Assessment of Chemotherapy-Induced Nausea and Vomiting in Pediatrics: Adequacy of Control and Adherence to Guidelines

Sameh Awwad[1], Abeer M.Ali[1], Fathia Shaik[1], and Mohammad Almotairi[1]

[1]King Fahad Medical City

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Abstract

Background: Chemotherapy-induced nausea and vomiting (CINV) is one of the most common side effects of chemotherapy in patients. Although sufficient evidence regarding its assessment and treatment in adults exists, CINV is more complicated in children. There are established guidelines for its prevention and treatment endorsed by several reputable organizations; however, their adherence varies between institutions. Therefore, this study aimed to assess the incidence and severity of CINV in pediatric patients receiving any form of chemotherapy in the acute and delayed phases and evaluated our institution's adherence to published guidelines endorsed by the Pediatric Oncology Group of Ontario. *Procedure*: This was a prospective longitudinal single-center study. A structured assessment was administered twice to patients or their caregivers during the acute and delayed phases. Baxter Animated Retching Faces scale was used. *Results*: A total of 186 patients completed 236 surveys, including those for acute and delayed phases. Incidence of acute nausea was reported in 33% patients of both phases, while vomiting was observed in 20.3% and 18.8% of the acute and delayed phases, respectively. A total of 31% patients met the criteria for proper adherence in case of prescribed appropriate antiemetic agent(s)/class irrespective of the dose. *Conclusion*: CINV is a major side effect among children who receive high and moderate emetogenic chemotherapy compared to those receiving minimal and low regimens. Despite the low rate of adherence to the guidelines, the incidence and severity of CINV reported in our study were acceptable and indicate good clinical practice. Further research should seek strategies to better implement and standardize these guidelines.

Introduction

Childhood cancer is the second leading cause of death by disease post infancy among children. The overall survival of the disease has greatly improved in the past few years[1–3], which has been distinctly observed in case of acute lymphoblastic leukemia, the most common childhood cancer; its overall survival has increased drastically from 40% to 50% in the early 1970–1980s to over 90% in recent years[4]. This improvement has been attributed to incorporation of increasingly intense chemotherapeutic courses associated with a high incidence of adverse events such as chemotherapy-induced nausea and vomiting (CINV). Despite the presence of highly effective antiemetics regimens, CINV remains a cause of distress for patients with cancer, especially those undergoing highly emetogenic chemotherapy (HEC) regimens. CINV occurs in up to 70% of the pediatric population undergoing rigorous chemotherapy. Studies have suggested that nausea and vomiting can be associated with extended hospital stay and decreased patient satisfaction. CINV influences the quality of life of children and their parents.

Symptoms such as nausea are highly subjective and often difficult to assess in the pediatric population; conversely, vomiting is usually much easier to assess mainly as it is a tangible and objective symptom that can be counted for frequency and measured for severity. Children lack the ability to describe how they feel or adequately rate their nausea severity and are often prescribed antiemetic medication as needed and may not receive it until commencement of vomitting. The Baxter Animated Retching Face (BARF) scale was

developed by Baxter et al. as a tool to assess and monitor the presence and severity of nausea in children aged between 4 and 18 years.

Several studies have examined the incidence of acute and delayed nausea and vomiting, particularly in children[12,21,24]. Despite the use of antiemetics, CINV continues to be a contributing factor in reducing patients' quality of life after undergoing highly and moderately emetogenic chemotherapy. Most studies that assessed the incidence of chemotherapy-induced nausea and vomiting (CINV) included patients who underwent HEC; however, studies on those undergoing chemotherapy with a moderate or low level of emetogenicity are rare. Similarly, data from Saudi Arabia's pediatric population are scarce, especially prospectively.

To bridge the knowledge gap, this study aimed to assess the incidence and severity of acute and delayed CINV in pediatric cancer patients who are receiving any form of chemotherapy. Furthermore, we examined our institution's adherence to the published Pediatric Oncology Group of Ontario (POGO) guidelines. Nausea and vomiting can have non-treatment-related causes. In our study, we focused only on treatment-related causes. Proactive assessment of CINV has a great potential for improving treatment tolerance and decreasing health care cost by reducing the number of re-admission secondary to excessive CINV. In addition, implementation of CINV guidelines can increase adherence to antiemetic guidelines and ultimately improving outcomes

Patients and methods

Study design and setting

This prospective longitudinal study was conducted over a 1-year period at a tertiary care hospital with a dedicated pediatric oncology unit that registers over 200 new cases each year.

Sample size calculation

An estimated sample size of 185 patients was calculated by our biostatistician using the Raosoft online calculator

Study participants

All pediatric patients (<14 years old) with confirmed hematology/oncology diagnoses and receiving high, moderate, low, and minimum emetogenic chemotherapy regimens as inpatients or outpatients were included in the study. We excluded patients with a history of vomiting or those who had received any antiemetic medication 24 h prior to commencement of chemotherapy.

Data collection

A structured assessment employing the BARF scale was administered twice to the patients or their caregivers during the acute and delayed phases, respectively. After obtaining official permission from the Institutional Review Board (IRB) at King Fahad Medical City (KFMC), the patient or guardian was initially approached by a familiar healthcare professional (a physician, nurse, or pharmacist) to explain the study, details of participation, and the potential value of the survey results. The patient/guardian was then provided with a patient information sheet and a consent form and provided with sufficient time to decide whether to participate in the assessment. The questionnaire was administered to the guardian/attendant if the child was <8 years old with due input from the child, while the assessment was obtained directly from the children aged between 8 and 14 years with parents' input. Subsequently, the patient was provided with the BARF and educated on how to use it. For inpatients, the assessment was performed two separate times: the first was conducted 1-day post-chemotherapy to assess for acute CINV, and the second was done 2–5 days post-chemotherapy to assess for delayed CINV. For outpatients, the assessment was given to the patient/caregiver during their visit and completed via telephonic conversation.

Survey instrument

Baxter et al. (2011) developed the BARF to assess the severity of nausea in children aged between 4 and 18 years. The BARF scale has been validated in postsurgical, oncology department, and emergency department patients. The scale has construct, content, and convergent validity as an instrument to measure nausea in

children, which helps clinicians to recognize and treat nausea and vomiting in pediatric patients more efficiently. The BARF consists of six faces, is an easy-to-use screening tool that provides an objective measure of nausea in young children and can be useful for assessing nausea in a variety of pediatric scenarios[19,20]. Nausea severity was classified based on the BARF scale as mild nausea=1–2; moderate nausea=3–5, and severe nausea=>6. Food tolerance/intolerance was classified based on nutrition intake assessment as mild=food intake below 50–75%, moderate=25–50%, and severe=0–25%, relative to normal food intake.

Validation of the survey instrument

The original tool is available in English; therefore, the tool was carefully and accurately translated into Arabic following a standardized method. The scale underwent forward and backward translations; three healthcare professionals from the KFMC (two consultant subspecialty physicians in pediatric oncology and one consultant clinical pharmacist) assessed the translated versions. The backward translation was conducted by a healthcare provider fluent in Arabic whose native language was English. The questionnaire was piloted on five patients before initiating official data collection.

Statistical analysis

All statistical analyses, including determination and measurement of frequencies, central tendency, and correlation, were performed using the Statistical Package for the Social Sciences (SPSS 25.0). In addition, descriptive statistical analyses such as frequencies and percentages were performed. The relationship between categorical data was examined using the Chi-squared (χ^2) test. Pearson's correlation coefficient was used to measure the associations between continuous variables. A two-sided p-value less than 0.05 was considered statistically significant.

Ethical consideration

Ethical approval was obtained from the KFMC ethics committee. The characteristics of the participants in this study remained confidential. Incentives or rewards were not provided to the participants.

Results

Sample characteristics

A total of 186 patients completed 218 assessments in the acute phase and 208 in the delayed phase of their chemotherapy regimens. This count included 41% female patients whose average age was 6.46 years. The complete demographics are provided in Table 1. Approximately 53% of the surveys were completed with inpatients, while the remaining 47% with outpatients. The most common diagnoses were leukemia/lymphomas (55.5%), followed by solid tumors (28.4%) and central nervous system (CNS) tumors (16.1%). The overall distribution of the types of chemotherapy regimens is provided in table 1, with moderately and highly emetogenic regimens accounting for 70% of them.

Incidence and severity of acute nausea and vomiting

Acute nausea was reported by 72 patients (33%) of whom 20 (27.7%) experienced mild, 32 (44.5%) experienced moderate, and 20 (27.7%) experienced severe nausea (table 1). Regarding emetogenic potential, most patients (58; 80%) who experienced acute nausea received either high or moderate emetogenic chemotherapy (table 7). In addition, a statistically significant association was found between a high emetogenic potential and incidence of acute nausea (P=0.003) (table7). Patients treated in an inpatient setting were found to be more likely to experience acute nausea (P=0.033) (table 3). No statistically significant correlation was found between age, sex, diagnosis, and presence of acute nausea (table 6). Contrary to our expectations, the association between adherence to guidelines and the occurrence of acute nausea was not statistically significant (P=0.289) (table 3). A distinct association was found between acute nausea and acute vomiting (P=0.001), delayed nausea (P=0.001), delayed vomiting (P=0.002), and food intake intolerance in both the acute and delayed phases (table 3).

Acute vomiting was reported in 44 patients (20.3%), of whom 34 (78%) experienced 1–2 vomiting episodes

while 10 (22%) experienced [?]3. Most patients (37; 84%) who experienced acute vomiting received either high or moderate emetogenic chemotherapy (table 3). However, the associations between the emetogenic potential and the occurrence of acute vomiting (P=0.109), and between treatment setting, age, sex, and presence of acute vomiting were not statistically significant. The association between adherence to guidelines and the presence of acute vomiting was statistically significant (P=0.052). Patients with leukemia/lymphoma and CNS tumors had a significantly higher incidence of acute vomiting. A distinct association was found between patients with acute vomiting and their tendency to develop delayed nausea (P=0.026), delayed vomiting (P=0.002), and food intake intolerance in the acute and delayed phases (P=0.001) (table 6 ,7).

Food intolerance in the cute phase was reported by 118 patients as follows: 54 (24.8%) assessments were found to be severe (tolerated <25% of normal intake), 24 (11%) moderate (tolerated 25–50% of normal intake), and 40 (18.3%) mild (tolerated 50–75% of normal intake). A strong association was found between food intolerance and type of chemotherapy emetogenicity (P=0.001) (table 1).

Incidence and severity of delayed nausea and vomiting

Delayed nausea was reported by 70 (33%) patients, of whom 27 (38.5%) experienced mild, 23 (33%) experienced moderate, and 20 (28.5%) experienced severe nausea (table 1, 4). A total of 39 (55.7%) patients who experienced delayed nausea had received highly emetogenic chemotherapy (HEC), while 21 (30%) underwent moderate, 4 (5.8%) low, and 6 (8.5%) minimal emetogenic chemotherapy. Furthermore, a significant association was observed between HEC and frequency of delayed nausea (P=0.001). Patients treated in the inpatient setting were more likely to experience delayed nausea compared to the outpatients (P=0.001). The correlation between age, sex, and presence of delayed nausea was not statistically significant. Surprisingly, guideline adherence was not associated with the incidence or degree of delayed nausea (P=0.001). A strong association was found between delayed nausea and delayed vomiting (P=0.001), and intolerance to food intake (P=0.001)) (table 6 and 7).

Delayed vomiting was reported in 39 (19%) patients, of whom 28 (72%) experienced 1–2 vomiting episodes while 11 (28%) experienced [?]3 vomiting episodes. The survey scores for high, moderate, low, and minimal emetogenic chemotherapy associated with delayed vomiting were 51.3%, 30.7%, 7.6%, and 10.3%, respectively) (table 5) . Notably, patients who received high and moderate emetogenic regimens showed a high association with the development of delayed nausea (P=0.037). Similar to delayed nausea, sex, age, treatment setting, and the rate of delayed vomiting were not found to be significantly related. No association was found between underlying diagnosis and delayed vomiting (P=0.185). The association between adherence to guidelines and the presence of delayed vomiting was not statistically significant (P=0.123).

A total of 106 patients experienced food intake intolerance during the later phase of their chemotherapy course. Thirty-seven (35%) of these patients reported severe intolerance i.e., tolerated <25% of normal intake), 24 (22.5%) showed moderate (tolerated 25–50% of normal intake), and 44 (42.5%) exhibited mild intolerance (tolerated 50–75% of normal intake). Logically, a strong association was found between food intolerance and type of chemotherapy regimen (P=0.002)) (table 6, 7).

Adherence to the CINV guidelines published by POGO was achieved for all 236 assessments. We only examined adherence as the number of patients who were prescribed the correct antiemetic agent(s)/class irrespective of the dose. A total of 73 patients were prescribed proper antiemetics (31%) as compared to 163 (69%) who were not prescribed proper antiemetics. Only 22% of patients who received highly emetogenic regimens and 27% of patients who received moderate regimens presented proper antiemetics' prescriptions. Analysis by age was not statistically significantly (P=0.774). This poor compliance remained the same regardless of whether the patient was in an outpatient or inpatient setting (P=0.221). The rate of adherence was statistically significant for patients diagnosed with solid tumors as compared to those diagnosed with CNS and leukemia (P=0.034). Association between nausea and adherence to guidelines (P=0.289), and between the presence of vomiting and non-adherence in the acute (P=0.052) and delayed phases (P=0.123) were not statistically significant) (table 6,7).

Discussion

To the best of our knowledge, this is the first comprehensive review of the incidence and severity of CINV, and the first pediatric study to evaluate the use of a validated tool to capture the incidence and severity of CINV in pediatric patients in Saudi Arabia. Aseeri et al. evaluated the use of prophylactic antiemetics in a single-center pediatric oncology patient receiving moderate and HEC and concluded that premedication was underutilized in two-thirds of the patients; however, they did not investigate the incidence or severity of CINV.

The overall diagnoses distribution in our study matched the estimated proportions of malignancies reported globally. Similarly, the distribution of age and sex were consistent with the globally reported pediatric malignancy statistics. The incidence and severity of CINV in children vary depending on the type of chemotherapy administered, with some regimens having higher rates than others. In our study, the incidence of acute and delayed nausea was 30–33%, which is either less or consistent with previously published studies. In addition, we found that most patients who experienced acute or delayed nausea and vomiting received either high or moderate emetogenic chemotherapy, which is similar to that in previously published literature locally and internationally.

Flank et al. explored the impact of CINV on the use of parenteral nutrition and whether CINV affected the incidence of gut graft-versus-host disease[10]. Their data showed that most patients (83%) had received HEC regimens. A distinct indication was found that patients who experienced nausea or vomiting in the acute phase were likely to develop delayed nausea and/or vomiting. Our findings also revealed the same important productions regarding the severity of nausea and emesis, and the direct association between the acute and delayed phases. Although this was an exploratory study, we report a link between CINV and food intake tolerance. As nausea is very difficult to assess, especially in such a sensitive population, we included food tolerance as an indirect indicator to potentially aid in a thorough assessment. Over 50% of the patients indicated that they had a certain degree of food intake intolerance. Food intolerance was high among the patients with severe nausea and vomiting, and it was strongly associated with the type of chemotherapy emetogenicity.

In 2012, the POGO guidelines for the prevention and management of CINV in children were endorsed by several pediatric organizations such as the Children's Oncology Group (COG). Incorporating these guidelines into clinical practice is imperative for better clinical outcomes. Similar to previously published studies, our study found a low rate of adherence to POGO guidelines. This finding showed that the rate of adherence differed depending on the diagnosis. Two main ways for the low rate of adherence were observed. The first was by using a 5-HT3 receptor antagonist (granisetron or ondansetron) for patients receiving minimal chemotherapy when none was indicated. The second was by not prescribing NK-1 antagonist for the patients receiving HEC. Clinicians are still cautious about potential drugs/drug interactions and prescribing medications, such as aprepitant, to prevent CINV. The primary reasons for non-adherence to the guidelines were the omission of dexamethasone in the patient's antiemetic prophylaxis and prescribing antiemetics for patients with minimal emetogenic potential for which no antiemetics were indicated. Further research should seek strategies to better implement and standardize these guidelines.

This study has strengths and limitations. The strengths include the report being prospective in nature, allowing for inclusion of heterogeneous populations with differing diagnoses, ages, and chemotherapy regimens, both in ambulatory and inpatient settings, since both are likely to experience CINV. In addition, we performed the assessment twice to evaluate acute and delayed CINV and ensure that these phases of therapy were captured. Moreover, we included food intake tolerance as a valuable indirect indicator of nausea because it is difficult to assess. The limitation includes this study being a single-center analysis, which posed a challenge in completing the survey during the delayed phase in the outpatient setting, resulting in approximately a 10% loss of follow-up.

Adherence to the CINV guidelines and building a standardized approach in the institutions can decrease food intake intolerance, prevent delays in the chemotherapy protocol, decrease hospitalization, and improve patient quality of life. In addition to ensuring the practice of the latest and best available evidence-based medicine in the hospital, this study laid the foundation for establishing local data to implement a CINV

assessment tool, which currently does not exist at our center. The study findings indicate the importance of integrating the BARF scale as an everyday assessment tool in pediatric oncology patients, and, therefore, preemptively treating children receiving chemotherapy before further deterioration. A proactive assessment approach will improve the patients' and their families quality of life. If implemented, the tool has great potential in decreasing healthcare costs by reducing the number of readmissions secondary to excessive CINV. Finally, the role of clinical assessment by healthcare professionals remains a strong path toward the most suitable and correct decisions in managing CINV.

Conclusion

CINV is the major side effect among children who receive high and moderate emetogenic chemotherapy compared to those receiving minimal and low regimens. Despite the low rate of adherence to the guidelines, the incidence and severity of CINV reported in our study are acceptable and indicate proper clinical practice.

Conflict of interest

The author(s) declare that they have no conflict of interests.

Acknowledgment

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References

Table 1. Patient characteristics, incidence, severity of acute and delayed nausea and vomiting

Variables	Description	n(n%)
Treatment setting	In patient	125 (53.0%)
	Outpatient	111 (47.0%)
Gender	Male	139 (58.9%)
	Female	97 (41.1%)
Age (years)	Mean ± SD	6.46 ± 3.59
Weight (kg)	Mean ± SD	21.46 ± 12.08
BSA	Mean ± SD	0.81 ± 0.28
Diagnosis	Leukemia/ lymphoma	131 (55.5%)
	Solid	67 (28.4%)
	CNS	38 (16.1%)
Emetogenic Potential	Minimal	49 (20.8%)
	Low	22 (9.3%)
	Moderate	93 (39.4%)
	High	72 (30.5%)
Follow guideline	Yes	73 (30.9%)
	No	163 (69.1%)
Acute Nausea	Yes	72 (33.0%)
	No	146 (67.0%)
Acute Nausea Degree categorize	Mild nausea	20 (27.7%)
	Moderate nausea	32 (45.5%)
	Severe nausea	20 (27.7 %)
Acute Vomiting	Yes	44 (20.3%)
	No	173 (79.7%)
Acute Vomiting Frequency	1-2 times	34 (15.7%)
	3 times or more	10 (4.6%)
	None	173 (79.7%)
Acute Food Tolerance	Yes	118 (54.1%)

Variables	Description	n(n%)
	No	100 (45.8%)
Acute Food Tolerance Degree (%) Categorize	Severe	54 (24.8%)
	Moderate	24 (11.0%)
	Mild	40 (18.3%)
	Normal	100 (45.9%)
Delayed Nausea	Yes	70 (33.8%)
	No	137 (66.2%)
Delayed Nausea Degree categorize	Mild nausea	27 (38.5%)
	Moderate nausea	23 (33%)
	Severe nausea	20 (28.5%)
Delayed Vomiting	Yes	39 (18.8%)
	No	168 (81.2%)
Delayed Vomiting Frequency	1-2 times	28 (13.5%)
	3 times or more	11 (5.3%)
	None	168 (81.2%)
Delayed Food Tolerance	Yes	122 (58.7%)
	No	86 (41.3%)
Delayed Food Tolerance Degree (%) Categorize	Severe	37 (17.8%)
	Moderate	24 (11.5%)
	Mild	45 (21.6%)
	Normal	102 (49.0%)

Note: Categorical data presented as frequency (%); * shows that P-value is significant at P<0.05.

Table – 2: Association between *acute nausea* with demographics

Variables	**Description**	**Acute Nausea**	**Acute Nausea**	**P -**
		Yes		
(n = 72)	**No**			
(n = 146)				
Treatment setting	In patient	47 (65.3%)	73 (50.0%)	*0.0
	Outpatient	25 (34.7%)	73 (50.0%)	
Gender	Male	39 (54.2%)	85 (58.2%)	0.57
	Female	33 (45.8%)	61 (41.8%)	
Diagnosis	Leukemia/ lymphoma	33 (45.8%)	84 (57.5%)	0.10
	Solid	27 (37.5%)	37 (25.3%)	0.06
	CNS	12 (16.7%)	25 (17.1%)	0.93
Acute Nausea Degree categorize	No Nausea	0 (0.0%)	146 (100.0%)	*<0
	Mild nausea	20 (27.8%)	0 (0.0%)	*<0
	Moderate nausea	32 (44.4%)	0 (0.0%)	*<0
	Severe nausea	20 (27.8%)	0 (0.0%)	*<0
Acute Vomiting	Yes	43 (59.7%)	1 (0.7%)	*<0
	No	29 (40.3%)	144 (99.3%)	
Acute Vomiting Frequency	1-2 times	33 (46.5%)	1 (0.7%)	*<0
	3 times or more	10 (14.1%)	0 (0.0%)	*<0
	None	28 (39.4%)	145 (99.3%)	*<0
Acute Food Tolerance	Yes	19 (26.4%)	102 (69.9%)	*<0
	No	53 (73.6%)	44 (30.1%)	

Variables	Description	Acute Nausea	Acute Nausea	P -
Acute Tolerate Feeding Degree (%) Categorize	Severe	34 (47.2%)	20 (13.7%)	*0.0
	Moderate	10 (13.9%)	14 (9.6%)	0.34
	Mild	14 (19.4%)	26 (17.8%)	0.76
	Normal	14 (19.4%)	86 (58.9%)	*<0
Delayed Nausea	Yes	50 (72.5%)	17 (12.8%)	*<0
	No	19 (27.5%)	116 (87.2%)	
Delayed Nausea Degree Categorize (%)	No Nausea	19 (26.4%)	116 (79.5%)	*<0
	Mild nausea	14 (19.4%)	12 (8.2%)	*<0
	Moderate nausea	22 (30.6%)	3 (2.1%)	*<0
	Severe nausea	17 (23.6%)	15 (10.3%)	*0.0
Delayed Vomiting	Yes	24 (34.8%)	13 (9.8%)	*<0
	No	45 (65.2%)	120 (90.2%)	
Delayed Vomiting Frequency	1-2 times	16 (23.2%)	11 (8.3%)	*0.0
	3 times or more	8 (11.6%)	2 (1.5%)	*0.0
	None	45 (65.2%)	120 (90.2%)	*0.0
Delayed Food Tolerance	Yes	24 (34.3%)	96 (72.2%)	*<0
	No	46 (65.7%)	37 (27.8%)	
Delayed Food Tolerance Degree (%) Categorize	Severe	23 (32.9%)	13 (9.8%)	*<0
	Moderate	12 (17.1%)	10 (7.5%)	*0.0
	Mild	20 (28.6%)	25 (18.8%)	0.06
	Normal	15 (21.4%)	85 (63.9%)	*<0

Note: Categorical data presented as frequency (%); * shows that P-value is significant at P<0.05.

Table – 3: Association between *acute vomiting* and demographics

Variables	Description	Acute Vomiting	Acute Vomiting
		Yes	
(n = 44)	**No**		
(n = 173)			
Treatment Setting	In patient	25 (56.8%)	94 (54.3%)
	Outpatient	19 (43.2%)	79 (45.7%)
Gender	Male	22 (50.0%)	102 (59.0%)
	Female	22 (50.0%)	71 (41.0%)
Diagnosis	Leukemia/ lymphoma	21 (47.7%)	96 (55.5%)
	Solid	16 (36.4%)	47 (27.2%)
	CNS	7 (15.9%)	30 (17.3%)
Acute Nausea Degree categorize	No Nausea	1 (2.3%)	144 (83.2%)
	Mild nausea	8 (18.2%)	12 (6.9%)
	Moderate nausea	18 (40.9%)	14 (8.1%)
	Severe nausea	17 (38.6%)	3 (1.7%)
Acute Vomiting Frequency	1-2 times	34 (77.3%)	0 (0.0%)
	3 times or more	10 (22.7%)	0 (0.0%)
	None	0 (0.0%)	172 (100.0%)
Acute Food Tolerance	Yes	11 (25.0%)	109 (63.0%)
	No	33 (75.0%)	64 (37.0%)
Acute Food ToleranceDegree (%) Categorize	Severe	23 (52.3%)	31 (17.9%)
	Moderate	6 (13.6%)	18 (10.4%)

Variables	Description	Acute Vomiting	Acute Vomiting
	Mild	7 (15.9%)	32 (18.5%)
	Normal	8 (18.2%)	92 (53.2%)
Delayed Nausea	Yes	27 (64.3%)	40 (25.2%)
	No	15 (35.7%)	119 (74.8%)
Delayed Nausea Degree Categorize (%)	No Nausea	15 (34.1%)	119 (68.8%)
	Mild nausea	5 (11.4%)	21 (12.1%)
	Moderate nausea	13 (29.5%)	12 (6.9%)
	Severe nausea	11 (25.0%)	21 (12.1%)
Delayed Vomiting	Yes	19 (45.2%)	18 (11.3%)
	No	23 (54.8%)	141 (88.7%)
Delayed Vomiting Frequency	1-2 times	11 (26.2%)	16 (10.1%)
	3 times or more	8 (19.0%)	2 (1.3%)
	None	23 (54.8%)	141 (88.7%)
Delayed Food Tolerance	Yes	15 (34.9%)	104 (65.4%)
	No	28 (65.1%)	55 (34.6%)
Delayed Food Tolerance Degree (%) Categorize	Severe	15 (34.9%)	21 (13.2%)
	Moderate	6 (14.0%)	16 (10.1%)
	Mild	15 (34.9%)	29 (18.2%)
	Normal	7 (16.3%)	93 (58.5%)

Note: Categorical data presented as frequency (%); * shows that P-value is significant at P<0.05.

Table – 4: Association between *delayed nausea* and demographics

Variables	Description	Delayed Nausea	Delayed Nausea	P - v
		Yes		
(n = 70)	**No**			
(n = 137)				
Treatment setting	In patient	54 (77.1%)	66 (48.2%)	*<0.
	Outpatient	16 (22.9%)	71 (51.8%)	
Gender	Male	36 (51.4%)	80 (58.4%)	0.339
	Female	34 (48.6%)	57 (41.6%)	
Diagnosis	Leukemia/ lymphoma	28 (40.0%)	82 (59.9%)	*0.00
	Solid	28 (40.0%)	36 (26.3%)	*0.04
	CNS	14 (20.0%)	19 (13.9%)	0.254
Acute Nausea Degree categorize	No Nausea	17 (25.4%)	116 (85.9%)	*<0.
	Mild nausea	14 (20.9%)	4 (3.0%)	*<0.
	Moderate nausea	19 (28.4%)	12 (8.9%)	*<0.
	Severe nausea	17 (25.4%)	3 (2.2%)	*<0.
Acute Vomiting Frequency	1-2 times	19 (28.4%)	13 (9.6%)	*0.00
	3 times or more	8 (11.9%)	2 (1.5%)	*0.00
	None	40 (59.7%)	120 (88.9%)	*<0.
Acute Feeding Tolerance	Yes	21 (31.3%)	90 (66.7%)	*<0.
	No	46 (68.7%)	45 (33.3%)	
Acute Food Tolerance Degree (%) Categorize	Severe	30 (44.8%)	20 (14.8%)	*<0.
	Moderate	10 (14.9%)	12 (8.9%)	0.222
	Mild	10 (14.9%)	28 (20.7%)	0.279
	Normal	17 (25.4%)	75 (55.6%)	*<0.

Variables	Description	Delayed Nausea	Delayed Nausea	P - v
Delayed Nausea Degree Categorize (%)	No Nausea	0 (0.0%)	137 (100.0%)	*<0.
	Mild nausea	27 (38.6%)	0 (0.0%)	*<0.
	Moderate nausea	26 (37.1%)	0 (0.0%)	*<0.
	Severe nausea	17 (24.3%)	0 (0.0%)	*<0.
Delayed Vomiting	Yes	36 (51.4%)	3 (2.2%)	*<0.
	No	34 (48.6%)	134 (97.8%)	
Delayed Vomiting Frequency	1-2 times	25 (35.7%)	3 (2.2%)	*<0.
	3 times or more	11 (15.7%)	0 (0.0%)	*<0.
	None	34 (48.6%)	134 (97.8%)	*<0.
Delayed Food Tolerance	Yes	15 (21.4%)	106 (77.4%)	*<0.
	No	55 (78.6%)	31 (22.6%)	
Delayed Food Tolerance Degree (%) Categorize	Severe	29 (41.4%)	8 (5.8%)	*<0.
	Moderate	14 (20.0%)	10 (7.3%)	*0.0
	Mild	16 (22.9%)	28 (20.4%)	0.687
	Normal	11 (15.7%)	91 (66.4%)	*<0.

Note: Categorical data presented as frequency (%); * shows that P-value is significant at P<0.05.

Table – 5: Association between *delayed vomiting*and demographics

Variables	**Description**	**Delayed Vomiting**	**Delayed Vomitin**
		Yes	
(n = 39)	**No**		
(n = 168)			
Treatment setting	In patient	31 (79.5%)	89 (53.0%)
	Outpatient	8 (20.5%)	79 (47.0%)
Gender	Male	18 (46.2%)	98 (58.3%)
	Female	21 (53.8%)	70 (41.7%)
Diagnosis	Leukemia/ lymphoma	17 (43.6%)	93 (55.4%)
	Solid	13 (33.3%)	51 (30.4%)
	CNS	9 (23.1%)	24 (14.3%)
Acute Nausea Degree categorize	No Nausea	13 (35.1%)	120 (72.7%)
	Mild nausea	5 (13.5%)	13 (7.9%)
	Moderate nausea	9 (24.3%)	22 (13.3%)
	Severe nausea	10 (27.0%)	10 (6.1%)
Acute Vomiting Frequency	1-2 times	12 (32.4%)	20 (12.1%)
	3 times or more	7 (18.9%)	3 (1.8%)
	None	18 (48.6%)	142 (86.1%)
Acute Food Tolerance	Yes	14 (37.8%)	97 (58.8%)
	No	23 (62.2%)	68 (41.2%)
Acute Food Tolerance Degree (%) Categorize	Severe	16 (43.2%)	34 (20.6%)
	Moderate	5 (13.5%)	17 (10.3%)
	Mild	4 (10.8%)	34 (20.6%)
	Normal	12 (32.4%)	80 (48.5%)
Delayed Nausea Degree Categorize (%)	No Nausea	3 (7.7%)	134 (79.8%)
	Mild nausea	12 (30.8%)	15 (8.9%)
	Moderate nausea	11 (28.2%)	15 (8.9%)
	Severe nausea	13 (33.3%)	4 (2.4%)

Variables	Description	Delayed Vomiting	Delayed Vomitir
Delayed Vomiting Frequency	1-2 times	28 (71.8%)	0 (0.0%)
	3 times or more	11 (28.2%)	0 (0.0%)
	None	0 (0.0%)	168 (100.0%)
Delayed Food Tolerance	Yes	8 (20.5%)	113 (67.3%)
	No	31 (79.5%)	55 (32.7%)
Delayed Food Tolerance Degree (%) Categorize	Severe	19 (48.7%)	18 (10.7%)
	Moderate	7 (17.9%)	17 (10.1%)
	Mild	8 (20.5%)	36 (21.4%)
	Normal	5 (12.8%)	97 (57.7%)

Note: Categorical data presented as frequency (%) while continuous data expressed Mean ± SD

Table – 6: Association between following guidelines and demographics

Variables	Description	Follow guideline	Follow guideline
		Yes	
(n = 73)	**No**		
(n = 163)			
Treatment setting	In patient	43 (58.9%)	82 (50.3%)
	Outpatient	30 (41.1%)	81 (49.7%)
Gender	Male	44 (60.3%)	95 (58.3%)
	Female	29 (39.7%)	68 (41.7%)
Diagnosis	Leukemia/ lymphoma	39 (53.4%)	92 (56.4%)
	Solid	27 (37.0%)	40 (24.5%)
	CNS	7 (9.6%)	31 (19.0%)
Acute Nausea	Yes	20 (28.2%)	52 (35.4%)
	No	51 (71.8%)	95 (64.6%)
Acute Nausea Degree categorize	No Nausea	51 (71.8%)	95 (64.6%)
	Mild nausea	8 (11.3%)	12 (8.2%)
	Moderate nausea	6 (8.5%)	26 (17.7%)
	Severe nausea	6 (8.5%)	14 (9.5%)
Acute Vomiting	Yes	9 (12.7%)	35 (24.0%)
	No	62 (87.3%)	111 (76.0%)
Acute Feeding Tolerance	Yes	44 (62.0%)	77 (52.4%)
	No	27 (38.0%)	70 (47.6%)
Acute Tolerate Feeding Degree (%) Categorize	Severe	12 (16.9%)	42 (28.6%)
	Moderate	10 (14.1%)	14 (9.5%)
	Mild	13 (18.3%)	27 (18.4%)
	Normal	36 (50.7%)	64 (43.5%)
Delayed Nausea	Yes	19 (27.9%)	51 (36.7%)
	No	49 (72.1%)	88 (63.3%)
Delayed Nausea Degree Categorize (%)	No Nausea	49 (67.1%)	88 (54.0%)
	Mild nausea	9 (12.3%)	18 (11.0%)
	Moderate nausea	6 (8.2%)	20 (12.3%)
	Severe nausea	9 (12.3%)	37 (22.7%)
Delayed Vomiting	Yes	8 (11.8%)	31 (22.3%)
	No	60 (88.2%)	108 (77.7%)
Delayed Food Tolerance	Yes	43 (63.2%)	79 (56.4%)
	No	25 (36.8%)	61 (43.6%)

Variables	**Description**	**Follow guideline**	**Follow guideline**
Delayed Food Tolerance Degree (%) Categorize	Severe	7 (10.3%)	30 (21.4%)
	Moderate	8 (11.8%)	16 (11.4%)
	Mild	18 (26.5%)	27 (19.3%)
	Normal	35 (51.5%)	67 (47.9%)

Note: Categorical data presented as frequency (%); * shows that P-value is significant at P<0.05.

Table – 7: Association between Emetogenic potential and demographic

Variables	Description	Emetogenic potential	Emetogenic potential	E
		Minimal		
(n = 49)	**Low**			
(n = 22)	**Moderate**			
(n = 93)	**High**			
(n = 72)				
Treatment setting	In patient	13 (26.5%)	12 (54.5%)	5
	Outpatient	36 (73.5%)	10 (45.5%)	4
Gender	Male	31 (63.3%)	14 (63.6%)	5
	Female	18 (36.7%)	8 (36.4%)	3
Diagnosis	Leukemia/ lymphoma	33 (67.3%)	12 (54.5%)	6
	Solid	10 (20.4%)	7 (31.8%)	2
	CNS	6 (12.2%)	3 (13.6%)	5
Follow guideline	Yes	16 (32.7%)	16 (72.7%)	2
	No	33 (67.3%)	6 (27.3%)	6
Acute Nausea	Yes	8 (18.2%)	6 (30.0%)	2
	No	36 (81.8%)	14 (70.0%)	6
Acute Nausea Degree categorize	No Nausea	36 (81.8%)	14 (70.0%)	6
	Mild nausea	2 (4.5%)	4 (20.0%)	8
	Moderate nausea	6 (13.6%)	0 (0.0%)	1
	Severe nausea	0 (0.0%)	2 (10.0%)	6
Acute Vomiting	Yes	4 (9.1%)	3 (15.0%)	1
	No	40 (90.9%)	17 (85.0%)	6
Acute Vomiting Frequency	1-2 times	4 (9.1%)	2 (10.0%)	1
	3 times or more	0 (0.0%)	1 (5.0%)	3
	None	40 (90.9%)	17 (85.0%)	6
Acute Food Tolerance	Yes	29 (65.9%)	15 (75.0%)	5
	No	15 (34.1%)	5 (25.0%)	3
Acute Food Tolerance Degree (%) Categorize	Severe	8 (18.2%)	3 (15.0%)	1
	Moderate	3 (6.8%)	2 (10.0%)	8
	Mild	6 (13.6%)	5 (25.0%)	1
	Normal	27 (61.4%)	10 (50.0%)	4
Delayed Nausea	Yes	6 (14.6%)	4 (23.5%)	2
	No	35 (85.4%)	13 (76.5%)	6
Delayed Nausea Degree Categorize (%)	No Nausea	35 (71.4%)	13 (59.1%)	6
	Mild nausea	5 (10.2%)	3 (13.6%)	1
	Moderate nausea	0 (0.0%)	0 (0.0%)	8
	Severe nausea	9 (18.4%)	6 (27.3%)	1
Delayed Vomiting	Yes	4 (9.8%)	3 (17.6%)	1

Variables	Description	Emetogenic potential	Emetogenic potential	E
	No	37 (90.2%)	14 (82.4%)	7
Delayed Vomiting Frequency	1-2 times	3 (7.3%)	2 (11.8%)	1
	3 times or more	1 (2.4%)	1 (5.9%)	2
	None	37 (90.2%)	14 (82.4%)	7
Delayed Vomiting Volume	A lot	2 (5.1%)	1 (5.9%)	4
	Little	0 (0.0%)	1 (5.9%)	4
	Some	2 (5.1%)	1 (5.9%)	3
	None	35 (89.7%)	14 (82.4%)	6
Delayed Food Tolerance	Yes	30 (73.2%)	10 (58.8%)	5
	No	11 (26.8%)	7 (41.2%)	2
Delayed Food Tolerance Degree (%) Categorize	Severe	2 (4.9%)	3 (17.6%)	1
	Moderate	4 (9.8%)	2 (11.8%)	8
	Mild	7 (17.1%)	7 (41.2%)	1
	Normal	28 (68.3%)	5 (29.4%)	4