DOI:10.31557/APJCC.2023.8.1.21

RESEARCH ARTICLE

A Qualitative Study to Explore Patient's experiences on Chemotherapy-induced Nausea and Vomiting: Focusing Impact on Daily Life

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Abstract

Background: This study aimed to explore the experience of cancer patients about chemotherapy-induced nausea and vomiting and its effect on patients' daily life. Methods: A descriptive qualitative study was conducted on cancer patients who experience nausea and vomiting due to chemotherapy. Semi-structured interview guide consisting of eight questions was used as a study tool and thematic analysis was done using QDA Miner lite software. Results: Twenty-five participants were included in the final analysis. The median age of the participants was 53 (IQR-15) years and most of the patients were Hindu. All the patients were newly diagnosed. Approximately 80% of patients had received three cycles of chemotherapy by the time of their interviews. Adriamycin, Cyclophosphamide (AC), Docetaxel (T), Paclitaxel and Carboplatin (P+C) were the chemotherapy drugs administered. Our findings suggest that chemotherapy-induced nausea and vomiting has affected many aspects of patient's lives, especially those related to eating, physical, emotional, and social functioning, but the degree of impact was unique to each patient. Conclusion: The individual experiences of nausea and vomiting during chemotherapy treatment may have a profound effect on treatment compliance and future outcomes. Specific assessment and innovative approaches for its subsequent management are highly needed while considering the complexity of these symptoms.

Keywords: Cancer, Chemotherapy- Nausea- Vomiting- Quality of life

Asian Pac J Cancer Care, 8 (1), 21-28

Submission Date: 09/24/2022 Acceptance Date: 11/26/2022

Introduction

There are various types of cancer treatment. The types of treatment that patients receive will depend on the type of cancer and its stage. Some patients with cancer will have only one treatment, but most patients have a combined modality of treatments, such as surgery along with chemotherapy and radiation therapy. Chemotherapy-induced nausea and vomiting (CINV) can have a deteriorating effect on further cancer treatment [1].

Chemotherapy is an important treatment in cancer care and is associated with numerous side effects such as myelosuppression, increased susceptibility to infection, nausea and vomiting, nephrotoxicity, loss of appetite, loss of hair and occasional episodes of diarrhoea. Nausea and vomiting due to chemotherapy are still the most distressing symptoms [2,3] and are associated with devastating effects on routine life including effects on diet intake, loss of

weight, dehydration, sleeping deprivation, and anxiety [1,4].

In cancer patient care, previously in 1981 introduction of metoclopramide improve emesis, then in the early 1990s development of serotonin (5-HT3) antagonists along with concomitant use of corticosteroids came intothe picture which further improved nausea and vomiting [5,6]. In recent advances few newer drugs like neurokinin (NK-1) receptor antagonists has been shown to have a promising effect on preventing chemotherapy-induced nausea and vomitingin patients treated with chemotherapeutic agents [7].

Study aim

This study aimed to acquire an overall understanding of symptoms experienced by cancer patients with a focus on nausea and vomiting during chemotherapy treatment and

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its consequences on their daily life.

Materials and Methods

Study design

A qualitative descriptive study was conducted in the oncology department of Government Bundelkhand Medical College, Sagar, Madhya Pradesh. This study was conducted to obtain in-depth descriptive data on patient experiences related to chemotherapy-induced nausea and vomiting (CINV) symptoms and their impact on patient's daily life. Permission to conduct this study was obtained from the Institutional Ethical Committee of Government Bundelkhand Medical College, Sagar.

Study tool

A semi-structured interview guide consisting of eight questions was used as the study tool (Table 1). The interview guide was developed after an extensive literature review [1,4,8,9] to create and identify the questions with specific probes while keeping the questions as open as possible to give patients maximum opportunity to express their views.

Sample

- A. Inclusion criteria: Patients were selected based on purposive sampling and saturation principles using the following inclusion criteria:
- 1) Patients age 18 years and above with confirmed diagnosis of cancer at any stage,
- 2) Patients received chemotherapy treatment alone and had experienced nausea and/or vomiting of any severity
 - 3) Gave consent in written format for participation.
- B. Exclusioncriteria: Patients who were undergoing concurrent radiotherapy and not gave written informed consent were excluded from the study.

Data collection

Patient's medical records were collected including age, sex, diagnosis, duration since cancer diagnosis, number of chemotherapy cycle done and chemotherapeutic agent used. Patients who met the inclusion criteria were invited verbally to participate in the study, and written informed consent was obtained from those who agreed to participate. Patients who provided consent were interviewed about their experience of nausea and vomiting related to chemotherapy. According to the convenience of the patient, the interviews were conducted in a private room at the hospital. Face-to-face interviews were conducted during follow-up visits it lasted for 40-60 minutes, depending on the information obtained from the interview and the depth of data collection. Since in this qualitative study we generally focused on a homogeneous patient population, data saturation was estimated to be achieved with a minimum of 25 patient's interview.

Data analysis

Interviews were transcribed verbatim and analyzed using the QDA Miner lite software to spot the central

theme from the content. A coding manual supported the areas of interest covered within the interview guide was developed. The eight questions were used because the interview guide became themes around which the information was later organized, and also the responses associated with all of those themes were grouped. Codes and sub-codes were developed for every broad theme. The codes were compared, whereby the similarities and differences in understanding and interpretation were discussed.

Results

Patients' characteristics

Of the 35 patients who were approached to participate in this study, 30 accepted our invitation; however, only 25 were included in the final analysis because five were afflicted by low data quality due to the lack of response. Reasons for declining included "not interested" or "too tired". Characteristics of the patients are summarized in Table 2.

The median age of the participants was 53 (IQR-15) years, ranging from 28 to 70 years. Most of the patients, i.e., 19, were Hindu and the rest were Muslim. All of the patients were newly diagnosed. Approximately 80% of patients had received three cycles of chemotherapy by the time of their interviews. The chemotherapy drugs administered were Adriamycin, cyclophosphamide (AC) and Docetaxel (T) and Paclitaxel, Carboplatin (P+C) as chemotherapy protocols.

Theme 1: Nausea and vomiting in patients' words

For most patients, it was difficult to describe nausea in their own words. Patients generally describe nausea as there is a feeling of vomiting but nothing comes out. They also describe it as something that wants to come out but nothing comes out. Few patients describe putting one hand on the throat and abdomen as an unpleasant feeling sensation. Some patients describe it as an unpleasant facial expression or saying that not feeling well.

- ".... Nausea....umm....feeling come tried to vomit but nothing comes out..." (P10)
- "....after chemotherapy, I feel an unpleasant sensation in my throat..." (P15)
- ".... I feel something want to come out from my stomach and throat...this started after chemotherapy..." (P19)
- ".... I felt that my stomach contents were shaken up repeatedly after chemotherapy..." (P20)
 - "....impulse to vomit but nothing comes out...." (P25)

On other hand, vomiting was more easily expressed by the patients. Vomiting was generally described as the act of throwing up of the content of stomach. Patients explained it as "the food all comes out which was eaten". Some patients described it in their own words as "the food along with water comes out". Few of the quotes of patients are as follows:

- "....all food along with water comes out of stomach...." (P16)
- "...whatever I ate, all was coming out of stomach..." (P18)

Table 1. Interview Guidelines

1	To define nausea and vomiting in patients' words					
2	Patients experience on chemotherapy-induced nausea and vomiting (CINV)					
2a	Patients experience on chemotherapy-induced nausea and vomiting in terms of previous history of nausea and vomiting					
2b	Patients experience on chemotherapy-induced nausea and vomiting in terms of severity and duration					
2c	Patients experience on chemotherapy-induced nausea and vomiting along with the association of other symptoms.					
3	Problems experienced by patients along with CINV					
3a	Nutritional problems experienced by patients along with CINV					
3b	Physical and psychological symptoms experienced by patients along with CINV					
3c	Other problems experienced by patients along with CINV					
4	What and how they ate when they were nauseated?					
4a	Frequency of meals during CINV					
4b	Consistency, nature, smell, taste, type and amount of food preferred by patients during					
4c	Foods avoided by patients during CINV					
4d	Nutritional supplements taken by patients during CINV					
5	How much CINV has affected their lives					
5a	How much CINV has affected their lives in terms of social life and family support?					
5b	How much CINV has affected their lives in terms of emotions					
6	Patient belief in God during CINV					
7	How do they manage the symptoms?					
7a	Symptoms management via dietary strategies					
7b	Antiemetic medication to prevent CINV					
7c	Non-pharmacological approach to manage CINV (e.g., aromatherapy, herbs)					
8	How much CINV has affected their lives in terms of eating patterns?					
8a	Eating patterns pre-chemotherapy cycle					
8b	Eating patterns during chemotherapy					
8c	Eating pattern post-CINV period					

"....vomiting started just after chemotherapy was started..." (P21)

"...something came out from stomach after the chemotherapy drug was administered, I started to vomit" (P24)

Theme 2: Experience on chemotherapy induced nausea and vomiting

Theme 2a: Experience on chemotherapy induced nausea and vomiting in terms of previous history of nausea and vomiting

Some patients experienced more nausea and vomiting in previous chemotherapy cycle as compare to recent chemotherapy cycle. Few patients had experienced similar nausea and vomiting in previous chemotherapy cycle and in recent chemotherapy cycle. Even some patients felt relief after vomiting. However, a handful of patients did notexperience any episode of nausea and vomiting. While few patients experienced both nausea and vomiting, few experienced only nausea. One woman experienced severe emesis commented as aches pointing the abdomen. A patient commented as nothing was left in my stomach. One patient commented that he continuously felt nauseous but didn't vomit till late in night. However, in our study we found that female patients experienced more nausea and vomiting as compare to male patients.

Theme 2b: patients experience on chemotherapy induced nausea and vomiting in terms of severity and

duration.

Some patients experienced one or two episodes of chemotherapy induced nausea and vomiting in a day after receiving chemotherapy which last for one week. Some patients experienced only two episodes of chemotherapy induced nausea and vomiting in a day after receiving chemotherapy last for 2-3 days. However, few patients experienced even six or more episodes of chemotherapyinduced nausea and vomiting in a single day after receiving chemotherapy which last for one day only. While some patients did not experienced any episodes of chemotherapy induced nausea and vomiting after receiving chemotherapy. Some patients experienced chemotherapy induced nausea and vomiting on same day of receiving chemotherapy while some experienced it one day after receiving chemotherapy while some experienced two to three days after when they reach at home.

Theme 2c: Patients experience on chemotherapy induced nausea and vomiting along with association of other symptoms.

Though few patients experiencedabdominal pain, headache, dizziness and generalized weakness. Some patients did not experience any associated symptoms along with CINV.

Theme 3: Problems experienced by patients along with CINV

Theme 3a: Nutritional problems experienced by

Table 2. Characteristics of the Participants

Sl no.	Patients' ID	Age (years)/ Gender	Occupation	Cancer stage	Duration since cancer diagnosis (months)	Chemotherapy cycle	Chemotherapeutic agents
1	P4600	60/M	Labour Work	II	3	Second	P+C
2	P6821	55/F	Housewife	IV	6	Third	AC
3	P0496	56/F	Housewife	II	3	Third	AC
4	P0904	45/F	Housewife	III	4	Second	AC
5	P5484	47/F	Housewife	III	3	Second	P+C
6	P2196	28/F	Housewife	III	10	Sixth	T
7	P2202	65/F	Housewife	II	3	Second	P+C
8	P2194	45/M	Labour Work	III	8	Fourth	P+C
9	P2287	62/F	Housewife	II	5	Third	AC
10	P2309	60/F	Housewife	IV	7	Sixth	T
11	P2322	50/F	Housewife	IV	3	Third	P+C
12	P2397	62/M	Labour Work	III	3	Second	P+C
13	P2331	53/F	Housewife	III	5	Third	AC
14	P2419	65/F	Housewife	III	9	Fifth	T
15	P2503	52/F	Housewife	IV	6	Second	AC
16	P2516	50/M	Labour Work	II	6	Fourth	P+C
17	P2518	60/M	Labour Work	III	3	Second	P+C
18	P2515	56/M	Labour Work	III	4	Second	P+C
19	P2522	42/F	Housewife	IV	6	Third	AC
20	P2545	70/F	Housewife	II	4	Third	P+C
21	P2054	50/F	Housewife	II	3	Second	AC
22	P2167	62/F	Housewife	III	4	Third	AC
23	P2160	45/F	Housewife	II	8	Fifth	T
24	P2152	35/F	Housewife	III	3	Third	AC
25	P5687	50/M	Labour Work	III	3	Second	P+C

Abbreviation, AC-Adriamycin; Cyclophosphamide; T-Docetaxel; P+C- Paclitaxel; Carboplatin.

patients along with CINV.

Patients experienced number of nutrition related problems, which includes loss of appetite (n=20), constipation (n=15), bloating (n=10), loss of taste (n=7), mucositis (n=4), regurgitation (n=5).

Theme 3b: Physical and psychological symptoms experienced by patients along with CINV

Patients receiving chemotherapy experienced few psychological and physical problems including distress (n=11), depression (n=13), fatigue (n=15), hair loss (n=20).

Theme 3c: Other problems experienced by patients along with CINV

Includes flu like symptoms (n=10), sour throat (n=8), sleep disturbance (n=7), feeling hot and cold (n=6), sweating (n=5)

Some patients had clusters of symptoms like constipation, weakness, headache, fatigue, sleep disturbance, nausea, vomiting, and depression.

".... I felt repeated nausea, so I avoid eating food." (P15)

"...I felt tired because of repeated vomiting..." (P22) Theme 4:What and how they ate when they were nauseated?

On the day of chemotherapy most of patients unable to take any food items because of fear of nausea and vomiting, while some patients prefer semisolid to liquid food only. After many attempts they force themselves to eat something but unable to consume as much they want it is even hard for them to finish a simple meal like khichdi, and daliya. Thus, the food consumption is significantly decreased during and few days after chemotherapy due to CINV.

Theme 4a: Frequency of meal during CINV

Food and fluid intake was significantly reduced because of repeated nausea and vomiting during and after chemotherapy. Some patients couldconsume simple food like bread and biscuits with milk but some patientcouldn't consume even this simple food items. The following quote of a patientpoint out this fact:

"....I eat only once in a day...don't feel like eating, whatever I eat comes out..." (P11)

Theme 4b: Consistency, nature, smell, taste, type and amount of food preferred by patients during CINV

Patients generally prefer light and soft homemade food like daliya, rice, khichdi, fruit juices, and vegetables soups. Changes in taste also reported by few patients during and post chemotherapy period, and changes remains for 4-5 days than faded away. Some patients describe it as food become bitter in taste. Some patients also reported metallic taste of food during chemotherapy period which further limit their food intake.

- ".... I eat only daliya made in home and semi solid in consistency..." (P10)
- ".... I eat only one time in a day because what I eat taste bitter." (P17)
- ".... I am unable to eat food even 3-4 days after chemotherapy..."(P18)

Theme 4c: Foods avoided by patients during CINV Patients generally avoided spicy and heavy weight food like nonveg foods items.

"....I can't eat spicy and heavy food items..."(P19)

Theme 4d: Nutritional supplements taken by patients during CINV.

Very few patients were taking nutritional supplements like protein powder with milk and while few were on nutritional supplements and medicine provided from hospital. However, a small number of patients were avoiding any nutritional supplements because of repeated nausea and vomiting. Few quotes illustrated by patients are following:

- ".... I am unable to take any nutritional supplements because of nausea..." (P1)
- "....I stopped eating food after starting of my chemotherapy treatment." (P9)
- ".... I take only medicines which are provided from hospital but sometimes I am unable to take them also because of vomiting." (P13)

Theme 5: How much CINV has affected their lives

Theme 5a: How much CINV has affected their lives in terms of social life and family support.

Some patients received lot of support from their family members while some patients were left alone when they come for chemotherapy. Under mentioned quotes from patients illustrated that fact.

- "....after chemotherapy I feel nausea and vomiting for 2-3 days during that period my daughter and my son helped me a lot in household works and in cooking food" (P2)
- "....my mother takes care of my children and me during and after chemotherapy." (P8)
- "....my husband take care of me during chemotherapy also they help in cooking food." (P11)
- "....my husband left me after I was diagnosed with cancer.....I have only one daughter, she takes care of me now." (P21)

Theme 5b: How much CINV has affected their lives in term of emotions

Majority of the patients reported that, they were upset and distressed by these symptoms since they could not perform their normal activities. Due to CINV most of the patients not able to perform their daily activities, thus distress and tension is a commonly reported symptom in them. Some patients get emotional and starts crying. Fewer patients did not feel distress at all. Few of the quotes of patients are as follows:

"....sometime I get emotional and tensed, but these feeling wouldn't last long..." (P4)

"...sometimes, I feel nothing remain in life and life is too short." (P7)

Theme 6:Patients' belief in God during CINV

In most of patients there was an increase in their tendency of worshiping God especially after receiving chemotherapy, which was help in peace of mind and has also helped them to be more positive in dealing with their symptoms. Most of patients start worship of God. Some patients writing ram, ram, ram thousands of times in a copy. Some patients start counting beads whole day. Some patients start listen bhajan of god. They tried to relax and deal with the symptoms by devoting more time to worship. This help in dealing with the treatment side effects. Few of the quotes of patients are as follows:

- "....I always starts writing God name for peace of my mind." (P22)
- ".... I start listening bhajan it helps in deviation of my mind." (P25)

Theme7: How they manage the symptoms

Theme7a: Symptoms management via dietary strategies

Patients avoid heavy food items like fatty foods, non-vegetarianitems. They start consuming small meals at small duration of intervals. Some patients avoid eating and they just drank fruit juices, vegetable soups some patients start eating only fruits and add more water in their diet. Few of the quotes of patients are following

- "....I ate daliya and fruit juices only...could not eat anything else, feels like nauseating..." (P6)
 - "...I ate more fruits and water..." (P11)
 - "...I ate only dal and rice..." (P19)
 - "....I just drank water couldn't eat even rice...." (P22)

Theme7b: Antiemetic medication to prevent CINV

Most common strategy to prevent CINV is antiemetic. However, the experience of this antiemetic medication is different for different individuals. Majority of patients (90%) usedantiemetic provided from hospitals. Among them, 65% patients got relived from CINV, while remaining 35% patients were still experiencing it. Few of the quotes of patients are as follows:

- ".....I feel better after taking antiemetic...I can at least eat without having any nausea feeling..." (P8)
- ".....I still vomit...even after taking this antiemetic medication..." (P11)
- "...I have taken this antiemetic, but, still I feel nausea." (P23)

Theme7c: Non pharmacological approach to manage CINV

Non pharmacological approach like yoga, meditation, rest also use by patients. These approaches are effective only in some patients but these are not effective in all patients.

Theme 8: How much CINV has affected their lives in terms of eating pattern.

Theme 8a: Eating pattern pre-chemotherapy cycle

Eating pattern of most of the patients remains normal before receiving chemotherapy. Some patients decrease their normal meal due to anxiety of chemotherapy. These few comments by patients illustrated this fact

"...I eat fourchapattis in morning and four in evening."

(P8)

"I was taking meal three times before taking chemo.... and also having small snacks in between..." (P15)

Theme 8b: Eating pattern during chemotherapy

Eating pattern of most of the patients decreased during chemotherapy, while it is not affected in some patients. These quotes illustrated this fact:

- ".... Iavoid eating during chemotherapy because of fear of vomiting..." (P3)
 - ".... I eat only one time on day of chemotherapy." (P5) Theme 8c: Eating pattern post-CINV period

Eating pattern of most of the patients decreased post chemotherapy because of CINV.The quotes of patients illustrated this fact.

- "....after cancer diagnosis my diet is reduced too much..." (P9)
- "...before receiving chemotherapy, eats three times in a day...but now I take solid meal only once..." (P7)
- ".... I am not able to eat for 2-3 days after chemotherapy whatever I eat all comes out." (P10)
- "I feel nausea and vomiting only on the day of chemotherapy and it remains same for 1-2 after chemotherapy..." (P 15)
- "....I feel nausea till 6-7 days after chemotherapy therefore I take only fruit juices and daliya in whole day." (P17).

Discussion

The main objective of our study was to provide a deeper understanding of cancer patients' experience with nausea and vomiting and how CINV and associated symptoms affect the daily life of cancer patients. The qualitative data obtained from this study help in providing a detailed description of patients' experiences in terms of intensity, pattern, and impact of CINV. These findings suggest that during chemotherapy treatment experiences of nausea and vomiting have a profound effect on the cancer experience, and thus may influence future decisions relating to a new treatment. While not all patients expressed chemotherapyinduced nausea and vomiting as bothersome, most patients described the symptom as quite distressing. Challenges in communicating about CINV (particularly nausea) became evident through this study as patients do not have words to describe this symptom. Similar conclusions have also been reported by Molassiotis et al., [9] indicating that nausea is a complex symptom with which patients struggled to cope by themselves and also a difficult symptom to describe. As nausea is a patient-experienced and not observable symptom, effective communication between patients and healthcare professionals is essential for its proper management.

The focus of this study was to explore patients' experiences of nausea and vomiting. Most patients hada bad experience regarding CINV. How cancer diagnosis and treatment are experienced may enhance negative experiences of side effects and symptoms. Our body was perceived both as a friend and a foe during cancer treatment; this thought has also been described in a previous study by Richer [10]. "Everything is changed

by cancer" this statement is used most of the time by individuals who are diagnosed with cancer, to describe the impact of cancer on patients' lives. In this explorative study, we find that there is a close association between CINV and symptoms like fatigue, weakness, and loss of appetite. A similar conclusion was also reported in the study of Molassiotis et al. [9] who reported associations between such manifestations with several others (i.e., taste disturbance and intolerance of smell) and CINV in cancer patients who received chemotherapy.

In our study, we felt that there is great importance of family support, information regarding treatment, patient education and support, and instructions on how to use antiemetics. In 1993, astudy [11] reported that knowledge of treatment and its side effects forms a basic foundation for effective cop-up strategies in cancer patients. Appropriate and sufficient information is important for the patient's perception of being in control and experiencing some certainty in their situation [12]. 5HT3 receptor antagonist is currently the best treatment to control CINV symptoms. However, these conventional anti-emetics are more successful in preventing emesis than in preventing nausea [13]. By using dietary strategies the eating pattern can be improved. Some self-improvement strategies can be used by patients like mind distraction techniques, yoga, exercise, acupressure, and muscle relaxant. However, there is very limited research in the field of self-management strategies [14].

A study by Landmark and Wahl [15] also supported the need to be loved, cared and support for cancer patients by family and close relatives. There is a necessity to be properly understood, heard, and seen, it appears to be a great value in a person's life. In this study, we find that patients are unable to fulfill their domestic roles due to chemotherapy-induced nausea and vomiting. In most cases, family members did not fully understand what was happening, and cancer patients require family support in terms of financial and daily routine care. Family support plays a vital role in the care of cancer patients as it helps in decreasing stress, strengthening them and improving their coping behavior, and also helps in improving their quality of life. Similarly, Cohen et al. [3] and Hilarius et al. [16] found that CINV significantly interfered with patients' daily functioning. Similarly in the study of Rustoen et al. [17] found that family support was the most important aspect of the quality of life of patients.

Nausea and vomiting are still a big problem from a patient's point of view as it affects their daily activities and family life too. Similar findings have recently been reported in other studies [2,18,19]. In our study we found that nausea and vomiting had a drastic effect on a patient's life. It depends on the severity and duration of chemotherapy, for example, decreases food intake, weight loss, fatigue, depression, anxiety, disturbed sleep patterns, and decrease social interaction. Consistent with prior experience with CINV patients feel exhausted for long periods and also restrict eating after chemotherapy this will further prolong the recovery of patients between treatment cycles of chemotherapy [1,4,9]. Several factors further decrease food intake which causes malnutrition

in most cancer patients and these factors are changes in taste, mucositis, loss of appetite, smell intolerance, etc. Malnutrition is a major problem because the patient is not able to eat properly in between and after chemotherapy cycles.

The present study describes the subjective experience of the patient on CINV these help in adding up knowledge to our previous knowledge of CINV. However, our study has a few limitations. The chemotherapy regimens are limited becausethe patient cannot afford the chemotherapy injection not available in government hospitals. Secondly, the potential for bias did exist since our study which is interview-based qualitative tended to attract only those who want to speak and discuss their symptoms. Despite these limitations, the result should be seen as a contribution to an ongoing effort to fill the gap in the literature and to understand patients' experienceson CINV.

In conclusion, this qualitative study has provided a current perspective of cancer patients regarding their subjective experiences of nausea and vomiting during chemotherapy. Communicating about CINV, particularly nausea, was a challenge to this group of patients, but the individual dimensions of CINV symptoms burden were obvious. CINV has affected many aspects of patients' lives, especially those related to eating, physical, emotional, and social functioning, but the degree of impact was unique to each patient. The rich description of experiences of chemotherapy-induced nausea and vomiting gained from this study is expected to assist healthcare professionals to understand better about the necessity of patients and their concerns when experiencing this symptom. Specific assessment and innovative approaches for its subsequent management are highly needed while considering the complexity of these symptoms.

Acknowledgements

We are grateful to all the participants for helping us obtain information on key parameters related to this study. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of interest or conflict of interest

The authors declare no conflict of interest.

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