# Prevalence of Chemo-induced Nausea and Vomiting, and Its impact on Patients' Quality of Life at the Oncology Unit of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia


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This is to certify that the Thesis prepared by Dawit Negusu, entitled: Prevalence of Chemo-induced Nausea and Vomiting, and Its impact on patients' quality of Life after Highly or Moderately Emetogenic Chemotherapy at the Oncology unit of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia and submitted in partial fulfillment of the requirements for the degree of master of pharmacy in pharmacy practice complies with the regulations of the University and meets the accepted standards with respect to originality and quality.

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## Abstract

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Nausea and vomiting remain among the most distressing side effects of treatment with chemotherapy. Chemotherapy induced emesis (CIE) can impair quality of life (QOL) and poor control of emesis can interrupt or force withdrawal from critical chemotherapy. The prevalence of chemo-induced nausea and vomiting (CINV), and its impact on patients' QOL were not assessed in Ethiopia.The objective of this study was to assess the prevalence of CINV, and its impact on patients' QOL after highly or moderately emetogenic chemotherapy at the oncology unit of Tikur Anbessa Specialized Hospital (TASH).A descriptive prospective cross sectional study involving interview and case note review were conducted among patients evaluated and treated at oncology unit of TASH. The incidence of CINV and its impact on the patients' daily life were evaluated using the self-assessment tools. Patients who agreed to participate received a diary covering the day of chemotherapy administration (day 1) and the following 4 days (day 2 through 5). Patients were instructed to use the diary every day to record each emetic episode and to provide daily nausea assessments using a 100-mm visual analog scale (VAS) to rate the severity of nausea experienced during the preceding 24 h. Bi variate and Multivariate logistic regression was used to identify determinants of CINV. Independent t- test was used for comparison of group means between highly emetogenic chemotherapy (HEC) and moderately emetogenic chemotherapy (MEC). Differences in the proportion of patients that reported no impact on daily life (NIDL) between MEC and HEC treated patients were analyzed using $X^2$ tests (Fisher's exact test). A total of 220 patients were assessable (74 HEC patients, 146 MEC patients). Emesis was reported by 64.1% of patients (37.3 % acute, 50 % delayed) and nausea by 76.8 % (50.5 % acute, 65.5 % delayed). HEC patients reported significantly lower mean functional living index (FLIE) total score than MEC patients (89.7 *v* 102.4 respectively; $P < .001$). Among all patients, the nausea score was significantly lower than the vomiting score (46.5 and 51.6, respectively; $p < .001$).The prevalence of CINV at oncology unit of TASH was found to be high and it adversely affects patients' QoL despite antiemetic therapy even after treatment with only moderately emetogenic chemotherapy regimens. On the basis of the FLIE results in this study, nausea had a stronger negative impact on patients' daily lives than vomiting.



Key words:

chemo-induced nausea and vomiting (CINV), highly emetogenic chemotherapy (HEC) , moderately emetogenic chemotherapy (MEC). impact on daily life (NIDL) , Functional living index (FLIE),

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## List of abbreviations

| | |
|---|---|
| 5-HT3 | 5-Hydroxy tryptamin-3 receptor |
| ANV | Anticipatory nausea and vomiting |
| ASCO | American society of clinical oncology |
| ASHP | American society of health-system pharmacist |
| CIE | Chemo-induced emeses |
| CIN | Chemo-induced nausea |
| CIV | Chemo-induced vomiting |
| CTZ | Chemo receptor trigger zone |
| CINV | Chemo induced nausea and vomiting |
| CPG | Central pattern generator |
| FDA | Food and drug adminstration |
| FILE | Functional living index emesis |
| IRB | Institutional review board |
| MASCC | Multinational association for support care in cancer |
| NK1R | Neurokinn 1 receptor antagonist |
| NIDL | No impact on daily life |
| NTT | Nucleus of the solitary tracts |
| QoL | Quality of life |
| SP | Substance P |
| TASH | Tikur Anbesa specialized hospital |
| VAS | Visual analogue scale |
| RCT | Randomized clinical trial |

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# 1. Introduction

## 1.1. Background

### 1.1.1 Overview of chemo-induced nausea and vomiting.

CINV will be around as long as cytotoxic chemotherapy is used to treat cancer (1). Nausea and vomiting are common and feared symptoms among cancer patients, and up to 80% of patients will experience CINV without prophylactic therapy (2).

CINV is also a frequent cause of patient non-adherence to chemotherapy, which may impact control of cancer and survival of patients (3).In the past three decades, more effective antiemetic medications were introduced and widely adopted. Serotonin (5-HT3) receptor antagonists are considered safe and work alone or in combination with corticosteroids (eg, dexamethasone) or other agents. Most recently, neurokinin-1 (NK-1) receptor antagonists, a new class of antiemetic, have been studied. One such drug (aprepitant [Emend]) has been approved for use in combination with other antiemetics (4).

CINV can be described as acute, delayed and anticipatory according to time course. The acute form of CINV is the well-recognized form. It is also known as post-treatment CINV. Acute CINV is usually defined as nausea and/or vomiting within the first 24 h after administration of chemotherapy. Delayed CINV is usually defined as nausea and/or vomiting that begins after the first 24 h of administration of chemotherapy. Delayed CINV may last for as long as 120 h after chemotherapy administration. Anticipatory CINV occurs before the second or later course of chemotherapy. Anticipatory CINV is a learned or conditioned response to poorly managed CINV during previous courses of chemotherapy. As a learned response, anticipatory CINV has a strong psychological component and does not respond well to antiemetic prophylaxis or treatment. However, it has been shown to respond to behavioral interventions. The most effective approach to preventing anticipatory CINV is to prevent nausea and vomiting associated with the patient's earlier courses of chemotherapy (5, 6).

Risk factors for CINV fall into patient-related, disease related and treatment-related categories. Patient-related risk factors include age younger than 50 years, female sex, poor performance status, history of light alcohol use (heavier drinkers have less emesis), a prior history of nausea

and/or vomiting associated with pregnancy or motion sickness, increased anxiety, a history of CINV with prior exposure to Chemotherapy, and low social functioning (5, 7). Disease-related features such as the primary site of the cancer, the histological subtype, clinical stage, and presence of end organ dysfunction may further impact the probability of emesis.

The intrinsic risk of the chemotherapy regimen is the main risk factor for the overall degree of CINV and can vary depending on the class of drug, dose, schedule, and route of administration used. The current classification of the risk of emesis is mostly based on the intrinsic emetogenic potential of the chemotherapy regimen (7), which is stratified as follows: high emetogenic potential (>90% risk of inducing vomiting after chemotherapy administration), moderate emetogenic potential (>30–90% risk), low emetogenic potential (10–30% risk), and minimal emetogenic potential (<10% risk) (8). According to ASCO 2011, guidelines emetic potential of chemotherapy regimens are presented in Table1 (8).

**Table 1. Emetic risk of intravenous antineoplastic agent.**

| **High** | |
|---|---|
| Dacarbazine | Carmustin |
| Dactinomycin | Cisplatin |
| Mechlorethamine | Cyclophosphamide >1500mg/m2 |
| Streptozotocin | |
| **Moderate** | |
| Azacitidine | Idarubicin |
| Ifosfamide | carboplatin |
| Irinotecan | Cyclophosphamide < 1,500 mg/m2 |
| Oxaliplatin | Daunorubicin |
| Alemtuzumab | Epirubicin |
| Bendamustine | Doxorubicin |

Carboplatin

Clofarabine

Cytarabine > 1000 mg/m2

**Low**

5-Fluorouracil

Gemcitabine

Ixabepilone

Bortezomib

Methotrexate

Carbezetaxel

Mitomycin

Catumaxumab

Mitoxantrone

Cytarabine < 1,000 mg/m

Paclitaxel

Panitumumab

Temsirolimus

Pemetrexe

Docetaxel

Doxorubicin HCL liposome injection

Etoposide

**Minimal**

2-Chlorodeoxyadenosine

Vinorelbine

Bevacizumab

Vincristine

Bleomycin

Vinblastine

Busulfan

Cetuximab

Fludarabine

Rituximab

Pralatrexate

**1.1.2 Pathophysiology**

Multiple organs and different neurotransmitters are involved in the pathophysiology of CINV (Fig 1).The understanding about the mechanism of CINV has significantly evolved over the last three decades. Initially it was thought that the central site 'the vomiting center' in medulla served the final relaying center for all incoming emetogenic inputs (9). Subsequent studies revealed that an anatomically distinct vomiting center is unlikely to exist (10) rather a number of interconnected neuronal areas in medulla interact and mediate the emetic reflex and are known as "central pattern generator" (CPG) (11). There are two main source of afferent input to the CPG.

i) First input is from the bowel through afferent vagal impulses and from the vagus central nucleus known as nucleus of the solitary tract (NTS) localized in the dorsal brain stem. This input has the greatest relevance for CINV (12). Chemotherapy agents either by direct mucosal interaction or by blood born mechanisms stimulate entero endocrine cells to release mediators such as 5HT, NK-1, substance P (SP) and cholycestokinin (13). These mediators then bind to the appropriate receptors on the vagal nerve ending, leading to afferent stimuli that go to the NTS (4).

ii) The second input is from area postrema (AP), which is also known as chemoreceptor trigger zone (CTZ). This is also localized in the dorsal hindbrain at the caudal end of the fourth ventricle (14). This area is more permeable than the rest of the brain thereby this area is easily exposed to humoral stimuli in blood and cerebrospinal fluid. Animal studies have shown that opoid, serotonin, SP, cholycetokinin and dopamine binding in this area triggers the emetogenic reflex (15). This is believed that gut derived neuropeptides and metabolites of chemotherapy drugs can interact with this area and induce emesis (11).

Besides these two main afferent inputs sources of stimuli from the limbic forebrain and the amygdale have also been discovered.

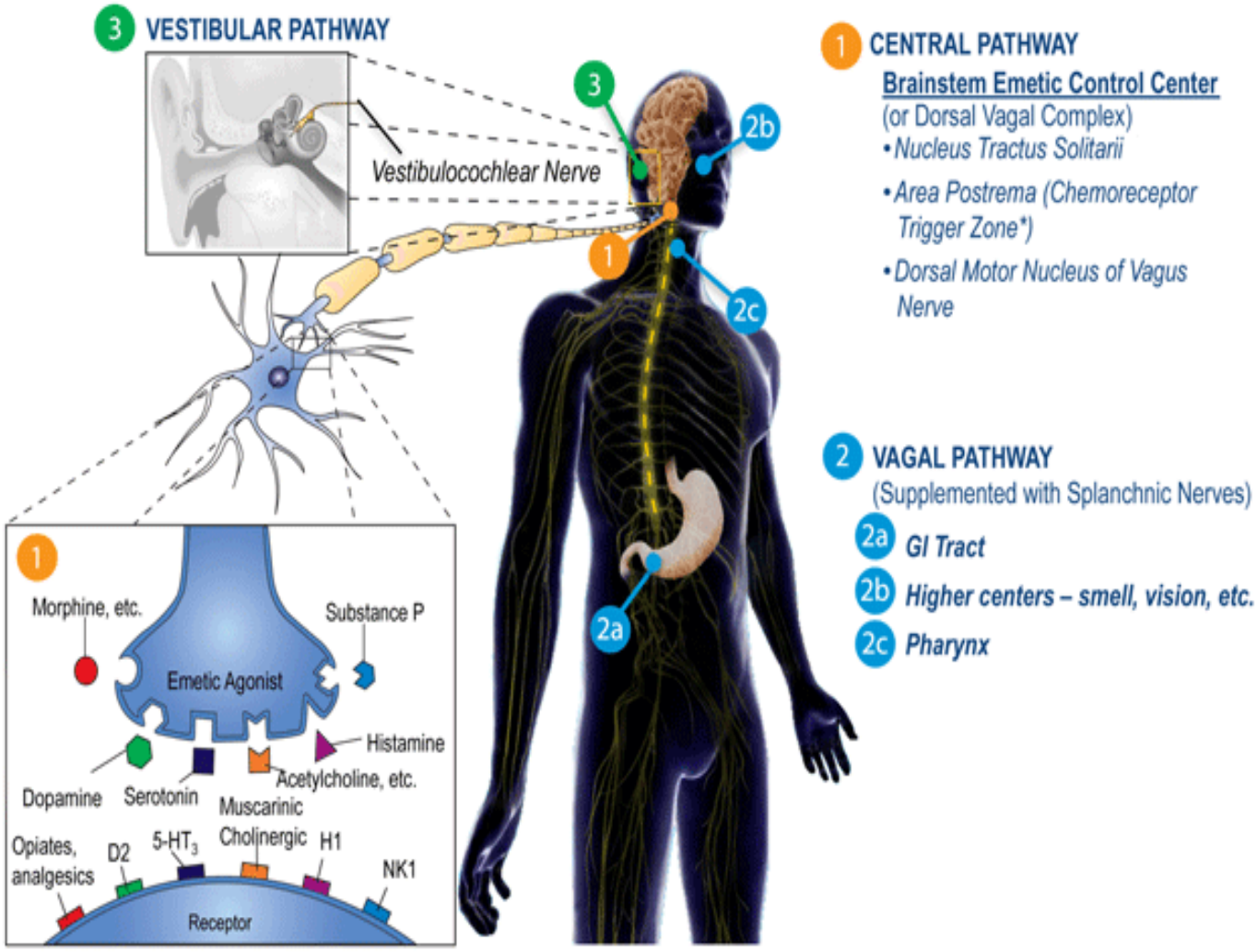


**Fig 1. Pathophysiology of chemo induced-nausea and vomiting**.

Vomiting is triggered by afferent impulses to the vomiting center, a nucleus of cells in the medulla. Impulses are received from sensory centers, such as the chemoreceptor trigger zone (CTZ), cerebral cortex, and visceral afferents from the pharynx and GI tract. When excited, afferent impulses are integrated by the vomiting center, resulting in efferent impulses to the salivation center, respiratory center, and the pharyngeal, GI, and abdominal muscles, leading to vomiting.

**Neurotransmitters Involved**

Several neurotransmitters are involved in the pathogenesis of CINV. The main neurotransmitters are dopamine, 5-HT, and SP. The initial works were focused on dopamine D2 receptors and dopaminergic antagonist such as metoclopramide was the 1st group of antiemetic that was used for the prevention of CINV. This agent showed limited efficacy in controlling CINV when used in high dose and significantly associated with side effect mainly as extrapyrmidal (16, 17).

The revolution in control of CINV made us recognize the role of 5-HT 3 receptor subtype and it has been found to mediate the acute phase of CINV (18, 19).The 5-HT3 receptors are located both centrally (NTS and AP) and in the periphery (GI) vomiting reflex arc (20). Subsequent development of selective 5-HT 3 antagonist led to significant success in control of CINV.

SP is also another relevant neurotransmitter in CINV. Three mammalian tachykinins have been isolated to date - SP, NK A, and NK B, which preferentially bind to the receptors NK- 1, NK-2, and NK-3, respectively. NK-1 receptors are widely distributed throughout the central nervous system, including the AP and the NTS, and are also found in peripheral sites such as the GI tract (21, 22). Several NK-1 receptor antagonists are developed with proven efficacy in controlling CINV (23).

Endocannabinoids constitute a fourth class of neurotransmitters that appear to be relevant to CINV. Unlike dopamine, 5-HT, and SP, which have a proemetic role, the endogenous cannabinoids exert antagonistic antiemetic effect. A number of clinical trials have shown that synthetic cannabinoids have antiemetic efficacy in patients with CINV (24).

### 1.1.3 Antiemetic Agents used

**5-HT3 antagonists**

The introduction of selective 5-HT3–receptor antagonists in the early 1990s revolutionized the Management of CINV. The first generation 5-HT3 antagonists in clinical use are: ondansetron, granisetron, tropisetron, and dolasetron. These agents have similar efficacy in controlling CINV and can be used interchangeably (25). These drugs form the cornerstone of prophylactic therapy for chemotherapy with moderate to high emetic potential. Multiple prospective, randomized trials have demonstrated the therapeutic equivalence of the four older 5-HT3 antagonists, a finding supported by a number of meta-analyses (26, 27).Their side effect profile is relatively mild and include mild headache, constipation, and transit elevation of liver enzymes (25).

Single-dose daily schedules are similar in efficacy to multiple dose daily schedules, and at the approved doses, the oral formulation is therapeutically equivalent to the intravenous route of administration (28). These 5-HT3 antagonists are very effective and accepted as standard for prophylactic use to prevent CINV as well as to treat acute emeses, but their efficacy in controlling acute CINV as a single agent is only 50-70% (29). About half of the patients receiving moderately to highly emetogenic chemotherapy will do poorly and still have significant acute and delayed CINV. Other studies showed that when 5-HT3 antagonists are used in combination with dexamethasone, the control of acute and delayed emeses further increase, and combination therapy of 5-HT3 and steroids has now become the standard regimen (30).

In 2003, a new 5-HT3 antagonist, palonoasetron, was approved by the Food and Drug Administration (FDA). It differs from the older 5-HT3 antagonists in its prolonged half-life (approximately 40 h) and it’s substantially greater binding affinity for the 5-HT3 receptor (31).In several randomized clinical studies; palonoasetron has been shown to be equivalent or superior as compared to first generation agents. In one study, palonoasetron was compared with ondasetron in 563 cancer patients. Palonosetron was shown to have a significant higher rate of complete response, defined as no emeses and requirement of antiemetic therapy during the acute, as well as delayed period (up to 120 days) after chemotherapy (32). On the other hand, in a study in 667 patients, palonosetron was found to be as effective as ondansetron (33).

**Neurokinin-1–Receptor Antagonists**

The NK-1–receptor antagonists represent the newest class of antiemetic agents that are effective for the prevention of CINV. Aprepitant (Emend, Merck), approved by the FDA in 2003 in an oral formulation, was the first available agent in this class. Fosapripitant was developed, which is an intravenously administered pro-drug form of aprepitant and it was approved in 2008.

Two prospective phase 3 trials conducted with highly emetogenic chemotherapy led to the approval of aprepitant. Both trials, of identical design, compared the three-drug combination of ondansetron, dexamethasone, and aprepitant, all administered before chemotherapy, with ondansetron and dexamethasone alone. In the standard-treatment group, dexamethasone alone was continued. Significantly better control of emesis was noted during the 5-day study period in both trials in the group that received aprepitant. The magnitude of the benefit (an approximate 50% reduction in the risk of emesis or need for rescue medications) established aprepitant as an important component of antiemetic management strategies for highly emetogenic chemotherapy (34, 35).

Superior control of emesis was again observed in the aprepitant group during the 5-day study period in another phase 3 trials that had an identical design, with the exception that the standard-treatment group received a daily dose of ondansetron as well as dexamethasone on days 2 through 4 after treatment with highly emetogenic chemotherapy (36).

Aprepitant has a complex metabolism. In vitro studies using human liver microsomes have shown that aprepitant is metabolized primarily through the cytochrome P-450 (CYP) 3A4 pathway, with minor metabolism by CYP 1A2 and CYP 2C9 (37). Aprepitant is also a moderate inhibitor and inducer of the CYP 3A4 pathway. This information is relevant when it is administered with corticosteroids, which are also metabolized through the CYP 3A4 pathway. Co-administration of aprepitant and dexamethasone increases the plasma concentrations of dexamethasone by fifity percent so the dose of aprepitant should be decreased by half when corticosteroids are administered with aprepitant (38).

**Corticosteroids**

Corticosteroids were first shown to be effective antiemetic agents more than 30 years ago (39). They can be effective when administered as a single agent in patients receiving chemotherapy of low emetic potential. Corticosteroids are most beneficial when used in combination with other antiemetic agents. This has been well demonstrated when corticosteroids have been used in combination with 5-HT3–receptor antagonists (40, 41).

Corticosteroids are effective for both acute and delayed emesis (42). Relatively little is known about the site or mechanism of action of corticosteroids as compared with the 5-HT3 antagonists and NK-1 antagonists. Many types of corticosteroids have been used as antiemetic agents. The widest experience has been reported with dexamethasone and methylprednisolone (43).

**Agents with Low Therapeutic Index**

A number of agents, including metoclopramide, butyrophenones, phenothiazines, cannabinoids, and olanzapine, are included among antiemetic agents with a lower therapeutic index. These drugs are generally characterized by lower efficacy and a greater potential for adverse effects, as compared with the agents with a high therapeutic index. In addition, the clinical database supporting their use is less robust (43, 44).

The phenothiazines constitute the oldest and most widely used agents in this category. They are appropriate for use as primary prophylaxis in patients receiving chemotherapy with a low emetogenic potential or for use as a salvage agent for patients in whom breakthrough emesis is developing. Metoclopramide, at standard doses, and the butyrophenones, like the phenothiazines, are also dopaminergic D2 antagonists and have a similar spectrum of use (44). The efficacy of metoclopramide improves with increasing doses, probably because of its capacity to inhibit 5-HT3 receptors at higher blood concentrations (45).

The synthetic cannabinoids, nabilone and dronabinol have also been shown to have antiemetic efficacy, especially for chemotherapy with low to-moderate emetic potential (46). Adverse effects such as postural hypotension and dysphoria limit their usefulness. Olanzapine, which antagonizes several neurotransmitter receptors, including dopamine and 5-HT receptors, has been shown in two phase 2 trials to be effective in preventing both acute and delayed CINV (47).

Benzodiazepines are another class of agents that may be helpful in some situations. Although benzodiazepines have modest antiemetic efficacy, their antianxiety properties can be useful in some settings .The most commonly used agent in the class is lorazepam, which is helpful in the prevention and treatment of anticipatory emesis and as an adjunct to other antiemetic agents when first-line agents fail (48).

### 1.1.4. Management of chemo-induced nausea and vomiting.

Practice guidelines from the American Society of Clinical Oncology (ASCO), the American Society of Health-System Pharmacists (ASHP), the Multinational Association for Supportive Care in Cancer (MASCC), and others have been developed to help standardize the use of antiemetic prophylaxis with chemotherapy (49, 50, and 51). These efforts have raised awareness of the continuing presence of CINV. However, problems with under treatment still persist. Management of CINV is summarized in (Annex 1 and 2) according to ASCO guidelines.

## 1.2. Statement of the Problem

Nausea and vomiting remain among the most distressing side effects of treatment with chemotherapy. CIE can impair quality of life and poor control of the emesis can interrupt or force withdrawal from critical chemotherapy (52). The use of selective 5-$HT_3$ receptor antagonists plus corticosteroid such as dexamethasone prevents acute emesis in 70% to 80% of patients in the first cycle of chemotherapy. Despite having reasonable protection from acute emesis, however, 25% to 40% of patients still experience vomiting and/or significant nausea in the delayed phase of their first cycle of chemotherapy (53). The addition of aprepitant is reported to be useful in preventing delayed emesis (54). However, the unavailability of this drug in Ethiopia has become a barrier in reducing the burden of nausea and vomiting associated with chemotherapy.

Two meta-analyses of clinical trials have shown that 5-HT3 receptor antagonists with or without corticosteroids are not effective against delayed emesis and nausea (55). The lack of adequate CINV control may be partly attributed to the fact that antiemetic treatment regimens are guided by risk factors, including level of emetogenicity of chemotherapeutic agents. Emetic risk categories are based on experience rather than specific data, and the categories refer to acute emesis only (55) Moreover, the neuropharmacologic mechanism of delayed CINV (>24 hours post chemotherapy) is not well understood, and prevention of delayed CINV has largely been based on empiric results (56).

CINV adversely affect patients' QOL (57). From a list of chemotherapy-related adverse effects, patients rated nausea as their first and vomiting as their third most feared symptom. In a recent study, ovarian cancer patients included complete to almost complete control from CINV among the most favorable health states, just below perfect health and clinical remission (58, 59).

According to the ethiopian cancer association, on average 60,000 up to 125,000 cancer patients visit TASH every year (60). This statistics indicates how cancer is becoming a major public health issue in Ethiopia. Since the most prominent problem associated with cancer treatments is CINV, the attention given to its accurate diagnosis and management in these setting is an important issue that must be examined.

The prevalence of CINV in the oncology unit of TASH, Addis Ababa, Ethiopia is reported to be 83%, this is not specific study on chemo-induced nausea and vomiting rather it was a study at

oncology unit of TASH on drug related problem (61). Antiemetic used to counteract CINV is limited to 5-HT3 antagonists in combination with dexamethasone, as aprepitant is not yet available in the country. There is also no local data generated showing the preventive effect of the combination for acute and delayed CINV. The aim of the present study was therefore to determine the prevalence CINV and its impact on patients quality of life (QOL) after highly or moderately emetogenic chemotherapy.

The outcome of the study will help identify at what level CINV after receiving HEC and/or MEC is within the hospital setting and based on the result determine what or whether an action is necessary to go from that stand point. Moreover, the result will directly guide CINV treatment for cancer patients in the direction that is set by the ASCO 2011 and other guidelines given such actual gaps are present. In addition, identifying the relationship between CINV management practice and potential predictive factors will help in focusing on the respective factors while managing the condition. The study will certainly help in drawing attention to the matter and in doing so help cancer patients get the required and adequate treatment for CINV.

## 1.3. Literature Review

### Prevalence of CINV

In 2004, Gunberg et al reported that greater than 35% of patients overall experienced acute nausea, whereas 13% experienced acute emesis. Delayed nausea and emesis were observed in 60% and 50% of HEC patients, respectively, and in 52% and 28% of MEC patients, respectively. Delayed symptoms appeared without acute symptoms after HEC (emesis, 38%; nausea, 33%) and MEC (emesis, 19%; nausea, 21%). Physicians and nurses accurately predicted the incidence of acute CINV but underestimated the incidence of delayed nausea and emesis after HEC by 21 and 28 percentage points, respectively, and delayed nausea after MEC by 28 percentage points. Greater than 75% of physicians and nurses underestimated the incidence of delayed CINV after both HEC and MEC (62).

The incidence of delayed CINV depends on the type of chemotherapy used, and the emetogenic potential of chemotherapy agents is one of the factors to be considered when decisions about prophylactic antiemetic are made (Table 2).

Table 2. Incidence of Emesis on Days 2 and 3 Following Chemotherapy (63).

| | CISPLATIN | FAC | CMF | CARBOPLATIN |
|---|---|---|---|---|
| Day 2 | 40% | >50% | 25% | 10%–20% |
| Day 3 | 61% | < 20% | < 10 | NA |

FAC = 5-fluorouracil, Adriamycin (doxorubicin), and cyclophosphamide;
CMF = cyclophosphamide, methotrexate, and 5-fluorouracil; NA = data not available.

Regardless of the regimen used, delayed CINV presents a more difficult treatment challenge than does acute CINV. Agents that are highly effective in preventing acute vomiting are less effective in preventing delayed vomiting. A review of three clinical studies compared the serotonin-antagonist ondansetron with the dopamine antagonist metoclopramide for the prevention of delayed emesis associated with non–cisplatin-based chemotherapy. The study results found that 34% (n = 152) of patients treated with metoclopramide experienced emesis on day 2 and 16% (n = 139) on day 3. Among patients treated with ondansetron, 17% (n = 149) experienced emesis on day 2 and 11% (n = 135) on day 3 (64).

The relationship between acute and delayed CINV is not completely understood, but the control of acute CINV appears to minimize the development of severe, delayed CINV Furthermore,

control of acute CINV minimizes the risk of a patient developing anticipatory CINV before subsequent courses of chemotherapy. When patients whose acute CINV was completely controlled were treated with dexamethasone plus ondansetron, 92% had complete control of delayed CINV. Among patients who experienced acute CINV, only 41% had complete control of delayed CINV (65).

A commonly reported consequence of post-treatment nausea or vomiting is the development of anticipatory nausea and vomiting (ANV). In most published works, nausea is reported to occur before chemotherapy drugs are administered by approximately 20% of patients at any one chemotherapy cycle and by 25–30% of patients by their fourth chemotherapy cycle. Most studies in adult patients strongly support the view that the development of ANV involves elements of classical conditioning. The best method to avoid development of ANV is to adequately prevent both vomiting and nausea from the first exposure to chemotherapy (66).

Data from 574 chemotherapy patients who received granisetron as their antiemetic treatment during repeat cycle chemotherapy less than 10% of patients displayed symptoms of anticipatory nausea and 2% or less had symptoms of anticipatory vomiting per treatment cycle. It is concluded that the use of granisetron as an antiemetic during the acute phase of chemotherapy may result in a lower incidence of ANV in patients undergoing repeat cycle chemotherapy (67).

A meta-analysis of 30 randomized studies comparing 5-HT3 antagonists with the conventional anti-emetics high dose metoclopramide, dexamethasone, diphenhydramine, lorazepam in the prophylaxis of acute vomiting induced by cytotoxic chemotherapy showed that 5-HT3 antagonists reduce the risk of acute vomiting in comparison to conventional anti-emetics both with cisplatin treatments (15 trials; odds ratio 0.60; 95% confidence interval 0.51-0.70 ) and with MEC (11 trials; odds ratio 0.47; 95% confidence interval 0.39-0.58). The risk of acute vomiting seems to be further reduced by 20 % when 5-HT3 antagonists are combined with dexamethasone (68).

A double-blind, randomized, crossover study conducted on 60 hospital admitted cancer patients to compare the efficacy and safety of high-dose dexamethasone with a combination of

dexamethasone, metoclopramide and diphenhydramine in the management of CINV after HEC showed that complete antinausea and antivomiting effects of high-dose dexamethasone were observed in 30 (50%) and 34 (57%), respectively and the combination therapy in 17 (28%) and 26 patients (43%) respectively. The difference was not statistically significant (P=0.09 and 0.24, respectively). Lack of significant difference between the two regimens was demonstrated irrespective of the administered cytotoxic drugs (69).

The combination therapy caused more adverse reactions than high-dose dexamethasone. While 27 patients (45%) experienced no side effects from high-dose dexamethasone, only 14 (24%) remained free of complications due to combination therapy (P=0.001). Furthermore, combination therapy produced more sedation, insomnia, headache, diaphoresis, dizziness and diarrhea than the high-dose dexamethasone. In addition it gave rise to more adverse effects on appetite and activity. Upon direct questioning, 37 patients (62%) expressed a preference for high-dose dexamethasone, 14 (23%) preferred the combination therapy and 9 (15%) found no difference between the two regimens (69).

A double-blind, randomized phase III trial performed for the treatment of breakthrough CINV in chemotherapy-naive patients receiving HEC comparing olanzapine to metoclopramide shows that during the 72-h observation period, 39 out of 56 (70 %) patients receiving olanzapine had no emesis compared to 16 out of 52 (31 %) patients with no emesis for patients receiving metoclopramide ($p<0.01$). Patients without nausea (0, scale 0–10, M.D. Anderson Symptom Inventory) during the 72-h observation period were those who took olanzapine, 68 % (38 of 56), and metoclopramide, 23 % (12 of 52) ($p< 0.01$). There were no grade 3 or 4 toxicities (70).

Two consecutive trial undertaken to evaluate the incidence, course and severity of delayed nausea and emesis after administration of cisplatin shows that that 38% of patients experienced acute vomiting after receiving cisplatin chemotherapy, and 61% of patients reported vomiting on days 2–3 after receiving cisplatin, despite treatment with metoclopramide, dexamethasone and diphenhydramine at the time that cisplatin was administered. Following cisplatin administration 120 h later, between 24% and 78% of patients reported nausea; the highest incidence of nausea,

like that of vomiting, was from 48 to 72 h after chemotherapy. Patients who had no emesis during the initial 24 h after cisplatin were less likely to experience delayed emesis (71).

**Impacts on Quality of Life.**

Both acute and delayed CINV had a significant impact on patients' daily functioning. Patients who developed both acute and delayed CINV reported that CINV significantly interfered with daily functioning to a greater extent than did patients who developed delayed alone or who did not have CINV (72).

One study in particular showed that delayed nausea had a negative impact on performance of daily living as measured by the functional living index (FLIE) questionnaire in 75% of patients receiving moderately to highly emetogenic chemotherapy (73). Another study reported that patients who vomited after chemotherapy reported significantly more impact on cognitive functioning, global QOL, fatigue, anorexia, dyspnea, and insomnia than did those who did not vomit (74). Patient satisfaction with antiemetic treatment also has been related significantly to psychological distress, physical symptom distress, activity level, and control of nausea and vomiting (75).

Overall, between 70% and 80% of patients who receive cancer chemotherapy experience nausea and/or vomiting almost 60% experience nausea after their first course of chemotherapy, and about 30% experience vomiting (76). These episodes of nausea and/or vomiting vary in severity but may significantly affect patients' lives. In particular, CINV that occurs during the 3-day period after chemotherapy, when the patient is at home, has negative effect on a patient's ability to care for him or herself. Patients may have difficulty preparing or eating meals, performing household tasks, or enjoying other daily activities (77). Furthermore, the experience of CINV may lead patients to postpone or withdraw from subsequent courses of chemotherapy, with negative effects on the management of their disease (78).

## 2. Objectives

### 2.1. **General objective**

- To assess the prevalence of CINV and its impact on patients QOL after highly or moderately emetogenic chemotherapy at the oncology unit of TASH.

### 2.2. **Specific objectives**

- To determine the prevalence of CINV.
- To assess the impact of CINV on patients' QOL.
- To identify the determinants of CINV

# 3. Methodology

## 3.1. Study design

The study was a prospective cross sectional quantitative study, including cancer Patients evaluated and treated at the inpatients and outpatients level.

### 3.2. Study setting and period

The study was conducted at oncology unit of TASH. TASH is a large referral teaching hospital, under the administration of Addis Ababa University, located in Addis Ababa, Ethiopia. The hospital has 800 beds and give diagnostic and treatment service for about 370,000-400,000 patients per year. The oncology unit of TASH is the only oncology unit for the country and has an outpatient department, which gives service to new and follow-up patients and an in-patients department, which has 19 beds. Professionally, the unit has 3 oncologists with palliative specialist, 1 general practitioner, 6 residents, and 12 nurses. The study was conducted over a five month period (from June to October 2014).

### 3.3 Population

#### 3.3.1. Source Population

All cancer patients evaluated and treated with highly or moderately emetogenic chemotherapy at the oncology unit of TASH during the study period and who did meet the eligibility criteria.

#### 3.3.2. Study Population

Cancer patients evaluated and treated with highly or moderately emetogenic Chemotherapy at the oncology unit of TASH who were met the eligibility criteria.

### 3.4 Inclusion and Exclusion Criteria

The inclusion criteria for the study were patients with cancer diagnosis, receiving highly or moderately emetogenic chemotherapy, who can read and write and who are willing to participate in the study. The exclusion criteria include patients, who are not mentally sound, have cognitive problem and those unable to record in the diary.

### 3.5 Sample size determination

The sample size for the study was determined by using single proportion population sample size determination. Since the prevalence of CINV in TASH is estimated to be 83%, 0.83 is used as the P value in the calculation and 5% is used as the error margin.

$$N = \frac{(1.96)^2 \times (0.83(1-0.83))}{(0.05)^2} = 217$$

So, the sample size of the study was 217.

**3.6. Study variables**

3.6.1. **Dependent Variable**

For this study the dependent variables were

Occurrence of CINV

Impact on QOL

3.6.2. **Independent Variables**

The independent variables included:

Socio demographics

Type of cancer

Alcohol consumption

Morning sickness

Motion sickness

Type of therapy

Type of chemo regimen

**3.7. Data collection and management**

### 3.7.1 Instrument

The incidence of CINV and its impact on the patients' daily life were evaluated using the self-assessment tools described below. The patients were given both oral and written instructions by the oncology nurse on using these tools

Patients who agreed to participate received a diary covering the day of chemotherapy administration (day 1) and the following 4 days (day 2 through 5). Patients were instructed to use the diary every day to record each emetic episode and to provide daily nausea assessments using a 100-mm visual analog scale (VAS) to rate the severity of nausea experienced during the preceding 24 h. Patients also recorded all rescue antiemetic medications, which were taken in addition to what was prescribed at baseline to prevent nausea and vomiting.

In addition, patients were asked to complete the function living index (FLIE), a self-administered questionnaire (Annex 3) used to evaluate the impact of CINV on patients' daily lives. The FLIE is a validated nausea- and vomiting-specific patient-reported outcome instrument composed of two domains (vomiting and nausea) with nine identical items in each domain. The FLIE-item score was assessed on the morning of day 6 post chemotherapy. The first item in each domain asked the patient to rate how much nausea and vomiting s/he had experienced during the previous 5 days. The remaining eight items covered different sections influencing the patient's quality of daily life (ie, "recreation or leisure activities," "make meal/do tasks," "ability to enjoy meal," "enjoy drinking fluids," "see family/ friends," "daily functioning," "personal hardship," "hardship on others")

The patients' sociodemographics, cancer type and stage, chemotherapy regimen, prescribed antiemetic medications (for acute and delayed phases), and comorbid conditions were recorded by the oncology nurses on a form (Annex 3) at study period.

### 3.7.2 Data collection techniques

Patient data was collected prospectively by medical chart review and patient interview by trained nurses who are currently working in the oncology unit of TASH using the pretested structured questioner. On days 2 to 6, daily telephone contact was made by data collector to confirm that patients are maintaining accurate records of diary and FLIE questioners.

### 3.7.3. Data quality assurance

The data collection checklist was pretested with 10% of subjects and questionnaires re-structuring was done prior to actual data collection. Data collectors were trained by principal investigator about ways of data collection and aim of the study. Data collectors were closely supervised by principal investigator, and the completeness of the checklist was checked at sites during data collection by supervisors.

### 3.7.4 Data processing and analysis

Data was entered by EP-Info version 7 and analyzed using SPSS version 20 software package. Descriptive and summary statistics were done for all variables. Bi variate and Multivariate logistic regression was used to identify determinants of CINV. Each independent variable with dependent variables was independently entered in to bivariate model and those variables that had p-value of $< 0.2$ were entered in to a multivariate model. In multivariate model, p-value of $\leq 0.05$ was used as a cut off point for identifying the significant determinants of CINV.

No nausea was defined as a VAS less than 5 mm on the 100-mm scale. A patient was considered to have had acute nausea or acute emesis if nausea (VAS_>5mm) or at least one episode of vomiting was reported during the first 24 hours after start of chemotherapy. Any episodes of nausea and/or vomiting thereafter up to 5 days after chemotherapy was considered delayed.

The FLIE-score was determined by summing the responses to the 18 questions on a seven-point analog scale. Therefore, the range of total scores possible is between 18 (all one responses on each scale) and 126 (all seven responses on each scale). A higher score corresponds to a higher QoL or less impact of CINV on daily life. No or minimal impact on daily life (NIDL) was defined as an average FLIE item score of more than 6 on the seven-point continuous visual analog scale or a total FLIE-Score of more than 108.

Independent t- test was used for comparison of group means between HEC and MEC. Differences in the proportion of patients that reported NIDL between MEC and HEC treated patients were analyzed using $x_2$ tests (Fisher's exact test).

### 3.8. Ethical Consideration

The study was undertaken after ethical clearance was obtained from the School of Pharmacy, College of Health Sciences, and Addis Ababa University's ethical review committee. In addition, the oncology unit was asked for permission to conduct the study. Participants of the study were also asked for consent before participating in the study and confidentiality was maintained throughout the study.

## 4. Results

A total of 298 cancer patients were interviewed, their case note were reviewed and a daily dairy for recording of nausea and vomiting were given to the patient. The data of 24 cancer patients were excluded from the study because of incompleteness of the data and 54 patients didn't return the dairy, bringing the number of the patient to 220.

### 4.1. Demographics characteristics

The patients had a mean age of 39.23±11.37 years (Table 3), and 72.3 % were female. Most patients (80.5 %) did not consume alcoholic beverages and about two-third of the patient did not experience motion or morning sickness. Majority of the patients (42.3 %) were attending primary education. The mean income level of cancer patient patients was 704.6 Ethiopian birr. With respect to destination, majority of the patient (53.2%) that was included in the sample were evaluated and treated at the outpatient department.

**Table 3: Socio demographic characteristics of the study participants**

| Demographic characteristic | Mean ± SD | Number of patient (%) |
|---|---|---|
| **Destination of the patient** | | |
| Inpatient | | 103(46.8) |
| Outpatient | | 117(53.2) |
| **Age (years)** | 39.23±11.37 | |
| **Sex** | | |
| Male | | 61(27.7) |
| female | | 159(72.3) |
| **Marital status** | | |
| Married | | 153(69.5) |
| Single | | 55(25) |

| | |
|---|---|
| Window | 6(2.7) |
| divorced | (2.7) |
| **Religion** | |
| Orthodox | 135(61.4) |
| Muslim | 49(22.3) |
| Protestant | 28(12.9) |
| catholic | 8(3.6) |
| **Educational status** | |
| Read and write | 17(7.7) |
| Primarily education | 93(42.3) |
| High school | 69(31.4) |
| Higher education | 41(18.6) |
| **Ethnicity** | |
| Amhara | 101(45.9) |
| Oromo | 63(28.6) |
| Tigre | 13(5.9) |
| SNNP | 43(19.6) |
| **Morning sickness** | |
| Yes | 59(26.8) |
| No | 100(62.8) |
| **Motion sickness** | |
| Yes | 59(26.8) |
| No | 161(73.2) |

| | |
|---|---|
| **Income** | **704.6**±1272 |
| **Alcohol use** | |
| No | 177(80.5) |
| < 5 days per week | 42(19.1) |
| >5 days per week | 1(0.5) |

SD: standard deviation

### 4.2 Clinical characteristics of the study participants.

Clinical Characteristics of the study participants is summarized in (Table 4). The most common primary cancer site was breast (60 %), followed by GI (9.5%). About 34% of the study participants received HEC and 66 % received MEC. Majority of the patients (75 %) took chemo and surgery concomitantly (Table 4). Of the 28.2 % of patient experiencing anticipatory nausea and vomiting, majority (10.9 %) of the patient had nausea and vomiting by seeing doctors, nurses, chemo drugs or the compound.

About 90% patients received 5-HT3 receptor antagonists, and 93 % received corticosteroids. No patient received prophylaxis for delayed CINV (> 24 hours post chemotherapy) and took rescue medication. The most common duration of 5-HT3 receptor antagonist therapy and corticosteroid therapy was 1 day, with 100 % of patients receiving 5-HT3 receptor antagonists and a corticosteroid.

**Table 4: clinical characteristics of the study particepants.**

| **Clinical characteristics** | **Number of patients (%)** |
|---|---|

| | |
|---|---|
| **Types of primary tumor** | |
| Breast | 132(60) |
| Gynecological | 18(8.2) |
| GI | 21(9.5) |
| Head and neck cancers | 20(9.09) |
| Others | 29(13.1) |
| **Concurrent illnesses** | |
| Yes | 45(20.5) |
| No | 175(79.5) |
| **Type of treatment** | |
| Chemo only | 41(18.6) |
| Chemo and surgery | 6(2.7) |
| Chemo and radiation | 165(75.0) |
| Chemo, radiation and surgery | 8(3.6) |
| **Chemotherapy** | |
| Highly emetogenic | 74(33.6) |
| Moderately emetogenic | 146(66.4) |
| **Antiemetic used** | |
| Dexamethasone | 204(92.7) |
| Metoclopramide | 78(35.4) |
| 5-HT3 antagonists | 198(90) |
| 5-HT3 antagonists plus dexamethasone | 136(61.8) |

| | |
|---|---|
| **Duration of antiemetic used** | |
| One day | 220(100 %) |
| **Anticipatory nausea and vomiting** | |
| Yes | 62(28.2) |
| No | 158(71.2) |
| **Occurrence of anticipatory nausea and vomiting** | |
| Looking | 24(10.9) |
| Smelling | 17(7.7) |
| Thinking | 19(8.6) |
| **Cycle of chemotherapy** | |
| 1st cycle | 64(29.1) |
| 2nd cycle | 38(17.3) |
| 3rd cycle | 34(15.5) |
| 4th cycle | 39(17.7) |
| 5th cycle | 24(10.9) |
| 6th cycle | 21(9.5) |

Others include.

### 4.3. Patient-reported outcomes

Patients recorded their mean VAS scores in both acute and delayed phases. Incidence rates of CINV as reported by patients in their diary and on the VAS scale are summarized in (Table 5 and 6). As depicted in these Tables, vomiting and nausea was reported by 64.1% and 76.8% participants respectively. About 37 % of the patients reported emetic episodes, and 50.5%

nausea, during the 24-hour period after administration of chemotherapy, whereas delayed emesis was reported by 50% of the patients and delayed nausea by 65.5%.

**Incidence of nausea**

About 67 % of HEC patients experienced acute (day 1, post chemotherapy) nausea and 80.8 % delayed nausea (days 2–5, postchemotherapy), despite antiemetic prophylaxis. Among MEC patients, 41.8% and 57.5% reported acute and delayed nausea, respectively. Patients treated with HEC or MEC reported nausea (VAS >5 mm) and significant nausea (VAS >25 mm) throughout the acute and delayed phases for a period of 5 days after chemotherapy, peaking on day 3. Slightly more patients treated with HEC reported higher levels of nausea (as measured by the VAS) than patients treated with MEC.

**Table 5**: **Nausea Assessment–Incidence and Severity**

| | All patients | | | | HEC patients | | | | MEC patients | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Days after chemotherapy | Missing value | Total no | % | Nausea mean±SD | Missing value | Total no | % | Nausea mean±SD | Missing value | Total no | % | Nausea mean±SD |
| 1(Acute Nausea) | 111 | 220 | 50.5 | 48±18.39 | 49 | 74 | 67.1 | 55.7±17.7 | 61 | 176 | 41.8 | 42±16.2 |
| 2 | 121 | 220 | 55 | 50.6±19.2 | 52 | 74 | 71.2 | 60±15.34 | 68 | 176 | 46.6 | 43±18.5 |
| 3 | 127 | 220 | 57.7 | 53±20 | 51 | 74 | 69.9 | 63±17.14 | 76 | 176 | 52.1 | 46.6±19.1 |
| 4 | 88 | 220 | 40 | 49±20.3 | 37 | 74 | 50.7 | 60.8±17.4 | 51 | 176 | 34.9 | 40.7±18.3 |
| 5 | 73 | 220 | 33.2 | 49±21 | 33 | 74 | 45.2 | 59±3719.34 | 40 | 176 | 27.4 | 40.8±18.56 |
| 2-5 (Delayed) | 144 | 220 | 65.5 | | 60 | 74 | 80.8 | | 84 | 176 | 57.5 | |
| 1-5(Overall) | 169 | 220 | 76.8 | | 62 | 74 | 83.7 | | 107 | 176 | 73.3 | |

NOTE. The measurements are based on a 100-mm VAS for nausea. No nausea was defined as nausea VAS score >5 mm. A total of 220 patients were Assessed. The number of patients reporting nausea reflects missing values.

Abbreviations: HEC, highly emetogenic chemotherapy; MEC, moderately emetogenic chemotherapy; VAS, Visual Analog Scale; SD, standard deviation

**Incidence of vomiting**

The incidence of vomiting (emesis) is also shown in (Table 6). Incidence rates of emesis in the acute phase averaged 59% and 26% in HEC and MEC patients, respectively, while in the delayed phase rates averaged 79.5 % and 34.9% respectively.

**Table 6: Frequency of Emetic Episodes during the 5-Day Period after Chemotherapy**

| | All patients | | | | HEC patients | | | | MEC patients | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Days after chemotherapy | Missing value | Total no | % | Episode No | Missing value | Total no | % | Episode No | Missing value | Total no | % | Episode No |
| 1(Acute emesis) | 82 | 220 | 37.3 | 126 | 43 | 74 | 59 | 63 | 38 | 146 | 26 | 61 |
| 2 | 81 | 220 | 36.8 | 160 | 47 | 74 | 64.4 | 96 | 33 | 146 | 22.6 | 61 |
| 3 | 86 | 220 | 39.1 | 191 | 45 | 74 | 61.6 | 100 | 41 | 146 | 28.1 | 91 |
| 4 | 46 | 220 | 20.9 | 106 | 22 | 74 | 30.5 | 50 | 24 | 146 | 16.4 | 56 |
| 5 | 28 | 220 | 17.7 | 55 | 15 | 74 | 20.5 | 29 | 13 | 146 | 8.9 | 26 |
| 2-5 (Delayed) | 110 | 220 | 50 | 233 | 59 | 74 | 79.5 | 124 | 51 | 146 | 34.9 | 109 |
| 1-5 (Overall) | 141 | 220 | 64.1 | 333 | 68 | 74 | 91.8 | 167 | 73 | 146 | 50 | 170 |

NOTE. A total of 220 patients were assessed. The number of patients reporting emesis reflects missing values.

Abbreviations: HEC, highly emetogenic chemotherapy; MEC, moderately emetogenic chemotherapy.

As opposed to nausea, post chemotherapy vomiting episodes peaked on day 4 with 46/220 patients (20.9%) vomiting on average 2.3 times (Fig. 2).

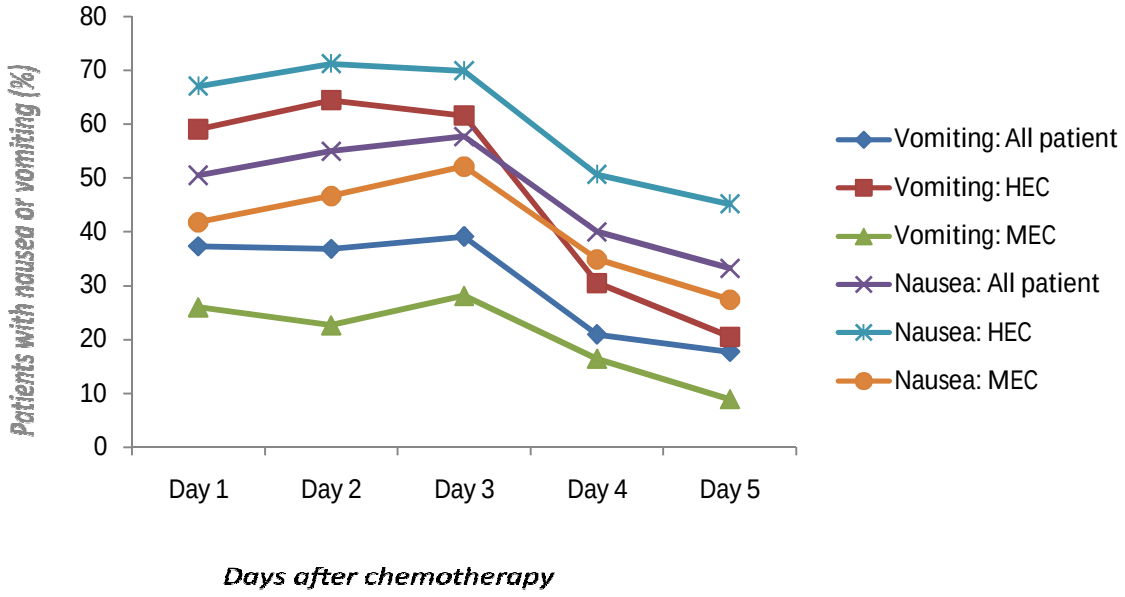


Fig 2: Frequency of nausea and vomiting during the 5-day period after chemotherapy. HEC, highly emetogenic chemotherapy; MEC, moderately emetogenic chemotherapy.

**4.4. Impact of nausea and vomiting on patient's quality of life**

In this study, HEC patients reported significantly lower mean FLIE total score than MEC patients (89.7 *v* 102.4 respectively; p < .001). Among all patients, the nausea score was significantly lower than the vomiting score (46.5 and 51.6, respectively; p< .001) (Table 7).

**Table 7: QoL assessment and Test of Differences in QoL by Treatment Type Based on Responses to the FLIE Questionnaire on Day 6 Post chemotherapy**.

| | All patient | | | | HEC | | | | MEC | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | No with NIDL | | | | No with NIDL | | | | No with NIDL | | | | | |
| FLIE Item | Missing value | Total no | % | FLIE score | Missing value | Total no | % | FLIE score | Missing value | Total no | % | FLIE score | FLIE score P* | FLIE score P† |
| FLIE total score | 119 | 220 | 54.2 | 98.14 | 30 | 74 | 40.5 | 89.7 | 89 | 146 | 60.9 | 102.4 | <0.001 | <0.001 |
| Nausea domain | 99 | 220 | 45 | 46.5 | 27 | 74 | 36.4 | 42.5 | 72 | 146 | 49.3 | 48.5 | <0.001 | <0.001 |
| Had nausea | 54 | 220 | 24.5 | 4.42 | 12 | 74 | 16.4 | 3.51 | 42 | 146 | 28.8 | 4.88 | <0.001 | 0.041 |
| Recreational or | 80 | 220 | 36.4 | 5.03 | 16 | 74 | 21.9 | 4.36 | 64 | 146 | 43.8 | 5.38 | <.001 | 0.01 |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| leisure activity | | | | | | | | | | | | | | |
| Make meal/do tasks | 102 | 220 | 46.4 | 5.35 | 21 | 74 | 28.8 | 4.79 | 81 | 146 | 55.2 | 5.62 | <0.001 | <0.001 |
| Ability to enjoy meal | 31 | 220 | 14.1 | 3.78 | 3 | 74 | 4.1 | 3.14 | 28 | 146 | 19.2 | 4.11 | <0.001 | 0.002 |
| Enjoy drinking flud | 90 | 220 | 40.9 | 5.07 | 22 | 74 | 30.1 | 4.53 | 68 | 146 | 46.6 | 5.34 | <0.001 | 0.0016 |
| See family/friends | 142 | 220 | 64.5 | 5.82 | 40 | 74 | 54.8 | 5.53 | 101 | 146 | 69.2 | 5.96 | 0.03 | 0.044 |
| Daily functioning | 83 | 220 | 37.7 | 5.20 | 24 | 74 | 32.9 | 5.01 | 59 | 146 | 40.4 | 5.29 | 0.073 | 0.249 |
| Personal hardship | 91 | 220 | 41.4 | 5.22 | 31 | 74 | 42.5 | 5.10 | 60 | 146 | 41.1 | 5.29 | 0.261 | 0.910 |
| Hardship on others | 220 | 220 | 100 | 6.62 | 74 | 74 | 100 | 6.4 | 146 | 146 | 100 | 6.84 | 0.11 | 0.821 |
| Vomiting domain | 139 | 220 | 63 | 51.64 | 33 | 74 | 44.9 | 47.2 | 106 | 146 | 72.5 | 53.9 | <0.001 | 0.02 |
| Had vomiting | 118 | 220 | 53.6 | 5.54 | 14 | 74 | 19.2 | 4.67 | 104 | 146 | 71.2 | 5.98 | <0.001 | <0.001 |
| Recreational or leisure activity | 128 | 220 | 58.2 | 5.66 | 24 | 74 | 32.9 | 5.16 | 104 | 146 | 71.2 | 5.91 | <0.001 | <0.001 |
| Make meal/do tasks | 154 | 220 | 70 | 5.83 | 43 | 74 | 58.9 | 5.42 | 110 | 146 | 75.3 | 6.03 | <0.001 | 0.015 |
| Ability to enjoy meal | 81 | 220 | 36.8 | 4.84 | 11 | 74 | 15.1 | 4.08 | 70 | 146 | 47.9 | 5.23 | <0.001 | <0.001 |
| Enjoy drinking flud | 127 | 220 | 57.7 | 5.56 | 28 | 74 | 15.1 | 4.08 | 70 | 146 | 47.9 | 5.23 | <0.001 | <0.001 |
| See family/friends | 168 | 220 | 76.4 | 6.09 | 50 | 74 | 88.5 | 5.75 | 117 | 146 | 80.1 | 6.25 | <0.001 | 0.064 |
| Daily functioning | 132 | 220 | 60 | 5.60 | 29 | 74 | 39.7 | 5.21 | 102 | 146 | 69.9 | 58 | <0.001 | <0.001 |
| Personal hardship | 136 | 220 | 63.2 | 5.80 | 34 | 74 | 46.6 | 5.45 | 104 | 146 | 71.2 | 5.98 | <0.001 | <0.001 |
| Hardship on others | 210 | 220 | 95.5 | 6.67 | 66 | 74 | 90.4 | 6.45 | 143 | 146 | 97.9 | 6.77 | ,0.001 | 0.013 |

NOTE. A total of 220 patients were assessed. The number of patients reporting Emesis and nausea reflects missing values .Abbreviations: QoL, quality of life; HEC, highly emetogenic chemotherapy; MEC, moderately emetogenic chemotherapy; FLIE, Functional Living Index-Emesis questionnaire; NIDL, average FLIE item score of > 6 on the seven-point scale.

*Based on t tests of the hypothesis that the mean scores of the FLIE items between MEC and HEC patients are not different.

†Based on $X^2$ tests of the hypothesis of no association between treatment type (MEC versus HEC) and effect on daily living measured by NIDL

When responses from FLIE questions were assessed study participants were suffered from both nausea and vomiting domain but more from nausea as shown in (Fig 3)

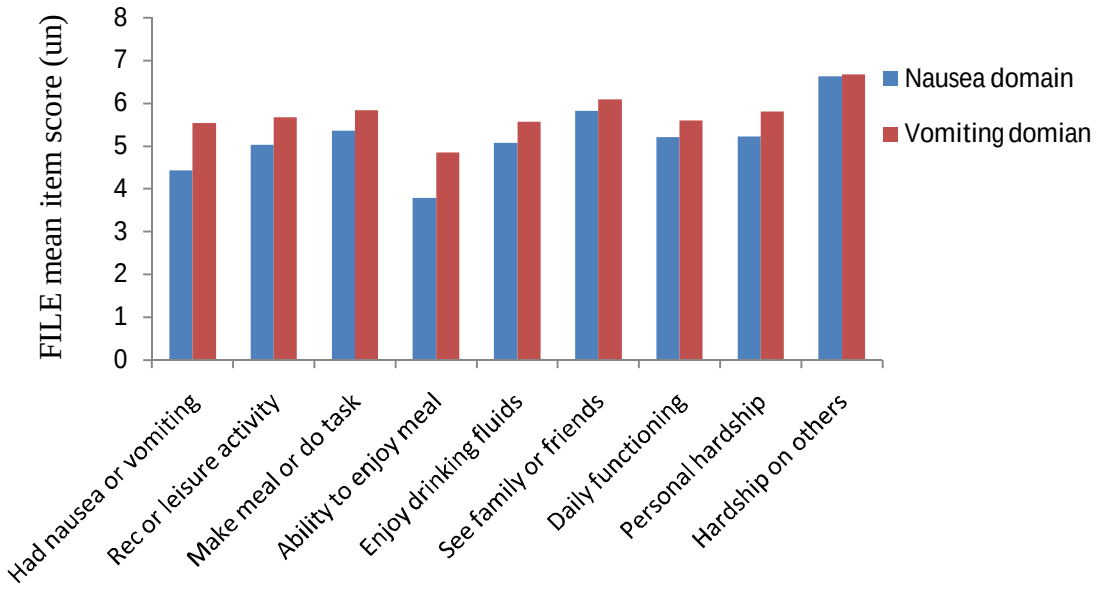


**Fig 3: Impact of nausea and vomiting on patient quality of life.**

### 4.5. **Bi -variety and Multivariate analysis of predictors of CINV.**

The association between prevalence of acute emeses and predictive factors was examined using bivariate and multivariate logistic regression. In bivariate analysis, acute emeses was significantly higher in female patient (p=0.035; OR=1.74), patients with morning sickness (p=0.02; OR=4.168), patients with motion sickness (p=0.029; OR=1.970), patients taking HEC (p=0.000; OR=4.168), and in patients who experiencing anticipatory nausea and vomiting (p=0.000, OR=3.716). There was, however no significant variation identified across other covariates (Table 8).

**Table 8: Bi-variants analysis of predictors of chemo-induce nausea and vomiting.**

| | P value | Odds Ratio | 95 %, CI | |
|---|---|---|---|---|
| | | | Lower | Upper |

| | | | | |
|---|---|---|---|---|
| Sex | | 1.74 | 0.374 | 0.854 |
| Male(reference) | | | | |
| Female | 0.035 | | | |
| Motion sickness | | 1.970 | 0.277 | 0.932 |
| No(reference) | | | | |
| Yes | 0.029 | | | |
| Morning sickness | | 2.882 | 1.477 | 5.624 |
| No(reference) | | | | |
| Yes | 0.02 | | | |
| Type of chemo | | 4.168 | 2.303 | 7.545 |
| HEC | | | | |
| MEC(reference) | 0.000 | | | |
| Anticipatory nausea and vomiting | | 3.716 | 2.012 | 6.860 |
| **No(reference)** | | | | |
| **Yes** | 0.000 | | | |

**CI, Confidence Interval**

In multivariate logistics regeration, only anticipatory nausea and vomiting was significantly associated with acute emeses with a P value of <0.001 and, odds ratio of 5.691 (Table 9).

**Table 9: Multivariate analysis of significant predictors of chemo induced nausea and vomiting.**

| | P value | Odds Ratio | 95 %, CI | |
|---|---|---|---|---|
| | | | Lower | Upper |

| | | | | |
|---|---|---|---|---|
| Sex | | | | |
| Male(reference) | | | | |
| Female | 0.109 | 0.105 | - | - |
| Motion sickness | | | | |
| No(reference) | | | | |
| Yes | 0.208 | 1.723 | 0.738 | 4.023 |
| Morning sickness | | | | |
| No(reference) | | | | |
| Yes | 0.243 | 1.659 | 0.709 | 3.881 |
| Type of chemo | | | | |
| HEC | | | | |
| MEC(reference) | 0.227 | 2.342 | 0.589 | 9.313 |
| Anticipatory nausea | | | | |
| and vomiting | | | | |
| **No(reference)** | | | | |
| **Yes** | **0.000** | **5.691** | **2.154** | **15.036** |

Bold; significant associations, CI; confidence int

## 5. Discussion

Adequate control of CINV is very important in determining patient compliance with either HEC or MEC. Marked progress in the prevention of CINV has been achieved over the past decade. Acute CINV is controlled successfully with a combination of a steroid and a 5-HT3 receptor antagonist or metoclopramide and delayed CINV is managed by NK-1 receptor antagonist. As a result, the prevalence of CINV is declining (76).

Emesis, or vomiting, is easily measured by counting the number of vomiting episodes, but levels of nausea can only be determined by the patient. Various questionnaires, using either VAS or

categorical scales, are in widespread use (79). The incidence of CINV and its impact on the patients' daily life were evaluated using the self-assessment tools.

In this study, overall 76.8% of patient experienced CIN with 50.5 % of acute and 65.5% of delayed, and 64.1 % of patient experienced CIV with 37.3% of acute and 50.5 % of delayed. These findings tell us CIN (76.8%) proved to be a more pervasive problem than CIV (64.1%). This is in agreement with other studies which reported that nausea occurred more often than vomiting (40, 80, 81).This is also in concordance with the finding that 5-HT3 receptor antagonists, such as ondansetron and granisetron, have been successful in preventing vomiting, but less effective in prevention of nausea (82).These findings also support the findings of 'first-generation 5-HT3 receptor antagonists have had only modest effectiveness in preventing delayed CINV' (30, 83).

Incidence rates of CINV in the study participants are in agreement with results from other studies. (62,76,83).The central findings from this study were that both HEC and MEC patients reported delayed nausea (80.8% vs. 57.5% ) and vomiting ( 79.5% vs. 34.9%) more often than acute nausea (67.1% vs. 41.8%) and vomiting ( 59 % vs. 26% ), respectively . Delayed emeses occurred in almost twice as many HEC as MEC patients (79.5% vs. 34.9%). Similarly, the rate of delayed nausea was high after HEC than MEC treatment (80.5 % *v* 57.5%, respectively). This indicates that level of emetogenicity is may be a strong a predictor of delayed nausea as might be assum

Nausea remains difficult to manage in clinical practice. Antiemetic in this study failed to provide adequate coverage. Even, those currently in use but not in Ethiopia including the NK-1 antagonists; have drawn no closer toward complete prevention of nausea. As studies reported antiemetic control has primarily focused on vomiting to the detriment of nausea. As the same time this offers a straightforward explanation for poor CIN outcomes, it ignores the more practical reasons underlying this state of affairs (80, 85). Our understanding of nausea is inconclusive. As studies reported CIN was frequently observed among patients without CIV, suggesting the involvement of different neural pathways in its etiology and the need for nausea and vomiting to be treated as separate entities requiring different drugs (40, 86).

Different reasons may be forwarded to explain poor CIN outcomes, including the subjective nature of nausea, inadequate assessment, underreporting among patients, and clinicians' underestimation of CIN incidence and its effect on patients' lives (80, 81). Indeed, patient's rate nausea as more distressing than vomiting as shown also in this particular study and others (87, 88) and it significantly impacts their QOL (87). Consequently, clinicians cannot effectively manage CIN unless they demonstrate a greater appreciation of the problem and make it as important a priority as CIV.

Independent risk assessment for both CIN and CIV is an important issues that clinician should follow to treat CIN or CIV independently. Several pretreatment factors were identified to help clinicians to identify patients at high risk of developing CIN or CIV. Independent predictors of CIN included high premorbid/anticipatory NV, M/HEC, longer treatment (>3 months, excluding surgery prior to adjuvant chemotherapy ± radiotherapy), female gender, surgery prior to adjuvant chemotherapy ± radiotherapy, private health insurance and low emotional functioning. Notably, CIN incidence increased three to fivefold if the patients had high premorbid/anticipatory NV or received M/HEC, and at least doubled if they possessed any of the remaining risk factors. Predictors of CIV included premorbid/anticipatory vomiting, M/HEC, female gender, cancer resection and low role functioning. Remarkably, CIV incidence increased more than tenfold if the patients experienced premorbid/anticipatory vomiting, and at least doubled if they held any of the remaining risk factors (except cancer resection) (89).

Adequately controlled CINV may have positive effects on patient QOL and ability to perform daily activities (72,90).One study showed that delayed nausea had a negative impact on performance of daily living as measured by the FLIE questionnaire in 75% of patients receiving moderately to highly emetogenic chemotherapy (73,91). Another study reported that patients who vomited after chemotherapy reported significantly more impact on cognitive functioning, global QOL, fatigue, anorexia, dyspnea, and insomnia than did those who did not vomit (74,92) Patient satisfaction with antiemetic treatment also has been related significantly to psychological distress, physical symptom distress, activity level, and control of nausea and vomiting( 75).

The result of this study is emphasized by the finding that nausea had a stronger negative impact on QoL than vomiting. This was consistent across all items of the FLIE score (Fig 3), and more patients experienced an impact on daily life from nausea than from vomiting (Table 3; Fig 2). This is in concordance with the finding that 5-HT3 receptor antagonists, such as ondansetron and granisetron, have been successful in preventing vomiting, but less effective in the prevention of nausea (82).Both absolute FLIE scores and the proportions of patients reporting NIDL were significantly different between HEC-and MEC-treated groups, demonstrating that HEC patients suffered from more of the impact.

In this study, the percentage of MEC patients who experienced an impact on daily living was as high as 39.1 for the FLIE total score, 27.5 for the vomiting score and 50.7 for the nausea domain score (corresponding to 60.9 %, 72.5% and 49.3 % NIDL, respectively). This indicates that nearly one in two patients suffered an impact on daily life, primarily from nausea, even though they received only moderately emetogenic regimens. The result findings highlight the need for adequate prevention of CINV, even after MEC. This finding also supports the notion that management of MEC patients may not have been adequately addressed, even in treatment guidelines for prevention of CINV (84).

When the answer to most individual FLIE questions were considered both nausea and vomiting had imposed more impact on patient quality of life primarily from ability to enjoy meal, daily functioning and recreational or leisure activity as shown in (Fig 4) and (Table 7) this result is in agreement with the study done by Baiiatori (77).

Because first-generation 5-HT3 receptor antagonists have had only modest effectiveness in preventing delayed CINV (30, 68) newer antiemetic that is more effectively prevent delayed CINV are highly desirable to maintain daily life activities and QOL.

Regarding the effects of demographic and clinical characteristic on CINV, several risk factors for acute emesis, some confirmed by multivariate analysis, have been shown to predict poor antiemetic control. These factors include age younger than 50 years, female sex, poor

performance status, history of light alcohol use (heavier drinkers have less emesis), chemotherapy regimen, a prior history of nausea and/or vomiting associated with pregnancy or motion sickness, increased anxiety, a history of CINV with prior exposure to Chemotherapy, and low social functioning, primary site of the cancer, the histological subtype, and clinical stage may further impact the probability of emesis (5, 7, 93, 94).

In this study, sex, type of chemo regimen, morning sickness, motion sickness and anticipatory nausea and vomiting were significantly associated with acute emeses in the bi-variety analysis. But, in the multivariate analysis only anticipatory nausea and vomiting was significantly associated with acute emeses (Table 7 and 8).

Surprisingly, younger age was not identified as a significant risk factor in the development of CIV, although other studies have also failed to do so (40, 95) and such patient factors can be inconsistent in their effects on CINV.

Sex, type of chemo regimen, morning sickness and motion sickness were significantly associated in the bi variety analysis but not in the multivariate mode which is probably due to presence of confounding factors. For instance, when sex was cross tabulated with type of chemo regimen it was found that most female patients (78%) were taking moderately emetogenic chemotherapy than male and more male patients (64%) were taking HEC. But, it is know that both being female patients and highly emetogenic chemotherapy were the risk factors for acute emeses. So, it means that sex is the confounding factor for type of chemo regimen and vice verse for this particular study.

Given the poor control of CIN exerted by antiemetic alone, clinicians should consider employing additional interventions (including combined pharmacological and non-pharmacological approaches) in attempts to improve management for their patients.

Supplementing antiemetic with interventions dealing with pre-existing anxiety (e.g. anxiolytics acupuncture/acupressure (97), and relaxation techniques (98) has been shown to reduce CINV in RCTs and should be offered to patients exhibiting such risk factors for CINV incidence when screened at pretreatment. While some non pharmacological approaches such as acupuncture are

time and labor intensive (and others like relaxation techniques are not), it should not preclude their regular use in antiemetic control by clinicians if significantly better outcomes can be achieved for patients (particularly in instances, such as CIN, where antiemetic alone have demonstrated limited efficacy). Finally, and in addition to supplementing antiemetic with other interventions, controlled antiemetic trials should seek to incorporate pretreatment risk factors in their evaluation of CINV development.

Inadequately control of CINV can lead to complications, such as anorexia and metabolite imbalance, and also contribute to a general deterioration of the cancer patient's psychological and physical condition (99). The impact of inadequately controlled nausea/vomiting on patient's quality of life is also substantial. One commonly reported consequence, caused by the conditioning effect created by frequent and/or severe posttreatment NV, is the advent of anticipatory NV (ANV). In this study, the occurrence of ANV is 62 (28%), which develop in approximately 40 % of patients by the fourth treatment cycle is in agreement with a study done by Morrow (100 ). ANV appears to Link psychological, neurological and physiological systems (101). Once they develop, ANV cannot be controlled by antiemetics, including the new 5-HT3 receptor antagonists. Fortunately, behavioral interventions have been effective in mitigating these side effects, and low doses of the anxiolytic agent alprazolam may be potentially useful as a pharmacological preventive intervention (102). Systematic desensitization (SD), or counterconditioning, is a well-developed, standardized behavioral technique that is effective against ANV associated with cancer chemotherapy (103). Hypnosis has been shown in several studies, most of them involving children and adolescents, to be effective in treating ANV. Patients can undergo chemotherapy while hypnotized (104).

## 6. Limitation of the study

Heterogeneity of the sample in terms of diagnosis, treatment received and antiemetic used could also limit the generalisability of results.

Baseline assessment of the FLIE item was not measured so that the difference of impact on quality of life before and after chemo regimen was not assessed.

Some risk factors were not assessed in these particular studies like psychological factors for instance the extent of anxiety. Additionally, information on the performance status and radiotherapy fractions would have provided greater insight into CINV outcomes in the present study (particularly given the heterogeneous sample), but unfortunately could not be utilized due to unacceptable amounts of missing/unavailable data.

## 7. Conclusion

The prevalence of CINV at oncology unit of Tikur Anbesa specialized hospital was found to be high and it adversely affect patients' QoL despite antiemetic therapy even after treatment with only moderately emetogenic chemotherapy regimens. On the basis of the FLIE results in this study, nausea had a stronger negative impact on patients' daily lives than vomiting.

## 8. Recommendations

- Oncology unit of TASH should consider using the recent antiemetic guidelines to improve the management of CINV.

- Clinicians should consider assessing the risk factors of the patient in the better management of CINV.
- The country should consider using newer antiemetic agents including NK-1 antagonist in the better control of CINV.
- Further study on the CINV which exclude the limitation of this particular study is needed to further explore the problem.

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**Annex 1. ASCO 2011 Guideline for the Treatment of Chemo Induce Nausea and Vomiting**

| **Chemotherapy induced nausea and vomiting** | **2011 recommendation of ASCO** |
|---|---|
| **Highly emetogenic agent** | The three-drug combination of an NK1 receptor antagonist (days 1-3 for aprepitant; day 1 only for fosaprepitant), a 5-HT3 receptor antagonist (day 1 only), and dexamethasone (days 1-3 or 1-4) is recommended for patients receiving Highly emetogenic chemotherapy. This |

| | |
|---|---|
| | recommendation is unchanged since the 2006 update, but re-worded for clarification.<br>The Update Committee also recommended reclassification of the combined anthracycline and<br>Cyclophosphamide regimen as highly emetogenic. |
| **Moderately emetogenic agents** | The two-drug combination of palonosetron (day 1 only) and dexamethasone (days 1-3) is recommended for patients receiving moderately emetogenic chemotherapy. If palonosetron is not available, clinicians may substitute a first generation 5-HT3 receptor antagonist, preferably granisetron or ondansetron. Limited evidence also supports adding aprepitant to the combination. Should clinicians opt to add aprepitant in<br>patients receiving moderate-risk chemotherapy, any one of the 5-HT3 receptor antagonists is appropriate. |
| **Low emetogenic agent** | A single 8 mg dose of dexamethasone<br>before chemotherapy is suggested. No change since 2006. |
| **Minimal emetogenic agents** | No antiemetic should be administered<br>Routinely before or after chemotherapy.<br>No change from the original guideline. |
| **Combination chemotherapy** | Patients should be administered antiemetics appropriate for the component |

| | |
|---|---|
| | chemotherapeutic<br>(antineoplastic) agent of greatest emetic risk. No change from the original guideline. Anthracycline-cyclophosphamide combinations are now classified as highly emetogenic. |
| **Adjunctive drugs** | Lorazepam or diphenhydramine are useful adjuncts to antiemetic drugs, but are not recommended as single agent antiemetics. No change since 2006. |
| **Complementary Therapy** | No published randomized controlled trial data which met inclusion criteria are currently available to support a recommendation about such therapies. |
| **Multi-day chemotherapy** | It is suggested that antiemetics appropriate for the emetogenic risk class of the chemotherapy be<br>administered for each day of the chemotherapy and for two days after, if appropriate. No change from the original guideline.<br>The Update Committee suggests, based on limited data, that patients receiving five-day cisplatin regimens be treated with a 5-HT3 receptor antagonist in combination with dexamethasone and aprepitant. |
| **Emesis or Nausea despite optimal** | Clinicians should:<br>(1) Re-evaluate emetic risk, disease |

| | |
|---|---|
| **prophylaxis** | status, concurrent illnesses, and medications;<br>(2) Ascertain that the best regimen is being administered for the emetic risk;<br>(3) Consider adding lorazepam or alprazolam to the regimen; and<br>(4) Consider adding olanzapine to the regimen or substituting high-dose intravenous metoclopramide for the 5-HT3 receptor antagonist or adding a dopamine antagonist to the regimen |
| **Anticipatory nausea and vomiting** | Use of the most active antiemetic regimens appropriate for the chemotherapy being administered to prevent acute or delayed emesis is suggested. Such regimens should be used with initial chemotherapy, rather than assessing the patient's emetic response with less effective treatment. If anticipatory emesis occurs, behavioral therapy with systematic desensitization is effective and suggested. No change since the original guideline. |

**Annex 2. Antiemetic Dosing by Chemotherapy Risk Category.**

| | Day of Chemotherapy | Subsequent Days |
|---|---|---|
| **Highly Emetic Risk (HEC)** | | |
| ***NK1 Antagonist*** | Aprepitant 125 mg oral 80 mg oral; | days 2 and 3 |
| | Fosaprepitant 150 mg IV | |
| ***5-HT3 Receptor*** | | |
| ***Antagonist*** | | |
| | Granisetron 2 mg oral OR | |
| | 1 mg or 0.01 mg/Kg IV | |
| | Ondansetron 8 mg oral twice daily OR | |
| | 8 mg or 0.15 mg/Kg IV | |
| | Palonosetron 0.50 mg oral OR | |
| | 0.25 mg IV | |
| | Dolasetron 100 mg oral ONLY | |
| | Tropisetron 5 mg oral OR 5 mg IV | |
| | Ramosetron 0.3mg IV | |
| ***Corticosteroid*** [a] | | |
| | Dexamethasone 12 mg oral or IV | 8 mg oral or IV; days 2 – 3 |
| | | or days 2 – 4 |
| **Moderate Emetic Risk (MEC)**[b] | | |
| ***5-HT3 Recepto*** | | |
| ***Antagonist*** | | |

| | | |
|---|---|---|
| | Palonosetron<br>0.25 mg IV OR<br>0.50 mg oral | |
| ***Corticosteroid*** | Dexamethasone 8 mg oral or IV | 8 mg; days 2 and 3 |
| **Low Emetic Risk** | | |
| ***Corticosteroid*** | Dexamethasone 8 mg oral or IV | |

For patients receiving multi-day chemotherapy**,** clinicians must first determine the emetic risk of the agent(s) included in the regimen. Patients should receive the agent of the highest therapeutic index daily during chemotherapy and for two days thereafter. Patients can also be offered the granisetron transdermal patch (Sancuso) that delivers therapy over multiple days rather than taking a serotonin antagonist daily.

a The dexamethasone dose is for patients who are receiving the recommended three-drug regimen for highly emetic chemotherapy. If patients do not receive aprepitant, the dexamethasone dose should be adjusted to 20mg on day 1 and 16 mg on days 2-4
b Clinicians who choose to utilize an NK1 antagonist should follow HEC dosing. Importantly, corticosteroid is **only** given on day one; dexamethasone dose is 12 mg.

## Annex 3. Data abstraction format

Addis Ababa University
College of Health Sciences
School of Pharmacy
Department of Pharmacology and Clinical Pharmacy

A questioner prepared for the assessment of CINV and its impact on patients' QOL after highly or moderately emetogenic chemotherapy at the inpatient and outpatient department of the unit of oncology of TASH.

**Id No----------**

Consent form

Hello dear respondent,

I am ……..,who is part of this research project entitled with the Prevalence of Chemo-induced Nausea and Vomiting, and Its impact on Quality of Life after Highly or Moderately Emetogenic Chemotherapy at Oncology Unit of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia. The objective of the research is assessing the Prevalence of Chemo-induced Nausea and Vomiting, and Its impact on Quality of Life in patient receiving higher and or moderately emetogenic chemotherapy like you. Thereby, major factors contributing to uncontrolled nausea and vomiting will be identified and accordingly ways of enhancing control of nausea and vomiting can be recommended, hence patient can improve their chemo induce nausea and vomiting prevention outcomes. In order to pursue this study and attain the set specific research objectives, the research project team found important that patient chart, diary and record reviews be conducted. This is the reason that you and other could be candidate for the study.

It is only through chance that you became part of the study like other: otherwise, if you don't want to be part of the study, you can refuse to participate .In doing so, you will not going to lose any service that you are getting from the clinic. Once after you decided to be part of the study and in case you don't want to continue, you still have the right to get out from the study at any time you want. In taking part in this study, you are not going to gain anything to, rather the finding from this study will enable us, we hope to improve chemo induce nausea and vomiting episodes in general, hence you will be benefited then indirectly.

I will be very grateful if you are going to be participate in this study and hence we, together can do something positive towards chemo induce nausea and vomiting episoides.Finaly, its my great pleasure to forward you deepest gratitude in advance for your kind cooperation you are going to have during the interview by giving your time with genuine information to me. Once again, I am assuring by any means, your confidentiality will not break and be kept secret and the data generated will be used for the purpose of this research only.

Once again, thank you

Are u agree

Yes no

Signatures of respondent……..

Interview date…….

If no go to the next patient

## Part 1: socio-demographic charctertics of the study participants.

1.1. Age_____

1.2. Gender

1. Male 2. Female

If your gender is male skip question number 1.3

1.3. Morning sickness

1. Yes 2. No

1.4. Religion

1. Orthodox 4. Protestant
2. Muslim 5. Non believer
3. Catholic 6.Others

1.5. Marital status

1. Single 3.Divorsed
2. Married 4.Window

1.6.Educational status

1. Can't read and write 4. Elementary class (7-8 grades)
2. Can read and write 5. High school (9-12 grades)
3. Elementary class (1-6 grades) 6. Higher education (certificate, diploma, first degree and above)

1.7. Ethnicity

1. Oromo 4. SNNP
2. Amhara 5. Other, pleas mention
3. Tigray

1.8.Monthly income_____

1.9.Drinking habit

1. No 2. Less than 5 days per week 3. Greater than 5 days per week

1.10. Motion sickness

1. Yes 2. No

## Part 2: Clinical Characteristics of the study participants

2.1 Type of cancer _____

2.2 Type of treatment(can circle more than once)

2.2.1 Chemotherapy

2.2.1.1. Name and dose of the drug of the drugs

_____

_____

_____

_____

2.2.1.2 Cycle of chemotherapy _____

2.2.2 Radiation

2.2.3 Surgery

2.3 Drug used for N/V prevention _____

_____

_____

2.4 Comorbide condition_____

2.5 Anticipatory nausea and/ vomiting? If any, how it occurs.

## Part 3. Data collection form for nausea and vomiting

### Part 3.1: data collection form for vomiting

Day 1 ( / / )

Please write the episode of vomiting.

Day 2 ( / / )

Please write the episode of vomiting.

Day 3 ( / / )

Please write the episode of vomiting.

Day 4 ( / / )

Please write the episode of vomiting.

Day 5 ( / / )

Please write the episode of vomiting

## Part 3.2：Data collection form for nausea

Please write the severity of nausea including time and amount from 0 (no nausea) up to 100(severe nausea) within 5 days of chemotherapy.

Day 1 ( / / )

0mm 5mm 10mm 15 mm 20mm 25mm 30mm 35 mm 40mm 45 mm 50mm 55mm 60mm

65mm 70mm 75mm 80mm 85mm 90 mm 95mm 100mm

time ---------- amount…….

time ---------- amount …….

time ---------- amount …….

time ---------- amount …….

time ---------- amount …….

Day 2 ( / / )

0mm 5mm 10mm 15 mm 20mm 25mm 30mm 35 mm 40mm 45 mm 50mm 55mm 60mm

_____

65mm 70mm 75mm 80mm 85mm 90 mm 95mm 100mm

time ---------- amount…….

time ---------- amount …….

time ---------- amount …….

time ---------- amount …….

time ---------- amount …….

Day 3 ( / / )

0mm 5mm 10mm 15 mm 20mm 25mm 30mm 35 mm 40mm 45 mm 50mm 55mm 60mm

_____

65mm 70mm 75mm 80mm 85mm 90 mm 95mm 100mm

time ---------- amount…….

time ---------- amount …….

time ---------- amount …….

time ---------- amount …….

time ---------- amount …….

day 4 ( / / )

0mm 5mm 10mm 15 mm 20mm 25mm 30mm 35 mm 40mm 45 mm 50mm 55mm 60mm

_____

65mm 70mm 75mm 80mm 85mm 90 mm 95mm 100mm

time ---------- amount…….

time ---------- amount …….

time ---------- amount …….

time ---------- amount …….

time ---------- amount …….

day 5 ( / / )

0mm 5mm 10mm 15 mm 20mm 25mm 30mm 35 mm 40mm 45 mm 50mm 55mm 60mm

65mm 70mm 75mm 80mm 85mm 90 mm 95mm 100mm

time ---------- amount…….

time ---------- amount …….

time ---------- amount …….

time ---------- amount …….

time ---------- amount …….

**Part 3.3. Please write any breakthrough medication including the name, amount and day taken for the treatment of CINV within 5 days of chemotherapy**.

Name of the drug _____

Amount of the drug: _____

Time and date taken _____

## Part 4 □**Diary prepared for the assessment of the impact of CINV on Patients' QOL.**

Please write the impact of CINV on your day to day life within the past five days. For each questions circle from 1 (had more impact) to 7 (no impact) on day to day life's.

---

## 4.1. Nausea related questions

4.1.1 Amount of nausea

1 2 3 4 5 6 7

4.1.2 Recreation or leisure activities

1 2 3 4 5 6 7

4.1.3. Make meal/do tasks

1 2 3 4 5 6 7

4.1.4. Ability to enjoy meal

1 2 3 4 5 6 7

4.1.5. enjoy drinking fluids

1 2 3 4 5 6 7

4.1.6. See family/ friends

1 2 3 4 5 6 7

4.1.7. Daily functioning

1 2 3 4 5 6 7

4.1.8. Personal hardship

1 2 3 4 5 6 7

4.1.9. Hardship on others

1 2 3 4 5 6 7

## 4.2. Vomiting related questions

4.2.1 Amount of vomiting

1 2 3 4 5 6 7

4.2.2 Recreation or leisure activities

1 2 3 4 5 6 7

4.2.3 Make meal/do tasks

1 2 3 4 5 6 7

4.2.4 Ability to enjoy meal

1 2 3 4 5 6 7

4.2.5 enjoy drinking fluids

1 2 3 4 5 6 7

4.2.6 See family/ friends

1 2 3 4 5 6 7

4.2.7 Daily functioning

1 2 3 4 5 6 7

4.2.8 Personal hardship

| | | | | | | |
|---|---|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 | 6 | 7 |

4.2.9 Hardship on others

| | | | | | | |
|---|---|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 | 6 | 7 |

## መረጃ መሰብሰቢያ መዝገብ

**ክፍል 1፡ የማስታወክ ምልክት መረጃ መሰብሰቢያ መዝገብ**

---

**ቀን** 1 ( / / )

**እባክዎን ትውከት የተከሰተበትን ሰአት እና ደቂቃ ይጻፉ**

---

**ቀን** 2 ( / / )

**እባክዎን ትውከት የተከሰተበትን ሰአት እና ደቂቃ ይጻፉ**

**ቀን** 3 (  /  /  )

**እባክዎን ትውከት የተከሰተበትን ሰአት እና ደቂቃ ይጻፉ**

**ቀን** 4 (  /  /  )

**እባክዎን ትውከት የተከሰተበትን ሰአት እና ደቂቃ ይጻፉ**

**ቀን** 5 (  /  /  )

**እባክዎን ትውከት የተከሰተበትን ሰአት እና ደቂቃ ይጻፉ**

**ክፍል 2፡ የማክለሽለሽ ምልክት *መረጃ መሰብሰቢያ መዝገብ***

**እባክዎን ኬሞቴራፒ ከወሰዱበት ቀን 1 እስከ ቀን 5 *ያጋጠሞትን* የማክለሽለሽ ስሜት *መጠን* ከ 0 (ምንም *ማክለሽለሽ* አልነበረም) እስከ 60 (እጅግ በጣም ከፍተኛ *ማክለሽለሽ*) *መ*ርጠው እስከተከሰተበት ሰአት እና ደቂቃ ይጻፉ።።**

**ቀን** 1 (  /  /  )

0mm 5mm 10mm 15 mm 20mm 25mm 30mm 35 mm 40mm 45 mm 50mm 55mm 60mm

65mm 70mm 75mm 80mm 85mm 90 mm 95mm 100mm

**ሰአት** ---------- ***መጠን***.....

**ሰአት** ---------- ***መጠን*** .....

**ሰአት** ---------- ***መጠን*** .....

**ሰአት** ---------- ***መጠን***.....

ሰአት ---------- መጠን……

---

ቀን 2 ( / / )

0mm 5mm 10mm 15 mm 20mm 25mm 30mm 35 mm 40mm 45 mm 50mm 55mm 60mm

_____

65mm 70mm 75mm 80mm 85mm 90 mm 95mm 100mm

ሰአት ---------- መጠን……

ሰአት ---------- መጠን ……

ሰአት ---------- መጠን ……

ሰአት ---------- መጠን……

ሰአት ---------- መጠን……

---

ቀን 3 ( / / )

0mm 5mm 10mm 15 mm 20mm 25mm 30mm 35 mm 40mm 45 mm 50mm 55mm 60mm

_____

65mm 70mm 75mm 80mm 85mm 90 mm 95mm 100mm

ሰአት ---------- መጠን……

ሰአት ---------- መጠን ……

ሰአት ---------- መጠን ……

ሰአት ---------- መጠን……

ሰአት ---------- መጠን……

---

ቀን 4 ( / / )

0mm 5mm 10mm 15 mm 20mm 25mm 30mm 35 mm 40mm 45 mm 50mm 55mm 60mm

65mm 70mm 75mm 80mm 85mm 90 mm 95mm 100mm

**ሰአት** ---------- **መጠን**……

**ሰአት** ---------- **መጠን** ……

**ሰአት** ---------- **መጠን** ……

**ሰአት** ---------- **መጠን**……

**ሰአት** ---------- **መጠን**……

**ቀን** 5 ( / / )

0mm 5mm 10mm 15 mm 20mm 25mm 30mm 35 mm 40mm 45 mm 50mm 55mm 60mm

65mm 70mm 75mm 80mm 85mm 90 mm 95mm 100mm

**ሰአት** ---------- **መጠን**……

**ሰአት** ---------- **መጠን** ……

**ሰአት** ---------- **መጠን** ……

**ሰአት** ---------- **መጠን**……

**ሰአት** ---------- **መጠን**……

**ክፍል 3፡ እባክዎን በነዚህ 5 ቀናት ውስት የወሰዱት የማቅለሽለሽ እና የማስታወክ ማስታገሻ መድሀኒት ካለ ስሙን፤ መጠኑን፤የተወሰደበት ቀን እና ሰአት ይግለጹ፡፡**

**የመድሀኒቱ ስም፡ _____**

**የመድሀኒቱ መጠን፡ _____**

**የተወሰ ደበት ቀን እና ሰአት፡ _____**

**ክፍል 2፡ የማቅለሽለሽ እና የማስታወክ ምልክቶች በተቀን ተቀን ህይወትዎ ላይ ያመጣውን ተፅኖ ለመመርመር የተዘጋጀ መጠይቅ**

**እባክዎን ባለፉት 5 ቀናት ውስጥ የተከሰቱት የማቅለሽለሽ እና የማስታወክ ምልክቶች ምን ያህል የተቀን ተቀን ህይወትዎ ላይ ተፅኖ እደፈጠረ ይግለፁልን፡፡ ለእያንዳንዱ ጥያቄዎች ከተቀመጡት ቁጥሮች መካከል ከ 1 (እጅግ በጣም ተፅኖ ፈጠርዋል) እስከ 7 (ምንም ተፅኖ አልፈጠረም) መርጠው ያክብቡ፡፡**

---

2.1. **የማቅለሽለሽ የሚመለከቱ ጥያቄዎች**

2.1.1 **የማቅለሽለሽ ምልክት መጠን**

1 2 3 4 5 6 7

2.1.2 **በትርፍ ሰአት የሚደረጉ የደስታ እና ሌሎች ክንዋኔዎችን የማድረግ ብቃት**

1 2 3 4 5 6 7

2.1.3. **ምግብ የመስራት እና ትና□ሽ የቤት ስራዎችን የማከናወን ብቃት**

1 2 3 4 5 6 7

2.1.4. **ምግብ በመመገብ የመደሰት ሁኔታ**

1 2 3 4 5 6 7

2.1.5. ፈሳሽ በመጠጣት የመደሰት ሁኔታ

1 2 3 4 5 6 7

2.1.6. ከቤተሰብ ወይንም ከጎደኛ ጋር አብሮ ሰአት ለማሳለፍ ፈቃደኝነትን

1 2 3 4 5 6 7

2.1.7. የተቀን ተቀን አድራጎቶችን ማወክ

1 2 3 4 5 6 7

2.1.8. ርስዎ ላይ ያመጣው የህይወት ክብደት

1 2 3 4 5 6 7

2.1.9. ሌሎች ሰዎች ህይወት ላይ ያመጣው ተፅኖ

1 2 3 4 5 6 7

**2.2. ማስታወክ የሚመለከቱ ጥያቄዎች**

2.2.1 የማስታወክ ምልክት መጠን

1 2 3 4 5 6 7

2.2.2 በትርፍ ሰአት የሚደረጉ የደስታ እና ሌሎች ክንዋኔዎችን የማድረግ ብቃት

1 2 3 4 5 6 7

2.2.3 ምግብ የመስራት እና ትናትሽ የቤት ስራዎችን የማከናወን ብቃት

1 2 3 4 5 6 7

2.2.4 ምግብ በመመገብ የመደሰት ሁኔታ

1 2 3 4 5 6 7

2.2.5 ፈሳሽ በመጠጣት የመደሰት ሁኔታ

1 2 3 4 5 6 7

2.2.6 ከቤተሰብ ወይንም ከጎደኛ ጋር አብሮ ሰአት ለማሳለፍ ፈቃደኝነትን

| | | | | | | |
|---|---|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 | 6 | 7 |

2.2.7 **የተቀን ተቀን አድራጎቶችን ማወክ**

| | | | | | | |
|---|---|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 | 6 | 7 |

2.2.8 **ርስም ላይ ያመጣው የህይወት ክብደት**

| | | | | | | |
|---|---|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 | 6 | 7 |

2.2.9 **ሌሎች ሰዎች ህይወት ላይ ያመጣው ተፅኖ**

| | | | | | | |
|---|---|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 | 6 | 7 |