Factors Associated with Adverse Effects in Elderly Women Receiving Chemotherapy for Breast Cancer

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ABSTRACT

Objective: To analyze the factors associated with adverse effects in elderly women receiving chemotherapy for breast cancer.

Study Design: Comparative Cross-sectional Study.

Place and Duration of Study: Oncology Department, Combined Military Hospital (CMH), Rawalpindi Pakistan, from Dec 2020 to Nov 2021.

Methodology: This study was conducted on 145 female patients (>65 years) with breast cancer who were taking chemotherapy of any type and had undergone one cycle. All the study participants underwent detailed clinical evaluation by a consultant oncologist to assess the presence of various adverse effects of chemotherapy. In addition, the association of Anthracycline use, >3 months of treatment, low haemoglobin at baseline and abnormal liver functions at baseline were studied with adverse effects in the study participants.

Results: The final analysis included one hundred forty-five elderly female patients with breast cancer receiving chemotherapy. The mean age of the patients was 69.731±8.794 years. 89(61.4%) patients had no adverse effects, while 56(38.6%) had one or more adverse effects during chemotherapy. Anaemia 26(17.9%) was the commonest adverse effect, followed by fatigue 18(12.4%) and abnormal liver function tests 18(12.4%). It was revealed that the use of Anthracycline-based chemotherapy and long duration of chemotherapy were statistically significantly associated with adverse effects (*p*-value<0.05) in our study participants.

Conclusion: Considerable number of elderly patients with breast cancer undergoing chemotherapy showed the presence of adverse effects. In addition, patients using Anthracycline-based chemotherapy and taking chemotherapy for more than three months were more at risk of developing adverse effects.

Keywords: Adverse effects, Breast cancer, Chemotherapy.

INTRODUCTION

Epidemiological data from around the world suggest that the prevalence and incidence of malignant illnesses of various types rank high among non-communicable diseases.[1] One of the commonest organs which fall prey to this lethal illness is the breast.[2] There have been multiple factors related to the prognosis of these patients.[3] Patient-related, illness-related and treatment-related factors prone the patients who have breast cancer towards various adverse effects.[4]

A multidisciplinary team usually manages breast cancer, including various treatment modalities. However, surgery and chemotherapy are these patients' most commonly used treatment modalities.[5] Much data has been published regarding various adverse events resulting from treatment modalities in patients suffering from breast cancer.[6] Treating team needs to be aware of these adverse effects to address them promptly.

Many breast cancer patients have reported various musculoskeletal adverse effects, including osteoporosis and osteopenia, using aromatase inhibitors. Ramaswamy *et al.* in 2003, highlighted that postmenopausal women taking adjuvant chemothe-rapy are more at risk of adverse events. There may be multiple side effects of chemotherapy in these patients. However, osteoporosis was the most concerning for them in their study participants.[7] Zanuso *et al.* 2020 conducted a cohort study regarding the side effects of adjuvant chemotherapy and their impact on outcomes in elderly breast cancer patients. They concluded that cardiotoxicity was the most serious adverse effect observed in their study participants, followed by leukopenia and neutropenia. Nausea and vomiting were also seen in many patients included in their analysis.[8] EA Perez, in 2007, studied the safety profile of aromatase inhibitors and concluded that these medications were associated with several side effects, including serious side effects, which may grossly affect the quality of life of the patients and may result in early discontinuation of medications. They also observed that if these adverse effects were intervened early,

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their impact was not to the extent that the cycle had to be discontinued.[9]

Weighing the risks and benefits of treatment options for malignant conditions like breast cancer has been the primary role of the treating team. Clinicians worldwide have different opinions regarding the efficacy and safety profile of various chemotherapeutic agents used to treat breast cancer. Changani *et al*. in 2017 conducted a study on the patients of Karachi highlighting that adverse events during chemotherapy had an inverse relationship with the overall quality of life in patients suffering from various types of cancer, including breast cancer.[10] Limited local data has been available which evaluates these factors specifically in the high-risk elderly population. Therefore, we planned this study to analyse the factors associated with adverse effects in elderly women receiving chemotherapy for breast cancer.

METHODOLOGY

This comparative cross-sectional study was conducted at the Oncology Department of Combined Military Hospital, Rawalpindi Pakistan from December 2020 to November 2021. Ethical approval was taken from the Ethical Review Board Committee of Combined Military Hospital, Rawalpindi, before the start of this study. The sample was gathered by using the non-probability consecutive sampling technique. The sample size was calculated using the WHO sample size calculator by using the prevalence of adverse effects in patients of breast cancer receiving chemotherapy as 79.3%,[11] and precision required as 10%.

Inclusion Criteria: All female patients between the age of 65 to 80 years suffering from Stage-I to III carcinoma of the breast undergoing any chemotherapy with at least one cycle completed were included in the study.

Exclusion Criteria: Patients having the first cycle of chemotherapy, patients who had a history of other primary tumours were excluded from the study. Patients with a history of autoimmune illness or any major uncontrolled systemic illness prior to chemotherapy were also excluded from the study.

After written informed consent from the participants, patients with Stage-I to III breast cancer and fulfilling the inclusion criteria were included in the study. Diagnosis and staging of breast cancer were made by consultant oncologist based on clinical, radiological and pathological criteria. Chemotherapy was given to all the patients in the Oncology Department under the supervision of the consultant oncologist based on the clinical profile of all the patients in accordance with the current international guidelines. Most patients got the combination of Doxorubicin and Cyclophosphamide followed by weekly Paclitexal in the neo-adjuvant regimen for ER PR positive tumors.[12] Herceptin was added with Paclitaxel in the same regimen for Her 2 neu positive tumours.[13,14]

All statistical analysis was performed using the Statistics Package for Social Sciences version 24.0 (SPSS-24.0). Mean and standard deviation were calculated for the age of patients. Frequency and percentages were calculated for the qualitative variables described in the study. Pearson Chi-square test was applied to look for the association of Anthracycline use, >3 months of treatment, low haemoglobin at baseline and abnormal liver functions at baseline with the presence of adverse effects among the elderly female suffering from breast cancer taking chemotherapy. The *p*-values less than or equal to 0.05 were taken as significant to establish an association among the study variables.

RESULTS

The final analysis included one hundred forty-five elderly female patients with breast cancer receiving chemotherapy. The mean age of the patients was 69.731±8.794 years. 89(61.4%) patients had no adverse effects, while 56(38.6%) had one or more adverse effects during chemotherapy. Table-I showed the general characteristics of patients. Out of 145 patients, 65(44.8%) patients received neo-adjuvant therapy while 80(55.2%) received adjuvant therapy.

Table-I: Characteristics of Patients with Breast Cancer Receiving Chemotherapy Included in the Study (n=145)

Study parameters	n (%)
Age (years)	
Mean±SD	69.731±8.794 years
Range (min-max)	65-79 years
Marital Status	
Married	122 (84.1)
Never married	08 (5.5)
Divorced	08 (5.5)
Widow	07 (4.6)
Hormonal Receptor Positive	
No	35 (29.1)
Yes	110 (70.9)
Her 2 Neu Positive	
No	105 (77.5)
Yes	35 (22.5)
Treatment Setting	
Neo-adjuvant	65 (44.8)
Adjuvant	80 (55.2)
Planned Duration of Treatment	
<3 months	72 (49.6)
>3 months	73 (50.4)

Table-II showed the adverse events experienced by study participants. Anaemia 26(17.9%) was the commonest adverse effect, followed by fatigue 18 (12.4%) and abnormal liver function tests 18(12.4%).

Table-II: Adverse Effects Experienced by Patients Included in the Study (n=145)

Adverse Effects	n(%)
Anemia	26 (17.9)
Thrombocytopenia	5 (3.4)
Leucopenia	9 (6.2)
Neutropenic sepsis	13 (8.6)
Fatigue	18 (12.4)
Abnormal liver functions	18 (12.4)
Thromboembolism	5 (3.4)
Hyponatremia	3 (2.1)
Diarrhea	9 (6.2)
Nausea/vomiting	9 (6.2)
Hypokalemia	8 (5.5)
Neuropathy	8 (5.5)
Syncopy	7 (4.8)
Sudden death	2 (1.4)
Others	3 (2.1)

Table-III showed that the use of Anthracycline-based chemotherapy and long duration of chemotherapy were statistically significantly associated with adverse effects (*p*-value<0.05) in our study participants.

Table-III: Association of Various Factors with Presence of Adverse Effects in Study Participants (n=145)

Factors	No Adverse Effects (n=89) n (%)	Presence of one or More Adverse Effects (n=56) n (%)	*p*-value
Anthracycline Use			
No	51(57.3)	13(23.2)	
Yes	38(42.7)	43(76.8)	<0.001
Duration of Treatment			
<3months	53(59.5)	19(33.9)	0.002
>3 months	36(40.5)	37(66.1)	
Low Baseline Hemoglobin			
No	70(78.6)	40(71.4)	0.325
Yes	19(21.4)	16(28.6)	
Abnormal Baseline Liver Functions			
	75(84.2)	45(80.3)	0.546
	14(15.8)	11(19.7)	

DISCUSSION

Chemotherapy is a mainstay of treatment for most types of malignant diseases. Breast cancer is no exception, and various chemotherapies are used depending on multiple factors. Physicians usually face problems with patients who are already at high risk, like patients of extreme ages or with multiple comorbidities. Elderly women are otherwise at high risk for multiple physical problems, and the risk may increase when they suffer from a malignant condition. We planned and conducted this study intending to analyze the factors associated with adverse effects in elderly women receiving chemotherapy for breast cancer at the oncology department of the tertiary care hospital of Rawalpindi.

Belachew *et al.* in 2016 summarized the adverse events reported in patients undergoing chemotherapy for various cancers, including breast cancer.[15] They concluded that haematological side effects were commonly seen in their patients, followed by fatigue and alopecia. Advancing age and more chemotherapeutic agents used were statistically significantly related to the presence and severity of adverse effects. Our results supported the findings generated by Belachew *et al*. as anaemia was the most commonly encountered adverse effect in our study participants, followed by fatigue. Anthracycline-based regimens appeared to be more toxic than others in our data set.

Prieto-Callejero *et al*.[16] in 2020 analyzed the relationship between chemotherapyinduced adverse reactions and various factors, including health-related quality of life in patients with breast cancer. They concluded that nausea, dysgeusia, peripheral neuropathy, loss of appetite, myalgia, and peripheral oedema were the commonest adverse effects in their patients. Our study was slightly different because we only included elderly female patients who have breast cancer undergoing chemotherapy. In addition, we found out that patients using Anthracycline-based chemotherapy and taking chemotherapy for more than three months were more at risk of developing adverse effects.

Chandler *et al*.[17] in 2020 studied elderly patients with breast cancer for the efficacy and adverse effects of chemotherapy. They revealed that more effective chemotherapy regimens increased toxicity but still improved survival. We did not study efficacy but found out that Anthracycline based treatment was associated more with the presence of adverse effects as compared to other chemotherapeutic regimens.

Weekly Docetaxel versus CMF as adjuvant chemotherapy for older women with early breast cancer was evaluated by Perrone *et al*.[18] in 2020. They suggested that haematological toxicity, mucositis and nausea were worse with CMF. In contrast, with docetaxel, allergy, fatigue, hair loss, onychopathy, dysgeusia, diarrhoea, abdominal pain, neuropathy, and cardiac and skin toxicity were worse. Our results supported the results of Perrone *et al.*

LIMITATIONS OF STUDY

Elderly women are a high-risk group for various physical health problems. A cohort or case-control study design may have yielded better results to establish the cause-and-effect relationship between chemotherapy and adverse effects. This remains one of the main limitations of our study. Assessing the patients before the start of therapy and then doing detailed assessments at various intervals during chemo-therapy may yield better results.

CONCLUSION

Many elderly patients with breast cancer undergoing chemotherapy showed adverse effects. Patients using Anth-racycline-based chemotherapy and taking chemotherapy for more than three months were more at risk of developing adverse effects.

Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

AR: Study design, data analysis, critical review, drafting the manuscript, critical review, approval of the final version to be published.

ZAA & MN: Drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

MU & AK: Conception, data acquisition, drafting the manu-script, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investi-gated and resolved.

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