Adıyaman Üniversitesi Sağlık Bilimleri Dergisi, 2024;10(3):225-235
doi:10.30569.adiyamansaglik.1481290

E-ISSN: 2458-9176

ADIYAMAN ÜNİVERSİTESİ SAĞLIK BİLİMLERİ DERGİSİ
JOURNAL OF HEALTH SCIENCES OF ADIYAMAN UNIVERSITY

Research Article/Özgün Araştırma

Determination of symptoms and symptom clusters in breast cancer patients receiving adjuvant chemotherapy treatment

Adjuvan kemoterapi tedavisi alan meme kanserli hastalarda görülen semptomlar ve semptom kümelerinin belirlenmesi

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Atıf gösterme/Cite this article as: Kurt B. Determination of symptoms and symptom clusters in breast cancer patients receiving adjuvant chemotherapy treatment. *ADYÜ Sağlık Bilimleri Derg*. 2024;10(3):225-235. doi:10.30569.adiyamansaglik.1481290

Abstract

Aim: To examine the symptom clusters in breast cancer patients receiving adjuvant chemotherapy treatment.

Materials and Methods: This descriptive study examined 128 female patients between February 2022-August 2023 using Memorial Symptom Assessment Scale, and EORTC QLQ-C30 Scale.

Results: In cluster analysis, 23 symptoms with a prevalence of >25% were selected, and six clusters were identified. First cluster is nausea, loss of appetite, and fatigue/loss of energy; second cluster is taste change, dry mouth, mucositis, vomiting, weight loss, and diarrhea; third cluster is worrying, feeling nervous, drowsy, and difficulty sleeping; fourth cluster is feeling bloated, shortness of breath, and difficulty swallowing; fifth cluster is alopecia, not look like herself, feeling irritable, sad; and last cluster includes problems with sexual interest, activity, pain, and sweating.

Conclusion: It may be recommended to plan and evaluate applications or interventions in breast cancer patients receiving adjuvant chemotherapy treatment for the six symptom clusters identified.

Keywords: Breast Cancer; Chemotherapy; Nursing; Symptom Cluster.

Öz

Amaç: Adjuvan kemoterapi tedavisi alan meme kanserli hastalarda görülen semptom kümelerini incelemektir.

Gereç ve Yöntem: Şubat 2022-Ağustos 2023 tarihleri arasında 128 kadın hasta ile gerçekleştirilen tanımlayıcı tipteki bu çalışmanın verileri Memorial Semptom Değerlendirme Ölçeği (MSDÖ) ve EORTC QLQ-C30 Yaşam Kalitesi Ölçeği kullanılarak toplandı.

Bulgular: Kümeleme analizinde >%25 prevalansı olan 23 semptom seçildi ve altı semptom kümesi belirlendi. *Birinci küme*; bulantı, iştahsızlık ve halsizlik/enerji kaybı, *ikinci küme*; yiyeceklerin tadını almada değişiklik, ağız kuruluğu, ağız yaraları, kusma, kilo kaybı ve ishal, *üçüncü küme;* endişelenme, kendini sinirli hissetme, uyumada zorluk ve kendini uykulu ya da sersemlemiş gibi hissetme, *dördüncü küme;* şişkinlik hissi, nefes darlığı ve yutma güçlüğü, *beşinci küme*; saç dökülmesi, kendine benzememe, hassas olma ve kendini üzgün hissetme iken *altıncı kümede*; cinsel istek veya aktivite ile ilgili sorunlar, ağrı ve terleme yer almaktadır.

Sonuç: Meme kanserli hastalardaki uygulamaların ya da girişimlerin belirlenen altı semptom kümesine yönelik planlanması ve değerlendirilmesi önerilebilir.

Anahtar Kelimeler: Hemşirelik; Kemoterapi; Meme Kanseri; Semptom Kümesi.

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Geliş Tarihi/Received:09.05.2024 **Kabul Tarihi/Accepted:**04.09.2024 **Yayım Tarihi/Published online:**31.12.2024

Introduction

Breast cancer is the most common type of cancer among women in our country, as in the rest of the world. In the country under study, the age-standard breast cancer incidence rate is 46.6 in a hundred thousand.[1] Breast cancer treatment is carried out using various treatment approaches such as cytotoxic chemotherapy, endocrine therapy, and immunotherapy taking into account the size of the tumor, the absence of lymph node retention, and receptor expression. Chemotherapy, commonly used in cancer treatment, aims to stop cancer from spreading or eliminate it.[2] Chemotherapeutic drugs used in the treatment of breast cancer cause significant symptoms in patients such as pain, fatigue, nausea-breathing, anxiety, depression, sleep problems, and shortness of breath, thereby adversely affecting the quality of life of patients.[3] After treatment, the symptoms associated with chemotherapy have physical effects and have a biopsychosocial adverse effect on the individual.[5] Recent studies have concentrated on symptom clusters to enhance the understanding of how symptoms manifest together. Symptom sets are groups of related symptoms that occur together due to a common cause or similarity. Symptoms that also occur in cancer patients can in themselves affect each other negatively. According to Clark and Talcott, more than one synergistically associated symptom occurring at the same time causes treatment to be ineffective and unexpected therapeutic consequences to occur. One symptom causes other symptoms to appear or become more severe.[4] However, Dong et al.[5] conducted a systematic observational study of symptom sets identified in patients with various types of cancer. This systematic review assessed thirty-three articles and identified many symptom groups with four common groups, including anxiety-depression, nausea-coughing, nausée-loss of appetite, and fatigue-breathing-sleepiness-pain.[5] The major problem that patients undergoing chemotherapy experience is the failure to manage the concomitant symptoms, and as a result, the treatment is adversely affected. In patients receiving chemotherapy, one symptom affects another symptom and even increases its severity.

There is a synergistic interaction between many symptoms, which can increase the morbidity rate of patients. For example, patients with nausea-induced lack of appetite, undernutrition, and proteins deficit may occur.[3,4] In addition, patients with nausea and vomiting may develop sleep disturbances and fatigue problems. Sleep disorders can result in impaired immune functions and increase the risk of infection. Collaborative efforts to address synergistic symptoms in chemotherapy patients have the potential for improvement.[6] This research aims to identify symptom clusters in breast cancer patients undergoing chemotherapy to apply the findings in clinical practice. It is crucial to thoroughly assess the frequency, severity, and discomfort of individual symptoms in clinical studies. Studies of the literature[3-6] show that only the frequency of symptoms has been determined. Studies targeting the frequency of symptoms show that the intensity of the symptoms and the discomfort caused by the symptoms are skipped. Furthermore, since these symptoms can be seen in groups or clusters, the identification of the relationship between the symptoms for effective measurements improves compliance with therapy. To identify the set of symptoms, it is necessary to customize the situations. The methods of selection should include a specific stage of treatment, individuals with a similar diagnosis or sexual relationships, the type of relationships, and the duration of symptoms. It is based on previous single-symptomatic studies for the creation of symptom sets for specific conditions or for the prediction of symptom sets. Literature reviews[5,6] have not found a study covering the whole group of symptoms associated with stage I-IIIA breast cancer patients receiving adjuvant chemotherapy. The concept of symptom grouping is argued to advance the understanding of the synergistic side effects caused by cancer treatment and increase effective nursing efforts. Although they have different indicators and may occur at different stages of the course of the disease, the symptoms often have a common etiology, which is a potential target for intervention. Understanding the set of symptoms associated with breast cancer in the adjuvant

chemotherapy process can be useful in developing effective care plans for affected patients. Symptom groups in this study are thought to influence the evaluation of symptoms as a whole and minimize symptom severity. These results are transferable to the clinical environment in the care of patients with BC undergoing chemotherapy.

This study aimed to draw attention to the importance of identifying and evaluating the symptoms and symptom groups experienced by breast cancer, on the severity of chemotherapy symptoms seen in patients receiving adjuvant chemotherapy therapy.

Research questions

- What symptoms comply with breast cancer patient's experience during chemotherapy treatment?
- What are the symptom clusters experienced by cancer patients during chemotherapy treatment?

Materials and Methods

Type of research

This study was designed as a descriptive study. The study was conducted at the Medical Oncology Department of the University of Hacettepe's Oncological Hospital's Day-Treatment Unit between 01 February 2022 and 07 August 2023. The universe of this research was created by female patients receiving adjuvant chemotherapy treatment at the Day-Treatment Unit of the Department of Medical Oncology of the University of Hacettepe's Oncological Hospital. The sample of the study consisted of female patients between the ages of 18 and 65, who received the Adriamicin-Siclofosphamide (AC) chemotherapy protocol, who knew that they had received at least the first course of chemo, who could communicate, who were willing to participate in the research and who were volunteer. Patients were excluded if they were already receiving AC, ceased participation in the study, their chemotherapy protocol changed, or their treatment was postponed by the doctor because the blood values were not suitable for chemotherapy. A pilot study of 20 patients was carried out using the G Power package program to calculate the number of samples, and the minimum number of patients to be included with 85% force was set at 128.

The Ethics Committee for Non-Interventional Clinical Research at the University of Hacettepe, after receiving written permits from the Directorate of Health and Nursing Services of the University's Oncology Hospital, has evaluated patients who have applied the adjuvant chemotherapy protocol from 1st February 2022 to the Day-Treatment Unit of the Researchers' Oncological Hospital at Hacettebe University, as regards the criteria for inclusion in the study. Patients included in the study were informed by the researcher about the purpose, duration, and method of the study during the admission of the patient. After the information, patients who voluntarily agreed to participate in the study were included in the sampling group with written and verbal permission. The sampled patients were monitored in the hospital when they came to receive treatment throughout the AC protocol. Patients will be interviewed face-to-face in the area where they are being treated. The questions Patient Information Form, The Memorial Symptom Assessment Scale (MSAS), and EORTC QLQ-C30 Quality of Life Scale were addressed to patients by the researcher, and the patient's responses were recorded by him. The patients were evaluated based on their symptoms and quality of life scores during the first week after each cycle. Data collection tools were completed in approximately 30 minutes.

Data collection tools

Patient information form; the patient information form, created by the researcher by scanning the literature, consists of two parts.[3-6] The first part consists of eight questions about the patient's characteristics, such as age, body surface area, number of treatments, civilian condition, the status of having children, educational status, occupation, and cancer in the family, and the second part of the question, the condition of the patient having another disease, the medicines he uses outside of chemotherapy and the type of breast surgery he has undergone.

The Memorial Symptom Assessment Scale (MSAS) was developed by Portenoy et al a 32-

dimensional multidimensional scale used to evaluate the symptoms experienced by cancer patients in the last week.[7] The scale includes three sub-dimensions, which include the frequency, severity, and discomfort of the 22 symptoms in the last week, and two dimensions, including the severity of the 8 symptoms and the decomposition they cause in the patient. The "heat" and "violence" levels of the symptoms are answered in the form of a liqueur of 4, while the "difficulty" levels are replied in a liquéur of 5. The scale consists of “physical symptoms” (insomnia, numbness or loss of energy, pain, feeling asleep or numb, constipation, dry mouth, nausea, vomiting, changes in taste, weight loss, feeling swollen, dizziness), “psychological symptoms" (sickness, feeling sad, feeling nervous, feeling sleepy or numbing, feeling sensitive, difficulty gathering attention) and “general fatigue index” (sense of sadness, anxiety, feelings of self-irritation, sensitivity, lack of appetite, emptiness or energy loss, the sensation of pain, constipating, dryness, feeling somnolent or cumulative). The Memorial Symptom Evaluation Scale (MSAS), conducted by Yildirim et al.[8], was used to evaluate post-chemotherapy symptoms in patients with NHL. MSAS, Cronbach found the alpha ratios between 0.71 and 0.75 for sub-scales and 0.84 for the total.

EORTC QLQ-C30 life quality index (EORTC QLQ-C30) was developed by European Organization for Research Treatment of Cancer[9] and the Turkish validity and reliability was conducted of the by Güzelant et al.[10]. EORTC QLQ-C30, was designed to assess a range of cancer-specific QoL issues relevant to a broad spectrum of cancer patients. This questionnaire consisted of 30 cancer-specific questions with multiple-point scales, including a global health status/QoL scale, 5 functional scales (physical, role, emotional, cognitive, and social), 9 symptom scales (fatigue, nausea, and vomiting and pain, dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulty). multiple-point scales were transformed into standard scores (from 0 to 100). High scores on global health status/QoL and functioning scales represented good QoL, while high scores on the symptom scales indicated more severe symptoms.

Analysis of data

Analyzes were evaluated in 25 package programs of SPSS (Statistical Package for Social Sciences; SPSS Inc., Chicago, IL). In the study, descriptive data are shown as n and % values in categorical data and mean ± standard deviation (mean ± SD) and median (minimum-maximum) values in continuous data.

There is no acceptance of the meaning of the association in determining the clusters of symptoms. Walsh and colleagues (2006) identified the symptoms, although symptoms with a frequency of less than 15% were not evaluated.[11] Kim et al.[12] investigated the connection of at least two symptoms to develop a set of symptoms. Cumulative analysis is a method for categorizing items (such as individuals) or variables (such as symptoms) into groups. Some similarity indicators should be applied to categorize the variables. Columns have been formed so that things in the same column are comparable while ones in separate columns are distinct. A cluster analysis of the symptoms was performed to identify symptoms that often occur together. For this study, each symptom was classed as either present or lacking. To keep the number of symptoms manageable, 23 symptoms with a prevalence of more than 25% were selected for cumulative analysis (Figure 1). A cluster hierarchical approach was applied, with each symptom treated as a single cluster of size one. Then, identical clusters were joined until a single cluster comprising all of the symptoms emerged. The average association approach was adopted, and the absolute value of correlation between symptoms was utilized to assess the similarity of symptom combinations. The final clusters were defined using a correlation score of ≥0.70. In our research, the collection of symptoms was determined using MVSP v.3.12 (Software Multi-Variate Statistical Package) and graphically represented using dendrograms. Dendograms are a type of data presentation that divides it into intrinsic parts at different levels. The vertical lines in the dendrogram refer to linked clusters. For

example, the location of the line on it indicates the distances where the clusters connect. The connection between items increases as their distance decreases.

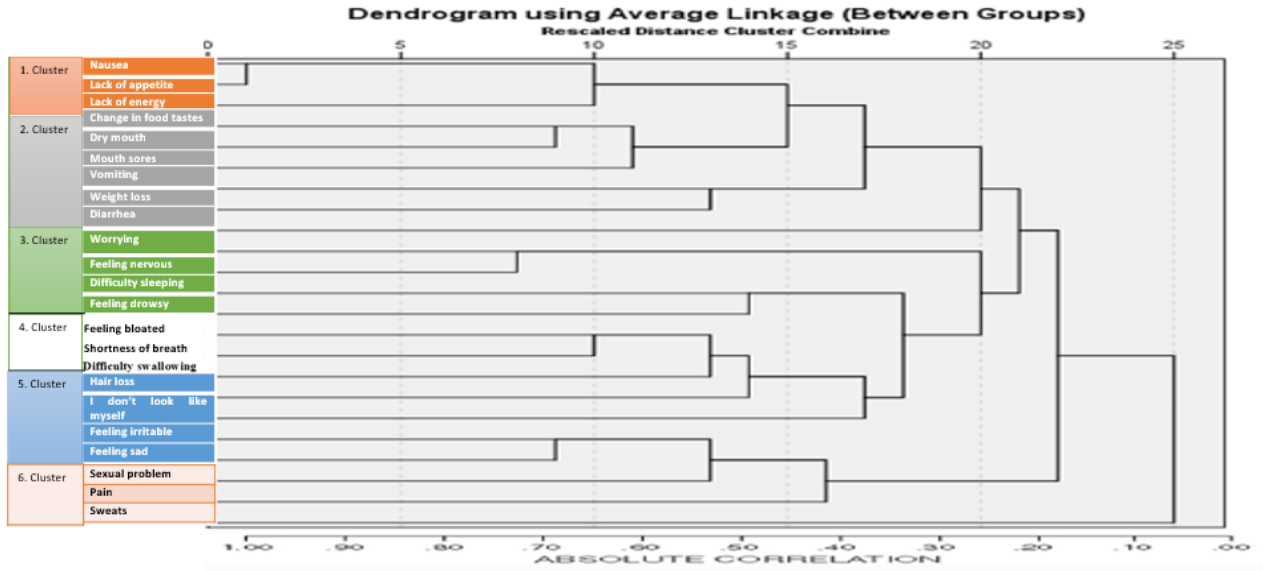

Figure 1. Dendogram.

Ethics committee approval

The ethics board of Hacettepe University Non-Interventional Clinical Research Ethics Committee (GO 21/1287) has authorized the study's conduct. The required permits have been obtained from the Administration of Health and Nursing at the University of Hacettepe Oncology Hospital, where the study was conducted, and material detailing what was learned from the research was submitted for approval. Furthermore, the study's participants provided both verbal and written permissions.

Results

Data on patient (n = 128) characteristics are presented as frequencies and percentages. The mean age of the patients in the study was 41.1 ± 5.3. 87.5% of patients were married. 53.1% of patients were 50 years of age or younger, and 64.9% of patients had a BSA of 1.60 to 1.79. While 67.2% of patients were primary school graduates, 67.2% were unemployed. While 75.0% of patients had a family history of cancer, 60.9% of them had no history of other diseases, and breast conservation surgery was performed in 51.6% of patients (Table 1).

Table 1. Demographic characteristics (n=128).

	n	%
Age		
Mean ± SD= 41.1 ± 5.3 (min: 32-max:58)		
≤50	68	53.1
>50	60	46.9
Chemotherapy Cycles= 1.3 ±1.1 (min:2-max:4)		
BSA		
1.40–1.59	28	21.8
1.60–1.79	83	64.9
1.80–1.99	17	13.3
Marital Status		
Married	112	87.5
Single	16	12.5
Education		
Primary education	86	67.2
High school	41	32.0
University	1	0.8
Occupation		
Unemployed	86	67.2
Public servant	12	9.5
Laborer	8	6.2
Other	22	17.1
A family history of cancer	96	75
Yes	32	25
No		
History of other diseases/Additional drugs	78	60.9
	50	39.1
Yes*		
No		
Surgery type		
Mastectomy	62	48.4
BCS	66	51.6

Abbreviation: BSA, Body Surface Area; BCS, Breast-Conservation Surgery; SD = Standard Deviation *Thyroid, , euthyrox

The number and percent of symptoms evaluated with the MSAS during treatment of first-time breast cancer patients (Table 2, Table 3). The most common symptoms during chemotherapy were nausea (93.2%), lack of appetite (85.1%), change in taste of food (79.6%), and dry mouth (70.3%). The symptoms with the lowest prevalence were coughing (15.6%), challenges focusing attention (14.1%), skin changes (14.1%), itching (14.1%), swelling of hands and feet (11.7%), drowsiness/deafness in hands and legs (11.7%), and problems urination (8.5%).

Table 2. Symptom frequency among patients in the study (n=128).

	Frequency				
Symptoms	**Yes** n (%)	**Rarely** n (%)	**Occasionally** n (%)	**Frequently** n (%)	**Almost constantly** n (%)
Nausea	120 (93.2)	4 (3.3)	2 (1.7)	10 (8.3)	104 **(86.7)**
Lack of appetite	109 (85.1)	1 (0.9)	1 (0.9)	98 **(89.9)**	9 (8.3)
Lack of energy	102 (79.6)	2 (2.0)	1 (1.0)	95 **(93.1)**	4 (3.9)
Change in food tastes	100 (78.1)	4 (4.0)	0 (0.00)	6(6.0)	90 **(90.0)**
Dry mouth	90 (70.3)	2 (2.2)	78 **(86.7)**	7 (7.8)	3 (3.3)
Mouth sores	85 (66.4)	5 (5.9)	10 (11.8)	60 (72.9)	8 (9.4)
Vomiting	85 (66.4)	12 (14.1)	5 (5.9)	62 (70.6)	8 (9.4)
Weight loss	81 (63.2)	1 (1.2)	5 (6.2)	20 (24.7)	55 (67.9)
Diarrhea	80 (62.5)	6 (7.5)	4 (5.0)	20 (25.0)	50 (62.5)
Worrying	76 (59.3)	1 (1.3)	0 (0.00)	55 (72.4)	20 (26.3)
Feeling nervous	76 (59.3)	6 (7.9)	9 (11.8)	50 (65.8)	11 (14.5)
Difficulty sleeping	74 (57.8)	6 (8.1)	10 (13.5)	48 (64.9)	10 (13.5)
Feeling drowsy	70 (54.6)	7 (10.0)	9(12.9)	44 (62.9)	10 (14.2)
Feeling bloated	66 (51.5)	3 (4.5)	6 (9.1)	35 (53.1)	22 (33.3)
Shortness of breath	66 (51.5)	13 (19.7)	0 (0.00)	35 (53.0)	18 (27.3)
Difficulty swallowing	63 (49.2)	0 (0.00)	17 (27.0)	31 (49.2)	15 (23.8)
Hair loss	60 (46.8)	0 (0.00)	8 (13.3)	22 (36.7)	30 (50.0)
I don’t look like myself	60 (46.8)	7 (11.7)	5 (8.3)	20 (33.3)	28 (46.7)
Feeling irritable	53 (41.4)	3 (5.7)	8 (15.1)	20 (37.7)	22 (41.5)
Feeling sad	50 (39.1)	0 (0.00)	8 (16.0)	22 (44.0)	20 (40.0)
Sexual problem	42 (32.8)	4 (9.5)	0 (0.00)	18 (42.9)	20 (47.6)
Pain	34 (26.5)	1 (2.9)	0 (0.00)	15 (44.2)	18 (52.9)
Sweats	34 (26.5)	3 (8.8)	0 (0.00)	13 (38.3)	18 (52.9)
Dizziness	32 (25)	1 (3.1)	0 (0.00)	13 (40.6)	18 (56.3)
Constipation	32 (25)	2 (6.2)	0 (0.00)	15 (46.9)	15 (46.9)
Cough	20 (15.6)	10 (50.0)	8 (40.0)	2 (10.0)	0 (0.00)
Difficulty concentrating	18 (14.1)	9 (50.0)	5 (27.8)	0 (0.00)	4 (22.2)
Skin Change	18 (14.1)	6 (33.4)	8 (44.4)	4 (22.2)	0 (0.00)
Itching	18 (14.1)	4 (22.2)	9 (50.0)	3 (16.7)	2 (11.1)
Swelling of arms or legs	15 (11.7)	7 (46.7)	4 (26.7)	3 (20.0)	1 (6.6)
Numbness/tingling	15 (11.7)	4 (26.7)	4 (26.7)	5 (33.3)	2 (13.3)
Problems with urination	11 (8.5)	2 (18.2)	5 (45.5)	3 (27.2)	1 (9.1)

The Memorial Symptom Assessment Scale, which examined the symptom frequency of breast cancer patients treated with adjuvant chemotherapy, identified that the symptoms experienced were "often" impotence or energy loss (93.1%) and appetite loss (89.9%), while nausea was experienced as "almost constant" (86.7%). Into the Memorial Symptom Assessment Scale, the symptom severity in breast cancer patients undergoing adjuvant chemotherapy included nausea categorized as "very severe" (91.6%), sores in the mouth (88.2%), and a change taste (84.0%).

When the Memorial Symptom Assessment Scale was applied to assess symptom lack in breast cancer patients undergoing adjuvant chemotherapy treatment, symptom nausea was regarded as "a little more" (85%), while symptom appetite loss was assessed as "too much" (77.3%).

Table 3. Symptom distress and severity among patients in the study (n=128).

Symptoms	Distress					Severity			
	Not at all n (%)	**A little bit** n (%)	**Somewhat** n (%)	**Quite a bit** n (%)	**Very much** n (%)	**Slight** n (%)	**Moderate** n (%)	**Severe** n (%)	**Very severe** n (%)
Nausea	1 (0.8)	0 (0.00)	0 (0.00)	102 (**85**)	17 (14.2)	1 (0.8)	3 (2.6)	6 (5)	**110 (91.6)**
Lack of appetite	0 (0.00)	0 (0.00)	0 (0.00)	10 (22.7)	55 (**77.3**)	3 (2.7)	7 (6.4)	**87 (79.8)**	12 (11.1)
Lack of energy	7 (6.8)	0 (0.00)	0 (0.00)	42 (54.9)	39 (38.3)	5 (4.9)	**81 (79.4)**	9 (8.8)	7 (6.9)
Change in food tastes	6 (6.0)	2 (2.0)	18 (18.0)	44 (44.0)	30 (30.0)	4 (4)	3 (3)	9 (9)	**84 (84)**
Dry mouth	2 (2.2)	1 (1.1)	35 (38.9)	38 (42.2)	14 (15.6)	6 (6.7)	**73 (81.1)**	5 (5.6)	6 (6.6)
Mouth sores	5 (5.9)	4 (4.7)	25 (29.4)	33 (38.8)	18 (21.2)	0 (0.00)	0 (0.00)	10 (11.8)	**75 (88.2)**
Vomiting	5 (5.9)	4 (4.7)	25 (29.4)	33 (38.8)	18 (21.2)	1 (1.2)	8 (9.5)	11 (12.9)	**65 (76.4)**
Weight loss	2 (2.5)	0 (0.00)	14 (17.3)	38 (46.9)	27 (33.3)	8 (9.8)	3 (3.8)	11 (13.6)	59 (72.8)
Diarrhea	0 (0.00)	0 (0.00)	12 (15.0)	24 (30.0)	44 (55.0)	6 (7.5)	4 (5)	12 (15)	58 (72.5)
Worrying	1 (1.3)	1 (1.3)	8 (10.5)	36 (47.4)	30 (39.5)	7 (9.3)	4 (5.3)	43 (56.5)	22 (28.9)
Feeling nervous	1 (1.3)	1 (1.3)	8 (10.5)	36 (47.4)	30 (39.5)	8 (10.5)	9 (11.9)	49 (64.5)	10 (13.1)
Difficulty sleeping	0 (0.00)	0 (0.00)	22 (29.7)	20 (27.1)	32 (43.2)	6 (8.2)	12 (16.2)	56 (**75.6**)	0 (0.00)
Feeling drowsy	3 (4.3)	2 (2.8)	0 (0.00)	38 (54.3)	27 (38.6)	9 (12.8)	9 (12.9)	52 (74.3)	0 (0.00)
Feeling bloated	3 (4.5)	3 (4.5)	3 (4.5)	35 (53.1)	22 (33.4)	4 (6.2)	7 (10.6)	30 (45.4)	25 (37.8)
Shortness of breath	3 (4.5)	3 (4.5)	3 (4.5)	35 (53.1)	22 (33.4)	3 (4.5)	6 (9.1)	35 (53.1)	22 (33.3)
Difficulty swallowing	0 (0.00)	0 (0.00)	5 (7.9)	34 (53.9)	24 (38.2)	14 (22.3)	6 (9.5)	34 (53.9)	9 (14.3)
Hair loss	1 (1.7)	4 (6.7)	6 (10.0)	34 (56.6)	15 (25.0)	3 (5)	4 (6.7)	43 (71.7)	10 (16.6)
I don't look like myself	1 (1.7)	4 (6.7)	6 (10.0)	34 (56.6)	15 (25.0)	7 (11.7)	5 (8.4)	25 (41.6)	23 (38.3)
Feeling irritable	11 (20.8)	3 (5.7)	8 (15.1)	8 (15.1)	23 (43.3)	12 (22.6)	7 (13.3)	25 (47.2)	9 (16.9)
Feeling sad	1 (2.0)	2 (4.0)	2 (4.0)	24 (48.0)	21 (42.0)	10 (20)	7 (14)	23 (46)	10 (20)
Sexual problem	0 (0.00)	0 (0.00)	19 (45.2)	19 (45.2)	4 (9.6)	4 (9.6)	5 (11.9)	12 (28.5)	21 (50)
Pain	2 (5.9)	0 (0.00)	0 (0.00)	22 (64.7)	10 (29.4)	6 (17.6)	5 (14.8)	12 (35.2)	11 (32.4)
Sweats	2 (5.9)	0 (0.00)	0 (0.00)	22 (64.7)	10 (29.4)	7 (20.5)	2 (5.8)	15 (44.2)	10 (29.5)
Dizziness	0 (0.00)	0 (0.00)	0 (0.00)	26 (81.3)	6 (18.7)	1 (3.2)	2 (6.2)	15 (46.8)	14 (43.8)
Constipation	0 (0.00)	0 (0.00)	0 (0.00)	26 (81.3)	6 (18.7)	2 (6.2)	0 (0.00)	15 (46.9)	15 (46.9)
Cough	2 (10.0)	0 (0.0)	2 (10.0)	13 (65.0)	3 (15.0)	1 (5)	4 (20)	4 (20)	11 (55)
Difficulty concentrating	3 (16.7)	4 (22.2)	0 (0.00)	9 (50.0)	2 (11.1)	7 (38.8)	6 (33.4)	0 (0.00)	5 (27.8)
Skin Change	3 (16.7)	4 (22.2)	0 (0.00)	9 (50.0)	2 (11.1)	7 (39)	8 (44.4)	3 (16.6)	0 (0.00)
Itching	3 (16.7)	4 (22.2)	0 (0.00)	9 (50.0)	2 (11.1)	4 (22.3)	8 (44.4)	6 (33.3)	0 (0.00)
Swelling of arms or legs	5 (33.4)	0 (0.00)	4 (26.6)	4 (26.6)	2 (13.4)	3 (20.1)	5 (33.3)	6 (40)	1 (6.6)
Numbness/tingling	2 (13.4)	0 (0.00)	6 (39.8)	5 (33.4)	2 (13.4)	3 (20.2)	4 (26.6)	7 (46.6)	1 (6.6)
Problems with urination	0 (0.00)	0 (0.00)	4 (36.4)	4 (36.4)	3 (27.2)	3 (13.7)	7 (49.9)	4 (36.3)	0 (0.00)

The Memorial Symptom Assessment Scale identified six separate groups of symptom clusters. A correlation of ≥0.70 was identified in determining a cluster (Figure 1). The table states that symptoms in each cluster have been grouped in decreasing order of total prevalence. The first group includes "nausea, appetite loss, and lack of weight/energy loss," the second group includes "changes in taste, dry mouth, mouth wounds, vomiting, weight loss, and diarrhea," the third group includes "depression, feeling nervous, difficulty sleeping, and feeling asleep or numb," the fourth group includes "sense of thirst, shortness of breath, and difficulty swallowing", the fifth group includes "hair loss, I don't like myself, feeling sensitive and sad", and the last group includes "problems with sexual desire or activity, pain, and sweating".

Discussion

Multiple symptoms in patients undergoing chemotherapy for breast cancer are different depending on what is causing the cancer. The patient's quality of life and the effect of the treatment have been impacted by symptom sets, whose effectiveness is following the particulars of the disease and the treatment strategy. Six clusters have been identified in the research we conducted based on the corresponding decrease in the patient's overall symptom prevalence. "Nausea, appetite loss, and intolerance/energy loss" are included in the first cluster. In literature studies, patients undergoing adjuvant chemotherapy commonly suffer from nausea, loss of appetite, or aggregation of energy loss. Moreover, ten symptoms that showed up in three of the six clusters strongly suggested the presence of digestive-related problems. The studies have shown that both before and during adjuvant therapy, there was negligible disparity between the quantity of symptoms and symptoms within a cluster in patients with breast cancer.[13-15] Kim et al. identified 10 symptoms using factor analysis. According to the research, a gastrointestinal (GI) cluster involving decreased appetite, nausea, and vomiting from the beginning of treatment until the fourth cycle has been identified in 44% of the women undergoing chemotherapy.[13] A three-point assessment was used in another research investigation to determine whether nausea is part of a set of symptoms. As a result of this, symptoms in the cluster that included nausea, dry mouth, drowsiness, lack of energy, and appetite loss were noted in the first measurement of chemotherapy. There is apprehension and a lack of energy at the end of the first treatment, and at the end of the second therapy, there is nausea and swelling along with a lack of energy.[14] The second and fourth clusters of gastrointestinal symptoms are also relevant to our study. It is consistent with the literature at this point.

The literature has shown that pain-fatigue-sleep occurs simultaneously with cancer treatments and as psychoneurological symptoms.[16-20] Differences in additional symptoms, such as nausea, that contributed to the psychoneurological symptom set were to be the result of differences in the number of symptomatic individuals used for the symptom clustering, the severity of the symptoms, the frequency of the symptoms, and the degree of symptom absence in an identifying-type study of 100 breast cancer patients undergoing stage I-IIIA chemotherapy treatment.[16] At least two of these psychological symptoms, known as psychological clusters, such as sadness, stress, and depression, occur before starting therapy. In addition, fatigue and/or insomnia have been associated with anxiety and sadness in this cluster.[21,22] Anxiety, sadness, worry, and anxiousness have all been linked to cancer treatment, and more than one of these symptoms may occur consecutively. These symptoms have the potential to result in a psychological cluster.[23-26] Since there are numerous symptoms in this psychological cluster, it becomes essential to thoroughly analyze these studies to verify consistency. Every cluster of these studies contains at least one of the psychological cluster symptoms. Our study in particularly, correlates the symptoms in the third cluster with the literature regarding "sickness, feeling anxious insomnia, and feeling asleep or fatigued." Although the underlying cause of these clusters of symptoms is unknown, pro-inflammatory cytokines, hyperactivation of the hypothalamic-hypofyse-adrenal (HPA) axis, and alterations

in the serotonin (5-HT) system might all contribute to psychoneurological symptoms.[27,28]

According to studies, women with breast cancer who accomplished treatment had a cluster known as the menopausal cluster, which included hot flashes, vaginal dryness, and at nocturnal sweats. Symptom sets were also brought about based on vasogenic symptoms with severity ranging from moderate to severe.[22,29] However, Li and Ark revealed that a collection of symptoms consisting only of hot flashes and nocturnal sweats does not include vaginal dryness.[30] In our study, the sixth category, known as vasomotor symptoms, has been identified as "problems with sexual desire or activity, pain, and sweating".

Known as adjuvant chemotherapy, women who have undergone surgery, specifically breast surgery, negatively influences their sexual behaviors throughout the treatment process. These adverse conditions could be influenced by changes in sexual development, changes in body image induced by cancer therapies (hair loss), and communication issues with the partner.[31,32] Our study's fifth cluster of symptoms, such as "hair loss, I don't look like myself, being sensitive and feeling sad about myself," are sexual life-related symptoms. An analysis comparing the sexuality of women with breast cancer with those without a history of cancer revealed that breast cancer patients had worse sexual functioning, decreased sexual desire, disliked sex, and other sexual issues.[33] Mastectomy is perceived as a loss of masculinity since the breast has become a symbol of beauty and sexuality in society, generating issues with body image and self-esteem.[34]

Symptom clusters are also considered crucial for clinical assessment the processes. If a particular treatment symptom impact is desired in a symptom control study, the other symptoms in that cluster should also be included as criteria for the result; otherwise, a meaningful therapy effect may be omitted. Our findings represent that it is indispensable and therapeutically relevant to investigate the association between symptoms not just among individuals, but also with other associated symptom features. The definition of symptom models is both intellectual and therapeutic, allowing us to get a better understanding of cancer's natural progression and offer more effective symptom management.

Limitations of the research

This study had certain limitations. Firstly, the data acquired in this research mainly represents the perspectives of patients at the hospital where the survey was conducted, therefore the conclusions cannot be generalized aside from sampling.

Second, this study was conducted in only patient receiving AC protocol. Therefore, other studies can determine the effect of the symptom clusters other chemotherapy protocols (oxaliplatin, taxol, etc.) and other cancer patients (stomach, lung, etc.).

Conclusion

The study we performed was conducted on a group of patients getting the same similar therapy to evaluate the set of symptoms, using female participants and standard tools. Clinical methods or initiatives emphasizing a particular symptom in breast cancer patients undergoing adjuvant chemotherapy could effectively manage multiple sub-symptoms within the six clusters to which the symptom belongs at affordable rates. It is additionally anticipated that the creation of individual therapies could supply the patient with vital information.

The assessment for specific biological stimulants during breast cancer therapy is advised based on subjective patient remarks and quantitative analytical data. Such research will assist us in identifying common biological pathways that underlie many reasons for symptom sets, as well as providing high-level information on efficient strategies for targeting these pathways. Our study results suggest the possibility of researching symptom clusters in different chemotherapy types and disease groups. The other studies can determine the effect of the symptom clusters on other chemotherapy protocols (oxaliplatin, taxol, etc.) and other cancer patients (stomach, lung, etc.).

Ethics Committee Approval

This study, approval was obtained from the Hacettepe University Non-Interventional Clinical Research Ethics Committee (Number GO 21/1287). All interventions were carried out following institutional ethical standards and the national research committee, including the 1964 Declaration of Helsinki and subsequent amendments. Furthermore, the study's participants provided both verbal and written permissions.

Informed Consent

Informed consent was obtained from the individuals participating in the study.

Conflict of Interest

The authors report no actual or potential conflicts of interest.

Author Contributions

Responsibility for the study design: BK; Responsibility for supervising the study: BK; Responsibility for data analysis: Statistics expert; Provision of peer review during the analysis process: Statistics expert, BK; Responsibility for manuscript writing: BK.

Acknowledgments

The author would like to acknowledge all patients who participated in this study.

Peer-review

Externally peer-reviewed.

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