, immediately proximal to the nail bed Ankle: top surface of the medial malleolus

Knee: overlying the medial epicondyle of the femur Hip: overlying the iliac crest

Finger: top surface of index finger, immediately proximal to the nail bed Wrist: surface of the ulnar styloid

Elbow: overlying the medial epicondyle Shoulder: overlying the acromion Below is a chart showing on how to score the with symptoms and signs of PN:

TNSc					
	0	1	2	3	4
Sensory symptoms	None	Limited to fingers or toes	Extend to ankle or wrist	Extend to knee or elbow	Above knees/elbows
Motor symptoms	None	Slight difficulty	Moderate difficulty	Require help/assistance	Disabled
Autonomic symptoms (n)	0	1	2	3	4 or 5
Pin sensation	Normal	Reduced in fingers or toes	Reduced up to wrist/ankle	Reduced up to elbow/knee	Reduced above elbow/knee
Vibration sensibility	Normal	Reduced in fingers or toes	Reduced up to wrist/ankle	Reduced up to elbow/knee	Reduced above elbow/knee
Strength	Normal	Mild weakness	Moderate weakness	Severe weakness	Paralysis
Tendon reflexes	Normal	Ankle reflex (AR) reduced	AR absent	AR absent and others reduced	All reflexes absent

Neuropathy profiling

Is there Neuropathy?	O Yes O No			
If Yes, What is the grade?	O 1	O 2	O 3	O 4
Grade 1 (TNS Score 2 – 5)	Grade 2 (TNS Score 6 – 9)			
Grade 3 (TNS Score 10 – 14)	Grade 4 (TNS Score >14)			

Appendix VI: Budget

Number	Item	Expense
1	Stationary	20,000
2	Research assistants (2)	30,000
3	Biostatistician	40,000
4.	Lab tests	120,000
5	Miscellaneous (10% of total)	21,000
	Grand Total	231,000

Appendix V: Hospital Approval (MTRH)



MOI TEACHING AND REFERRAL HOSPITAL

Telephone: (+254)-0532033471/2/3/4
 Fax: 0532061749
 Email: ceo@mtrh.go.ke/ceosoffice@mtrh.go.ke

NANDI ROAD
 P.O. BOX 3-30100
 ELDORET, KENYA

Ref: ELD/MTRH/R&P/10/2/V.2/2010

10th July, 2023

Dr. Hassan Abdi Mohamed,
 Moi University,
 School of Medicine,
 P.O. Box 4606-30100,
 ELDORET-KENYA.

PREVALENCE, SEVERITY AND FACTORS ASSOCIATED WITH PERIPHERAL NEUROPATHY AMONG CANCER PATIENTS ON CHEMOTHERAPY AT MOI TEACHING AND REFERRAL HOSPITAL, ELDORET KENYA

You have been authorised to conduct research within the jurisdiction of Moi Teaching and Referral Hospital (MTRH) and its satellites sites. You are required to strictly adhere to the regulations stated below in order to safeguard the safety and well-being of staff, patients and study participants seen at MTRH.

- 1 The study shall be under Moi Teaching and Referral Hospital regulation.
- 2 A copy of MTRH/MU-IREC approval shall be a prerequisite to conducting the study.
- 3 Studies intending to export human bio-specimens must provide a permit from MOH at the recommendation of NACOSTI for each shipment.
- 4 No data collection will be allowed without an approved consent form(s) to participants unless waiver of written consent has been granted by MTRH/MU-IREC.
- 5 Take note that data collected must be treated with due confidentiality and anonymity.

The continued permission to conduct research shall only be sustained subject to fulfilling all the requirements stated above.

The approval period is 10th July, 2023 – 9th July, 2024.

one 10/07/2023
 DR. WILSON K. ARUASA, MBS, EBS
 CHIEF EXECUTIVE OFFICER

c.c. - Senior Director, Clinical Services
 - Director, Nursing Services
 - HOD, HRISM



All correspondences should be addressed to the Chief Executive Officer

Visit our Website: www.mtrh.go.ke

TO BE A GLOBAL LEADER IN THE PROVISION OF EXCEPTIONAL MULTI-SPECIALTY HEALTH CARE, TRAINING AND RESEARCH

Appendix VI: IREC Approval



MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471/2/3

Reference: IREC/506/2023

Approval Number: 0004457

Dr. Hassan Abdi Mohamed,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.



MOI UNIVERSITY
COLLEGE OF HEALTH SCIENCES
P.O. BOX 4606
ELDORET
Tel: 33471/2/3
27th June, 2023

Dear Dr. Mohamed,

PREVALENCE, SEVERITY AND FACTORS ASSOCIATED WITH PERIPHERAL NEUROPATHY AMONG CANCER PATIENTS ON CHEMOTHERAPY AT MOI TEACHING AND REFERRAL HOSPITAL, ELDORET KENYA

This is to inform you that **MTRH/MU-IREC** has reviewed and approved the above referenced research proposal. Your application approval number is **FAN: 0004457**. The approval period is **27th June, 2023- 26th June, 2024**. This approval is subject to compliance with the following requirements;

- Only approved documents including (informed consents, study instruments, Material Transfer Agreements (MTA) will be used.
- All changes including (amendments, deviations, and violations) are submitted for review and approval by **MTRH/MU-IREC**.
- Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to **MTRH/MU-IREC** within 72 hours of notification.
- Any changes, anticipated or otherwise that may increase the risks or affected safety or welfare of study participants and others or affect the integrity of the research must be reported to **MTRH/MU-IREC** within 72 hours.
- Clearance for export of biological specimens must be obtained from **MOH at the recommendation of NACOSTI** for each batch of shipment.
- Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. Attach a comprehensive progress report to support the renewal.
- Submission of an executive summary report within 90 days upon completion of the study to **MTRH/ MU-IREC**.

Prior to commencing your study; you will be required to obtain a research license from the National Commission for Science, Technology and Innovation (NACOSTI) <https://oris.nacosti.go.ke> and other relevant clearances from study sites including a written approval from the CEO-MTRH which is mandatory for studies to be undertaken within the jurisdiction of Moi Teaching & Referral Hospital (MTRH) and its satellite sites.

Sincerely,

PROF. E. WERE
CHAIRMAN

INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc	CEO	-	MTRH	Dean	-	SOP	Dean	-	SOM
	Principal	-	CHS	Dean	-	SON	Dean	-	SOD

