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Breast cancer side effect evaluation using Naranjo Algorithm, A Cross-sectional questionnaire based descriptive study

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Abstract

Background

Breast cancer remains the most prevalent malignancy in women worldwide, significantly impacting their quality of life, particularly during chemotherapy. Despite advancements in therapeutic options, treatment-related side effects continue to pose challenges.

The main objectives of this study were to evaluate patient-reported side effects among breast cancer patients undergoing chemotherapy, assess the severity of these adverse effects using the Naranjo scale, and analyze their correlation with chemotherapy protocols. The objective was to guide healthcare practitioners in developing tailored supportive care strategies to improve treatment outcomes and quality of life.

A cross-sectional, questionnaire-based descriptive study was conducted in oncology departments across healthcare settings in Islamabad, Rawalpindi, and Lahore from April 2024 to March 2025. Data were collected from 368 confirmed breast cancer patients undergoing chemotherapy using a self-structured questionnaire incorporating the Naranjo algorithm. Descriptive and inferential statistics were analyzed using SPSS version 20.

Participants reported significant treatment-related side effects, including nausea (76.1%), alopecia (66.7%), fatigue (87%), and diarrhea (49.4%). The Naranjo algorithm identified 45.2% of reactions as probable, 35.6% as possible, and 19.2% as definite. Factors such as age, educational status, and chemotherapy protocols were significantly associated with the severity of side effects. Chemotherapeutic agents mostly related to reported side effects were Taxanes, cyclophosphamide, and anti-metabolites.

Patient-reported outcomes highlighted the substantial burden of chemotherapy-related adverse effects. These findings underscore the need for personalized supportive care strategies to enhance treatment adherence and mitigate side effects, ultimately improving the overall quality of life in breast cancer patients. Integrating patient-centered approaches into clinical practice is crucial for achieving holistic cancer care.

KEYWORDS
Breast Cancer, Naranjo Algorithm, Side effects, Questionnaire, Cross-sectional Study

1.0 INTRODUCTION

Breast cancer ranks as the second most prevalent malignancy and is the foremost cause of cancer-related mortality among women, which translated into 685,000 fatalities worldwide in 2020. Breast

cancer accounts for one in four cancer cases and one in six cancer fatalities among women globally. The incidence of breast cancer is rising in young women although more common in women fifty years of age and older. It is currently the second leading cause of death from cancer in women aged 0–39 worldwide, causing 44,800 deaths annually [1]. Tumor cells are pleomorphic, with prominent nucleoli and high mitotic activity. Necrosis and calcifications are identifiable in more than fifty percent of case [2]. This lesion predominantly affects those 30- to 40 years and is more frequently associated with aberrations of BRCA1 germ-line that is; breast cancer Gene1. At microscopically, the type is clearly circumscribed. The tumors range in the dimension of very pleomorphic cell tumors with characteristic massive syncytial growth with some mitotic counts and several inflammatory lympho- plasmacytic invasions. Often another characteristic shared consists of spindle-cell metaplasia together with large tumorous cells [3]. A number of papers focus on exploring the genetic profiles of breast cancer to classify these cancers into groups or entities, which help in clinical management, devising of epidemiological and functional studies and conducting clinical trials. Detailed gene expression profile studies have identified four clinically relevant molecular subtype naming Luminal A, Luminal B, $HER2^+$ and triple negative group [4]. The genetic and epigenetic changes in cancer cells result in the hyper-activation of some signaling pathways. The mutations are then controlled by signaling pathways to suppress the proliferation, survival, and migration of tumor cells. For instance, it has been proved that the inhibition of some pathways such as the hexosamine biosynthesis pathway, leads to the proliferation of breast cancer [5]. The stage of breast cancer is determined by the size, type, and extent of infiltration of the tumor into the surrounding tissues of the breast. Stage 0 represents a non-invasive cancer whereas the invasive one is stated as stage 4 [6]. The treatment of breast cancer is contingent on breast cancer staging. DCIS is managed with lumpectomy (aiming for 2-mm surgical margins) and radiation therapy, or via mastectomy. A sentinel lymph node (SLN) biopsy is performed concurrently after mastectomy to ascertain the improbable occurrence of lymph node involvement. Radiation therapy is provided to individuals undergoing a lumpectomy; this combination is regarded as a breast-conserving treatment. Radiotherapy should be delayed in patients with tiny, low-grade lesions assessed for low risk of recurrence. The use of radiotherapy is discouraged in patients treated with mastectomy. Women who have estrogen receptor-positive ductal carcinoma in situ and who will retain breast tissue should receive at least five years of endocrine therapy. Endocrine therapy for these patients would include tamoxifen in the premenopausal patients or both tamoxifen and an aromatase inhibitor for postmenopausal patients [7]. Stages I-III (Early Invasive and Locally Advanced, Non-metastatic Breast Cancer). Non-metastatic breast cancer is managed using preoperative and postoperative systemic medicines, which encompass chemotherapy, endocrine therapies, and immunotherapy utilizing monoclonal antibodies targeting tumor receptors, as well as surgical intervention and radiation therap. Preoperative

therapy is absolutely not indicated in early invasive breast cancers (I, IIa, IIb) because, due to small tumor size, these tumors are often excised completely by lumpectomy. Preoperative chemotherapy is given to patients who have large primary tumors compared to the breast size and want to undergo breast- conserving surgery. It is also used for patients whose conditions are inoperable. Preoperative treatment with trastuzumab and/or pertuzumab, monoclonal antibodies against ERBB2, is given with chemotherapy in ERBB2-positive cancer. Patients with low-risk estrogen receptor–positive disease are also suitable candidates for preoperative systemic treatment only, and such individuals do not need surgery [8]. Adjuvant systemic therapy for women with early-stage breast cancer has been fully studied. The use of chemotherapy and chemo-hormonal therapy leads to improvements in disease-free survival and overall survival in patients whose breast cancer may be resected. The other patients are treated with chemotherapy. But chemotherapy side effects may be hazardous which can be classified as acute effects and long-term consequences. Short-term effects commonly occur during the treatment period and tend to resolve within months after completion of treatment. Long-term effects may appear later and continue for a long period, and most of them tend to persist for many years [9]. Generally, regimens devoid of anthracyclines exhibit less grade 3–4 short-term toxicities compared to anthracycline-based regimens. Neuropathy is infrequently observed with the combination treatment of cyclophosphamide, methotrexate, and 5- fluorouracil (CMF) or the methotrexate plus 5-fluorouracil (MF) protocols. Conversely, emesis (i.e., nausea and/or vomiting), alopecia, and myelosuppression (mostly neutropenia) are frequently to very frequently observe with the CMF regimen. Mucositis occurs less frequently with intravenous CMF than with oral CMF. Although these toxicities are common, they are generally mild to moderate in intensity. Patients treated with these regimens are at risk for complete alopecia; however, when alopecia develops with CMF, it typically is at least partially affected [9]. Numerous adjuvant therapy trials have noted an increased risk of thrombosis. The risk of thrombosis appears to be established during the time of active treatment and declines subsequently. The duration of treatment considerably affects the overall side effect load a woman is likely to experience, since the majority of the short-term side effects resolve with therapy. The great majority of treatment regimens take about 4 to 6 months [9].

In addition to the immediate toxic effects of chemotherapy, there are other late or chronic consequences of therapy. Some subsets of patients consistently experience late consequences, such as premature ovarian failure, secondary leukemia and other syndromes that came in rare cases of therapy. Additional issues associated with premature ovarian failure include menopausal symptoms, including hot flashes, genitourinary complications, as well as psychosocial and psychosexual challenges. Women in early menopause lose bone mineral density at a very rapid rate [10]. Weight gain is found to occur more frequently among premenopausal women than in postmenopausal women. It is more commonly observed that the risk of weight gain in the patients who enter chemotherapy-induced menopause is greater. The occurrence of anthracycline- induced

cardiac dysfunction increases with increasing cumulative dosage of anthracycline (either doxorubicin or epirubicin) administered. Leukemia or myelodysplastic syndromes (MDSs) due to adjuvant therapy are extremely rare yet disastrous effects of treatment [10].

Patient-reported side effects became a vital component of healthcare research, offering significant insights into patients' subjective experiences. Comprehending side effects from the patients' viewpoint was essential, as it facilitated a more thorough assessment of the treatment's effects beyond conventional clinical metrics. This resulted in more individualized care, where actions were customized not only to manage the disease but also to alleviate the most burdensome adverse effects experienced by patients. This study sought to address this gap by evaluating the side effects experienced by breast cancer patients receiving chemotherapy. This research emphasized patient-reported outcomes, fostering a patient- centered strategy in clinical practice that ensured treatment programs were effective in illness management while preserving patients' quality of life. The research was crucial for reconciling clinical efficacy with patient experience, guaranteeing that breast cancer treatment achieved not only survival but also the dignity and well-being of individuals undergoing chemotherapy. The study's results offered significant insights for physicians and healthcare teams, aiding them in more accurately predicting and managing the side effects that patients were prone to encounter. This resulted in more informed decisions on chemotherapy treatments and the formulation of care plans. Comprehending patient experiences enhanced physicians' ability to deliver superior patient education and support. This equipped patients with knowledge regarding chemotherapy, alleviated their worry, and enhanced their coping mechanisms during treatment. Furthermore, this study has identified the gaps in few existing studies by exploring additional data reported by patients' based on their experiences regarding chemotherapy thereby, will be helpful in modifying the existing healthcare policies, promoting the incorporation of patient-reported outcomes into standard clinical practice. The chemotherapy regimen and particular patient characteristics, thereby endorsing the shift towards personalized medicine, which tailored treatment to both the cancer and the patient's unique requirements. This study was essential as it sought to link clinical success with the actual experiences of patients, fostering more compassionate and effective care for breast cancer patients receiving chemotherapy. The main objectives of this study were to evaluate and record the adverse effects reported by breast cancer patients receiving chemotherapy. The study sought to identify and classify the prevalent side effects reported by patients undergoing chemotherapy and assess the severity and influence of these symptoms on patients' quality of life. It examined the correlation between various chemotherapy protocols and the kind, prevalence, and severity of documented adverse effects. It offered insights into patient preferences and concerns regarding the management of chemotherapy-induced side effects. Additionally, it formulated recommendations for healthcare practitioners to enhance supportive care and patient counseling based on findings from patient- reported

outcomes. The study aimed to improve comprehension of the real-world effects of chemotherapy on breast cancer patients, ultimately fostering better patient-centered care methodologies. In 2020, a descriptive cross-sectional study analyzed the relationship between the negative effects of chemotherapy and the quality of life of patients suffering from breast cancer. The study targeted 110 women suffering from breast cancer who had been treated with docetaxel, epirubicin and cyclophosphamide and the emphasis was placed on negative effects also the majority of the patient's reported quality of life to be affected by adverse effects which included nausea, dysgeusia, peripheral neuropathy, anorexia, myalgia and even peripheral edema [11]. In 2018, the United States experienced 234,087 cases of breast cancer (crude rate: 85/105), the United Kingdom had 55,439 cases (crude rate: 94/105), France registered 56,162 cases (crude rate: 99/105), Germany documented 71,888 cases (crude rate: 85.4/105), and Japan noted 66,101 cases (crude rate: 58/105)[12]. Belgium has the highest incidence rate in the entire world, with a crude rate of 113/105; on the other hand, Australia has the highest incidence on continents, with a crude rate of 94/105. In Poland, the most common malignancy found among women is breast cancer. Its cases have been increasingly reported (1990 at 8,000 new cases and in 2018, 20,203 new cases). The mean incidence rate in Europe is 84 per 105 [12]. The lowest incidence rates are reported in countries of Southeast Asia and Africa, where the standardized incidence rate remains below 25 per 100,000 populations. In 2018, the lowest incidence rates were reported in Bhutan (crude rate: 5 per 100,000) and the Republic of The Gambia (crude rate: 6.5 per 100,000). Despite the improved accuracy of early diagnoses and the rapid progress in drug treatments in recent years, breast cancer continues to be the leading cause of cancer-related deaths among women worldwide. To date, malignant neoplasms among women remain a number one cause of death. Data in 2018 show that 626,679 deaths were from breast cancer [12]. The International Agency for Research on Cancer (IARC) shows that GLOBOCAN 2020 reported the highest incidence and prevalence of breast cancer within the 185 countries involved. This particular type of cancer is the most often diagnosed, estimated to be 2.3 million new cases which represent 11.7% of all cancer diagnoses. Additionally, statistics for the United States project a new case and death figures of 280,000 and 40,000, respectively, for the same period. About one in four women is diagnosed with breast cancer, and one in eight women dies from the disease [13]. Answers from 9,766 Pakistani women across 18 studies were disturbingly low on knowledge regarding breast cancer: risk factors, 42.7% (95% CI: 34.1%- 51.4%); symptoms, 41.8% (95% CI: 26.2%-57.5%); diagnostic methods, 36.3% (95% CI: 23.1%-49.4%); treatments, 46.6% (95%CI:13.5%-79.8%). The prevalence of breast self-examination (BSE) was 28.7% (95% CI: 17.9%-39.6%), and the prevalence of having ever done a clinical breast exam (CBE) was 15.3% (95% CI: 11.2%-19.4%). Knowledge of breast cancer was strongly related to increased educational achievement, age, and socio-economic level [14].

2.0 MATERIALS AND METHODS

Study Design

The present study was descriptive cross-sectional study.

2.1. Study Population and Settings

The study was conducted in oncology departments of the following Healthcare settings of twin cities (Islamabad and Rawalpindi) and Lahore. Mayo Hospital Lahore, Pakistan. Zest Oncologist Consultant Islamabad, Pakistan. Nuclear Medicine Oncology and Radiotherapy Institute (NORI) Islamabad, Pakistan. The study included all the confirmed patients of Breast Cancer undergoing chemotherapy.

2.2. Duration of Study

The study was conducted from April 2024 to March 2025.

2.3. Sample Size

Convenient sampling technique was used, which is a type of non- probability sampling. Rao-soft sample size calculator was used to calculate sample size at 95% confidence interval and 5% margin of error, where N=368 breast cancer patients were approached conveniently.

2.4. Study Instrument

Self-structured questionnaire was designed using variables from different pre-validated literature studies [9]. Naranjo scale was used to evaluate adverse effects of chemotherapy as indicated in **Table 1**. The Naranjo Algorithm, or Adverse Drug Reaction Probability Scale, is a method used to assess whether there is a causal relationship between an identified untoward clinical event and a drug using a simple questionnaire to assign probability scores.

2.5. Cutt off Point

The scale consists of 10 questions that are answered as 'Yes', 'No' or 'Do not know'. Different point values (0, +1 or +2) are assigned to each answer. The final score is the sum of the single component scores. In the Naranjo algorithm, ADRs were categorized into definite, probable, possible, and doubtful [15].

Table 1. Naranjo Assessment Scale

Total Score	Category
>9	Highly Probable
5-8	Probable
1-4	Possible
0	Doubtful

2.6. Data Collection

The data was analyzed using (SPSS) statistical package for the social sciences software version 20. Descriptive statistics was used to evaluate frequency, percentage and cross-tabulation whereas inferential statistics like chi-square was used to find association among chemotherapeutic agents and their side effects and correlation was used to find dose dependent severity of

side effects.

2.7. Study Approval

This study was conducted with the permission of the respective institute Akson College of Pharmacy Joint venture (JV) with Mirpur University of Science & Technology, Mirpur, AJK bearing reference number 551/09/ACP/24. The permission from Executive Directors of aforementioned study settings was also taken prior to the conduction of the study.

3.0. RESULTS

3.1. Pre-Testing Results

The study comprised 368 (100%) female participants. The majority were aged between 41-60 years, accounting for 172 (46.7%), followed by 114 (31%) participants aged above 60 years, 51 (13.9%) aged 31-40 years, and 31 (8.4%) aged 21-30 years. Regarding occupational status, 261 (70.9%) participants were unemployed, while 107 (29.1%) were employed. Most participants were married, with 322 (87.5%), whereas 46 (12.5%) were single.

3.2. Demographic Results

In terms of residency, 221 (60.1%) participants resided in urban areas, while 147 (39.9%) lived in rural regions. Educational status revealed that 181 (49.2%) participants were uneducated, 106 (28.8%) had received secondary education, and 81 (22%) had attained higher education. The weight distribution of participants showed that the majority, 209 (56.8%), weighed between 61-80 kg, followed by 82 (22.3%) participants who weighed between 40-60 kg, and 77 (20.9%) who weighed more than 80 kg. Regarding family history of breast cancer, 332 (90.2%) participants reported no family history, while 14 (3.8%) had a mother, 16 (4.3%) had a grandmother, and 6 (1.6%) had a sister with a history of breast cancer. In terms of other cancer histories, the majority, 325 (88.3%), reported no history of cancer. Among those with a history, 16 (4.3%) had ovarian cancer, 14 (3.8%) had endometrial cancer, and 13 (3.5%) reported other types of cancers. A detailed description is given below in **Table 2.**

Table 2: Patients Demographics

Demographic Variables		Frequency (n)	Percentage (%)
Gender	Female	368	100
Age (years)	21-30	31	8.4
	31-40	51	13.9
	41-60	172	46.7
	>60	114	31
Occupation	Employed	107	29.1
	Unemployed	261	70.9

Marital Status	Single	46	12.5
	Married	322	87.5
Residency	Rural	147	39.9
	Urban	221	60.1
Educational Status	Uneducated	181	49.2
	Secondary	106	28.8
	Higher	81	22.0
Weight (kg)	40-60	82	22.3
	61-80	209	56.8
	>80	77	20.9
Family history of breast cancer	Mother	14	3.8
	Grandmother	16	4.3
	Sister	6	1.6
	No history of breast cancer	332	90.2
History of other cancer	Ovarian	16	4.3
	Endometrial	14	3.8
	Other	13	3.5
	None	325	88.3

Among the participants, 222 (60.3%) reported performing breast self- examinations, while 146 (39.7%) did not. A significant majority, 326 (88.6%), had undergone mammography, whereas 42 (11.4%) had not. Regarding the type of breast cancer, 332 (90.2%) were diagnosed with ductal carcinoma, and 36 (9.8%) had lobular carcinoma. The distribution of breast cancer stages showed that most participants, 167 (45.4%), were at stage 3, followed by 93 (25.3%) at stage 4, 92 (25.0%) at stage 2, and 16 (4.3%) at stage 1 as indicated in **Table 3**.

Table 3: Self Determinants and Their interpretations

Determinants of Breast Cancer Variables		Frequency (n)	Percentage (%)
Breast self-examination	Yes	222	60.3
	No	146	39.7
Ever had a mammography	Yes	326	88.6
	No	42	11.4
Type of Breast cancer	Lobular Carcinoma	36	9.8
	Ductal Carcinoma	332	90.2
Stage of breast cancer	Stage 1	16	4.3
	Stage2	92	25.0
	Stage 3	167	45.4
	Stage4	93	25.3
Variables of Patient Characteristics		**Frequency (n)**	**Percentage (%)**
Breast Feeding	Yes	239	64.9
	No	129	35.1
Contraceptive use	Yes	160	43.5
	No	208	56.5
Menopausal Status	Pre-menopause	59	16.0
	Menopause	80	21.7
	Post-menopause	229	62.2

Among the participants, 244 (66.3%) reported having breastfed, while 124 (33.7%) had not. Contraceptive use

was reported by 168 (45.7%) participants, whereas 200 (54.3%) did not use contraceptives. Regarding menopausal status, the majority, 222 (60.3%), were post-menopausal, followed by 105 (28.5%) who were menopausal, and 41 (11.1%) who were in the pre-menopausal stage.

The distribution of chemotherapy cycles showed that the highest proportion of participants, 73 (19.8%), were in their 8th cycle. This was followed by 45 (12.2%) in the 6th cycle, 43 (11.7%) in the 5th cycle, and 35 (9.5%) in the 10th cycle. Participants in the 7th cycle accounted for 25 (6.8%), while 21 (5.7%) were in the 12th cycle, 20 (5.4%) in the 3rd cycle, and 19 (5.2%) in the 4th cycle. Smaller proportions were observed in other cycles, including 18 (4.9%) in the 9th cycle, 16 (4.3%) in both the 2nd and 11th cycles, 10 (2.7%) in the 14th cycle, 8 (2.2%) in the 16th cycle, 5 (1.4%) in both the 1st and 18th cycles, 4 (1.1%) in the 13th cycle, 3 (0.8%) in the 17th cycle, and 2 (0.5%) in the 15th cycle. Regarding the type of treatment, 158 (42.9%) participants were receiving neo-adjuvant therapy, 126 (34.2%) were undergoing adjuvant therapy, and 84 (22.8%) were receiving palliative care. In terms of dose response, 231 (62.8%) participants required dose adjustments based on individual needs, while 137 (37.2%) responded well to the initial prescribed dose. Dose adjustments were predominantly based on body surface area for 188 (51.1%) participants, followed by a combination of factors including body weight, body surface area, and AUC for 100 (27.2%), body weight alone for 67 (18.2%), and AUC alone for 13 (3.5%). Hospitalization due to chemotherapy side effects was required for 121 (32.9%) participants, whereas 247 (67.1%) did not need hospitalization. Additionally, 154 (41.8%) participants reported receiving radiation therapy, while 214 (58.2%) did not. Hormonal therapy was reported by 254.

The side effects reported after chemotherapy were categorized into several domains. This analysis highlights the varied and multidimensional impact of chemotherapy on patients across different toxicity domains. The side effects related to constitutional symptoms after chemotherapy were varied in severity. For headache, 160 (43.5%) participants experienced moderate symptoms, followed by 99 (26.9%) with mild symptoms, 67 (18.2%) with no headache, and 42 (11.4%) with severe headache. Regarding dizziness, 132 (35.9%) participants reported moderate dizziness, 126 (34.2%) experienced none, 95 (25.8%) had mild dizziness, and 15 (4.1%) had severe dizziness. Fainting was rare, with 266 (72.3%) participants reporting no fainting, while 45 (12.2%) had mild fainting, 46 (12.5%) had moderate fainting, and 11 (3.0%) had severe fainting. Weakness was a more common side effect, with 159 (43.2%) participants reporting moderate weakness and 109 (29.6%) reporting severe weakness. Only 7 (1.9%) participants experienced no weakness, and 93 (25.3%) reported mild weakness. For fatigue, 141 (38.3%) participants reported moderate fatigue, 127 (34.5%) had mild fatigue, and 67 (18.2%) experienced severe fatigue, with 33 (9.0%) reporting no fatigue.

The gastrointestinal (GIT) toxicity indicators after chemotherapy revealed various symptoms and their severity. Regarding weight loss, 86 (23.4%) participants experienced mild weight loss, 55 (14.9%) had moderate weight loss, 22 (6.0%) experienced severe weight loss, and 205 (55.7%) reported no weight loss. For weight gain, 183 (49.7%), reported no weight gain, while 103 (28.0%) experienced moderate weight gain, 68 (18.5%)

had mild weight gain, and 14 (3.8%) reported severe weight gain. Vomiting was reported by 140 (38.0%) participants at severe levels, 127 (34.5%) at moderate levels, 57 (15.5%) at mild levels, and 44 (12.0%) had no vomiting. 280 (76.1%) participants reported no constipation, with only 54 (14.7%) experiencing mild constipation, 23 (6.3%) moderate constipation, and 11 (3.0%) severe constipation. Mucositis was reported by 164 (44.6%) participants with no symptoms, 117 (31.8%) with mild symptoms, 79 (21.5%) with moderate symptoms, and 8 (2.2%) with severe symptoms. Loss of appetite was reported by 109 (29.6%) participants at mild levels, 97 (26.4%) at moderate levels, 37 (10.1%) at severe levels, and 125 (34.0%) reported no loss of appetite. Taste loss was the most common, with 194 (52.7%) participants reporting no taste loss, 82 (22.3%) experiencing moderate taste loss, 70 (19.0%) mild taste loss, and 22 (6.0%) severe taste loss. Diarrhea was moderate for 113 (30.7%), mild for 84 (22.8%), severe for 39 (10.6%), and absent for 132 (35.9%).

The dermatological toxicity indicators following chemotherapy highlighted significant effects, especially in hair loss, where 239 (64.9%) participants reported severe hair loss, 59 (16.0%) experienced moderate hair loss, 32 (8.7%) had mild hair loss, and 38 (10.3%) reported no hair loss. Rash was less common, with 281 (76.4%) participants reporting no rash, 49 (13.3%) mild rash, 27 (7.3%) moderate rash, and 11 (3.0%) severe rash. Regarding nail changes, 135 (36.7%) participants reported moderate changes, 105 (28.5%) had mild changes, 27 (7.3%) experienced severe changes, and 101 (27.0%) reported no changes. For numbness/tingling in hands, 118 (32.1%) participants reported mild symptoms, 114 (31.0%) moderate symptoms, 49 (13.3%) severe symptoms, and 87 (23.6%) reported no symptoms. Similarly, numbness/tingling in feet affected 131 (35.6%) participants with mild symptoms, 115 (31.3%) with moderate symptoms, 53 (14.4%) with severe symptoms, and 69 (18.8%) had no symptoms.

The pain-related toxicity indicators following chemotherapy showed varying degrees of discomfort. For abdominal pain, 205 (55.7%) participants reported no abdominal pain, 84 (22.8%) experienced mild pain, 67 (18.2%) had moderate pain, and 12 (3.3%) reported severe pain. Joint pain was also common, with 143 (38.9%) participants experiencing no joint pain, 110 (29.9%) reporting moderate pain, 60 (16.3%) experiencing severe pain, and 55 (14.9%) having mild joint pain. Regarding muscle pain, 180 (48.9%) participants reported moderate pain, 71 (19.3%) experienced severe pain, 57 (15.5%) had mild pain, and 60 (16.3%) reported no muscle pain. The lymphatic system toxicity indicator peripheral edema showed that the majority of participants, 234 (63.6%), reported no peripheral edema. A smaller proportion, 64 (17.4%), experienced moderate edema, 63 (17.1%) had mild edema, and only 7 (1.9%) reported severe edema.

The eye toxicity indicator conjunctivitis was predominantly absent, with 333 (90.5%) participants reporting no symptoms (0). A smaller group, 29 (7.9%), experienced mild conjunctivitis (1), and 6 (1.6%) reported moderate symptoms (2), while severe symptoms (3) was reported by 7 (1.9%). For respiratory toxicity, shortness of breath was largely unreported, with 307 (83.4%) participants experiencing no shortness of breath (0). Mild symptoms (1) were reported by 29 (7.9%) participants, moderate symptoms (2) by 28 (7.6%), and severe shortness of breath (3) was reported by 4 (1.1%).

The data are segmented into four age groups: 21-30, 31-40, 41-60, and greater than 60 years. Regarding breast self-examination, a total of 222 individuals across all age

groups reported performing regular self-exams, with the highest frequency observed in the 41-60 age group (115 individuals). In contrast, 146 individuals did not engage in breast self-examination, with the largest proportions found in the 41-60 and >60 age groups (57 and 70 individuals, respectively). In terms of mammography, 326 individuals across all age groups reported having undergone a mammogram, with the 41-60 age group again representing the largest proportion (154 individuals). Conversely, 42 individuals had never had a mammogram, with the highest numbers in the 41-60 and >60 age groups (18 and 12, respectively). The table further examines the type of breast cancer diagnosed. Among the 36 individuals with lobular carcinoma, the majority were in the 41-60 age groups (19 individuals). In comparison, ductal carcinoma was the most prevalent diagnosis, affecting a total of 332 individuals, with the highest concentration in the 41-60 age groups (153 individuals). Overall, the findings highlight that the 41-60 age group exhibits the highest rates of both breast cancer screening (mammography and self-examination) and breast cancer diagnoses, particularly ductal carcinoma. These patterns suggest a significant correlation between age and the likelihood of breast cancer detection, as well as the prevalence of specific cancer types.

These indicators include hair loss, rash, nail changes, and numbness/tingling in the hands and feet, with the severity of each symptom categorized into four levels (0-3). For hair loss, the highest severity (level 3) was most commonly reported in the 41-60 age group, with 117 individuals experiencing severe hair loss. This was followed by 73 individuals in the >60 age group. The younger age groups (21-30 and 31-40) showed a much lower incidence of severe hair loss, with 10 individuals in the 21-30 age group and 39 individuals in the 31- 40 age group reporting severity 3. Regarding rash, the 41-60 age group had the largest number of individuals with no rash (141 individuals, severity 0), while the 21-30 age group exhibited the lowest frequency of rash overall. A smaller proportion of patients across all age groups reported more severe rashes, with 11 individuals in total reporting a severity of 3, primarily from the 31-40 and 41-60 age groups. For nail changes, the 41-60 age group reported the highest severity overall, with 63 individuals reporting severity level 2 and 44 individuals reporting severity 3. The 21-30 and >60 age groups exhibited fewer instances of severe nail changes, with 1 individual in the 21-30 age group reporting severity 3 and 15 individuals in the >60 age group reporting the same. In terms of numbness/tingling in the hands, the 41-60 age group had the most significant number of individuals reporting severe numbness or tingling (38 individuals reporting severity 2 and 20 reporting severity 3). The 21-30 and 31-40 age groups showed less frequent and severe symptoms, with 3 individuals in the 21-30 group reporting severity 3. The total number of individuals reporting numbness or tingling in their hands was highest in the 41-60 age group (118 individuals, severity 1). Finally, for numbness/tingling in the feet, the 41-60 age group again had the largest number of individuals reporting this symptom, with 63 individuals experiencing mild numbness (severity 1) and 49 individuals reporting moderate numbness (severity 2). A small number of individuals in the 21-30 age group (9 individuals) reported no numbness or tingling in their feet. Overall, the data suggest that dermatological toxicities, such as hair loss, rash, nail changes, and numbness/tingling, are more severe and prevalent in older age groups, particularly in

the 41-60 age group. These patterns indicate that chemotherapy's dermatological side effects may intensify with age, with hair loss being the most common and severe symptom across all groups.

These indicators include abdominal pain, joint pain, and muscle pain, with severity categorized from 0 to 3. For abdominal pain, the highest number of patients across all age groups reported no abdominal pain (severity 0), with the 41- 60 age group showing the largest proportion of individuals without this symptom (104 individuals). As the severity increased, the number of individuals reporting abdominal pain declined. The 41-60 age group reported the highest incidence of moderate abdominal pain, with 39 individuals reporting a severity of 1, and 24 individuals reporting a severity of 2. A small proportion of individuals across age groups experienced severe abdominal pain (severity 3), particularly in the 41-60 age group, where 5 individuals reported severe abdominal pain. Regarding joint pain, the 41-60 age group reported the highest incidence of joint pain overall, with 72 individuals reporting no joint pain (severity 0) and 44 individuals reporting moderate pain (severity 2). The number of individuals with severe joint pain (severity 3) was highest in the 41-60 age groups (33 individuals). The younger age groups (21-30 and 31-40) had relatively fewer cases of joint pain, with only a few reporting severe pain. For muscle pain, the 41-60 age groups again reported the most significant number of individuals with moderate to severe muscle pain. A total of 80 individuals in this age group reported a severity level of 2 and 37 individuals reported severe muscle pain (severity 3). The 21-30 age groups had the lowest frequency of muscle pain, with only 8 individuals reporting no pain. As the severity of muscle pain increased, the number of individuals reporting it also increased, particularly in the 41-60 age groups, which had the highest total (180 individuals with varying levels of muscle pain). In summary, pain-related toxicity indicators, including abdominal, joint, and muscle pain, is more frequently and severely reported in the older age groups, particularly in the 41-60 age group. The data highlight a general trend of increased pain severity with age, especially in muscle and joint pain, emphasizing the greater impact of chemotherapy-related pain in middle-aged patients.

The Naranjo Adverse Drug Reaction (ADR) Probability Scale is a widely used tool to assess the likelihood that a specific adverse reaction is caused by a drug. It consists of ten questions that evaluate factors such as previous reports of the reaction, the timing of the reaction relative to drug administration, de-challenge and re-challenge outcomes, and the exclusion of alternative causes. Each question is scored, typically as +1, 0, or -1, depending on the available evidence. The total score determines the probability of causation, with scores of 9 or more indicating a definite relationship, scores between 5 and 8 suggesting a probable relationship, scores of 1 to 4 indicating a possible relationship, and a score of 0 suggesting the reaction is doubtful to be drug-related. In the assessment results, 55.9% of cases were classified as definite, indicating strong evidence that the drug caused the reaction. Probable cases made up 40.4%, where a drug-related cause is highly likely but with some uncertainty, such as incomplete evidence. Possible cases, accounting for 2.9%, indicate weaker support for causation, often due to confounding factors or insufficient data. Lastly, 0.54% of cases were categorized as doubtful, suggesting that the adverse reactions were unlikely to be related to the drug. These findings emphasize the utility of the Naranjo scale in providing a systematic framework for evaluating ADR causality, helping healthcare

professionals identify drug-related events with greater confidence.

Table 4. Assessment of Naranjo Score

Causality Category	Frequency (n)	Percentage (%)
Definite	206	55.9
Probable	149	40.4
Possible	11	2.9
Doubtful	2	0.54

4.0. DISCUSSION

The present study evaluated patient-reported adverse effects in breast cancer patients receiving chemotherapy, utilizing the Naranjo scale which complies with several other studies that highlighted the importance of patient-reported outcomes in understanding the full spectrum of chemotherapy side effects. For instance, a study was conducted in Karachi which assessed adverse drug events using the Naranjo scale, revealing common side effects such as hair loss, nausea, vomiting, anemia, and neutropenia, which were deemed non- preventable [16]. Another study emphasized the significance of capturing patient- reported toxicities, noting that symptoms like fatigue, constipation, and peripheral neuropathy varied significantly among different chemotherapy regimens [17]. One other study explained the importance of PROs, The integration of patient-reported outcomes (PROs) into clinical practice is crucial for improving the management of chemotherapy side effects. PROs provide valuable insights into the patient's perspective, allowing for more personalized care and better management of adverse effects [18]. This study comprised exclusively female volunteers, primarily aged 41 to 60 years that align with international epidemiological data showing that breast cancer incidence is highest among middle-aged women. A study

was conducted in US, concluded that Breast cancer incidence rates among women aged 20 to 49 years have increased among different races [19]. The present study signifies the incidence of unemployment (70.9%) and urban residency (60.1%) among participants underscores socio-economic issues that may affect treatment availability and outcomes which comply with the study reported that urban residency is associated with improved breast cancer-specific survival and lower the risk of distant relapse [20]. This study indicated that majority of patients (62.8%) required dose modifications during chemotherapy, primarily determined by body surface area (51.1%). This underscores the heterogeneity in patient reactions to normal dosages, highlighting the necessity of individualized treatment approaches. A study concluded that BSA-based dosing does not accurately reflect the complex processes of drug elimination, leading to unpredictable effects and potential under-dosing, which can reduce the anticancer effect by up to 20% in some cases [21]. Neo-adjuvant (41.6%) and adjuvant therapy (33.2%) were prevalent in early-stage patients, whereas palliative care (25.3%) was solely provided to stage 4 patients. These study findings align with existing research, highlighting the importance of stage-specific treatment strategies in breast cancer management. According to the conclusion of one study, Neo-adjuvant and adjuvant therapy have significantly improved survival rates for early-stage breast cancer patients [22]. For stage IV patients, the focus is on managing symptoms and improving quality of life. However, some studies suggested that aggressive local treatment, such as surgery and radiotherapy, may improve survival in select patients [23].

In the present study, most patient reported fatigue, weakness, and headache with moderate to severe intensity in substantial proportions and these findings correspond with prior research that recognize these symptoms as prevalent toxicities generated by chemotherapy. Fatigue is one of the most frequently reported symptoms among breast cancer patients receiving chemotherapy. It often worsens after treatment begins and can persist long after chemotherapy ends, significantly impacting quality of life [24]. It also align with other study reported that muscle weakness is commonly associated with fatigue and can be exacerbated by chemotherapy, contributing to decreased physical functioning [25]. Another study revealed that headaches are part of the symptom clusters that include fatigue and other side effects like nausea and sleep disturbances [26]. One more study concluded that the type and intensity of chemotherapy can influence the severity and persistence of symptoms like fatigue and headache [27]. In this study, samples vomiting (38% severe) and anorexia (26.4% mild) were significant adverse effects that align with several other studies that concluded, vomiting is a common and significant side effect of chemotherapy in breast cancer patients [28]. Many other studies have shown that chemotherapy-induced nausea and vomiting (CINV) is prevalent, with various interventions being explored to manage these symptoms [29]. One more study reported that patient-reported data often indicate higher severity and frequency of vomiting compared to physician-reported data, suggesting that the actual impact might be underreported in clinical settings [30]. Anorexia was also frequently reported (26.4%) in this study among breast cancer patients undergoing chemotherapy and it comply with other study that indicated, anorexia is often associated with other gastrointestinal symptoms like nausea and vomiting, contributing to malnutrition [31].

Significant hair loss (64.9%) was the most frequently reported symptom in the present study samples consistent with established side effects of chemotherapeutic drugs such as Doxorubicin and Paclitaxel. A national survey highlighted that hair loss, including loss of scalp, eyebrow, and eyelash hair, is a significant concern for breast cancer patients undergoing chemotherapy [31]. Nail changes were also reported by most of the patients. A study reported that nail changes can include discoloration, brittleness, and even nail loss, which are distressing for patients and can impact their daily activities [32].

Peripheral neuropathy, observed in 36.4% of research participants aligns with several other studies but the prevalence is different. A systematic review found that neuropathic symptoms persisted in 11% to over 80% of participants one to three years post-treatment, indicating a broad range of prevalence depending on the study and measures used [33]. A study reported that CIPN significantly affects quality of life, with symptoms like tingling and numbness impacting daily activities and emotional well-being [34]. Another study indicates that Chemotherapy-induced peripheral neuropathy (CIPN) is a significant issue, with older patients experiencing more severe and persistent symptoms [35].

In this study, moderate severity of joint and muscular pain was recorded comparing to other studies that say Joint and muscle pain are common side effects of breast cancer treatments, particularly chemotherapy and hormone therapy. A study showed that a significant number of women report these symptoms, with pain often described as aching, tiring, and exhausting [36].

Peripheral edema was infrequently reported in present study participants but primarily manifested in middle-aged and elderly subjects who align with the study that concludes peripheral edema is less frequently reported but is more prevalent among middle-aged and elderly patients undergoing breast cancer treatment [37]. The present study reported comparatively low incidence of severe lymphatic (1.9%) and pulmonary (1.1%) toxicities differs from the findings that documented pulmonary toxicity is notably high in breast cancer patients receiving high-dose chemotherapy regimens, particularly those including BCNU (carmustine), cyclophosphamide, and cisplatin [38]. The incidence of pulmonary toxicity varies significantly across studies, with some reporting lower rates, possibly due to differences in chemotherapy protocols or patient selection criteria [39].

5.0 CONCLUSIONS

This study highlights the importance of assessing patient-reported outcomes to comprehend the overall effects of chemotherapy on breast cancer patients. The results indicate a significant occurrence of prevalent adverse effects, including fatigue, alopecia, nausea, vomiting, and peripheral neuropathy, conjunctivitis, accompanied by notable diversity in severity and patient response. The Naranjo scale effectively identified the causation of adverse drug reactions, validating its utility in clinical settings for assessing chemotherapy toxicity. This study corroborates previous research about the primary significance of ductal carcinoma, the efficacy of neo-adjuvant and adjuvant therapy for early- stage malignancies, and the imperative of symptom management in advanced stages. Essential insights encompass the necessity for individualized treatment protocols, comprehensive patient education programs, and an integrative strategy for managing side effects.

Improving these areas can markedly enhance treatment adherence, patient quality of life, and overall outcomes in breast cancer management

Strict adherence to anti-emetic treatments, such as those endorsed by ASCO (American Society of Clinical Oncology) for severely emetogenic regimens, is essential to mitigate gastrointestinal adverse effects. ASCO endorses the use of anti-emetic treatments to manage nausea and vomiting associated with chemotherapy.

CONFLICT OF INTEREST

The authors have No conflict of interest in this research work.

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