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# A Retrospective Study on The Side-effects of Chemotherapy in Breast Cancer Patients in a Tertiary Care Hospital, Chennai

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## Abstract
Chemotherapy induced side effects among breast cancer can not only impact quality of life and tolerance of planned therapy, but also increases the cost of the therapy. The Aim and objective of our study was to identify and evaluate the frequency and severity of chemotherapy induced side effects in breast cancer patients. **Methods:** A retrospective observational study was carried out in a tertiary care hospital, Chennai over a period of 6 months from January to June 2020. A total of 150 breast cancer patients received chemotherapy were included in the present study. Patient's demographic details, cancer classification, drugs used to treat cancer, time of chemotherapy treatment, presence of associated diseases and data on side effects induced by different chemotherapeutic regimens were extracted from patients' case reports, which were collected from the medical record room. **Results:** A total of 150 patients were enrolled into the study in which 0.66 % were male and 99.3% were females. The majority were in the age range of 38 - 58 years (65.3%) The most commonly prescribed drug was trastuzumab 105 (70%), which was followed by docetaxel 101 (67.5 %). Majority of the patient (62.6%) took docetaxel, trastuzumab, carboplatin regimens. 27.5% (n=41) of patients were reported with nausea and vomiting as the major side effects followed by diarrhea (17.5%), fever (15%), and majority of the side effects (65%) occurred at the age group of 38-58. Skin irritation was the most common side-effect observed in the age group 58-78. **Conclusion:** Our study had revealed some of the chemotherapy-related side effects commonly experienced by local breast cancer patients. Nausea and vomiting were the major side effect observed and majority of the side effects have occurred in the age group 38-58.

**Keywords**
breast cancer, chemotherapy, side effects, cytotoxic drugs.

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## INTRODUCTION
Cancer originating from the breast is referred to as breast cancer, it is most commonly from the inner lining of milk ducts or the lobules that supply the ducts with milk. Cancer cells often have similarities to the cells of the organism from which they originated and have similar but not identical DNA and RNA, as a result in patients with low immunity the immune system may not attack the cancer cells. Breast cancer is a silently evolving condition. They are mostly discovered during their routine screening. Others may present themselves with abreast lump they accidentally discovered, change of breast shape or size, or nipple discharge. [1]

Globally, breast cancer is the second most common cancer i.e., around 2 million new cases in 2018.

Occurrence of cancer has increased from 0.6 million in 1991 to 1.4 million in 2015 in India. Among women the common form of cancer is, breast cancer (21.0%). [2] According to the Globocan (WHO), for the year of 2012, 70,218 deaths due to breast cancer was recorded in India, this is more than that of any other country in the world. [3]

**Chemotherapy:** Chemotherapy is an important component of treatment for many cancers, including breast cancer, and new anti-cancer drugs represent one of the largest areas of pharmaceutical development [4]. However, the nature of chemotherapy means that while damaging cancer cells it also damages healthy cells, leading to side effects [5]

Our understanding about side effects of chemotherapy and their frequency comes primarily from clinical trials [6]. However, this may not reflect the reality of chemotherapy side effects in real clinical practice.

There are several standard chemotherapy options, typically containing both an anthracycline and a taxane. In the United States, doxorubicin and cyclophosphamide for 4 cycles followed by paclitaxel for 4 cycles (AC-T) is a common regimen. Dose-dense (dd) AC-T given every 2 weeks with growth factor support after each chemotherapy cycle is superior to an older schedule of every 3 weeks. [7] Other optimal schedules of AC followed by a taxane include weekly paclitaxel for 12 weeks or every 3-weekly docetaxel for 4 cycles. [8] Another standard option is DAC, docetaxel with AC; however, this is not superior to the above regimens, and docetaxel is associated with more toxicity than paclitaxel and higher febrile neutropenia rates in particular. [9]

**Drug combinations in breast cancer therapy:** Use of combination of chemotherapy potentially provides advantages such as chances for the better efficacy and the dose reduction while increasing or maintaining efficacy, decreased toxicity, and reduced or delayed development of drug resistance. [10] Due to these advantages, combination chemotherapy has now become conventionally applied strategy in the clinical practice. [11] More recently, advances in the areas of isolation technology and the chemical synthetic capability, as well as the omics and cell biology, have also played an important role in the increasing the application of drug combinations in modern medical practice. [12]

The primary objectives of chemotherapy treatment have been predominantly focused on breast cancer outcome but at the same time, little attention has been given to the short term and long-term side-effects of these drugs [13] It is vital to address issues related to side effects that could affect the overall quality of patient survival. a better understanding of the whole spectrum of chemotherapy side effects, both short and long term would enable us to refine our use of such therapy, in terms of both scheduling and individual patients' risks and preferences. [14]

The objective of this study was to estimate the most common side effects experienced by the breast cancer patients receiving chemotherapy in a routine clinical care setting.

## METHODOLOGY

This retrospective observational study was carried out in a tertiary care hospital in Chennai for a period of four months. All patients confirmed with malignancy using mammography or Breast biopsy and received cancer chemotherapy in the department of oncology. A total number of 150 breast cancer patients who received chemotherapy were included in the study. Patients of both genders with age above 18 years and diagnosed as breast cancer using mammography or breast biopsy and receiving chemotherapy irrespective of their comorbidities were included in the study. The exclusion criteria include patients who are critically ill patients, pregnant and lactating and those receiving radiation therapy.

**Source of data and study material:** Data was collected from patient proforma. Medication details from, Lab investigation, Mammography or Breast biopsy reports from case sheets. Radio imaging study reports were also collected. The data was collected using a patient profile form.

**Treatment Plan:** The study consists of different regimens of treatment that were given to patients at various stages of breast cancer, tumor size, lymph node involvement and metastasis. The regimens of treatment applied were:

- Docetaxel 100mg/$m^2$ and carboplatin 600mg/$m^2$ every 3 weeks for 4 cycles followed by trastuzumab 440mg/$m^2$ every 3 weeks for 4 doses.
- Cyclophosphamide 600mg/$m^2$ and doxorubicin 80mg/$m^2$ every 3 weeks for 4 cycles followed by paclitaxel 250mg/$m^2$ every 3 weeks for 4 doses.
- Cyclophosphamide 600mg/$m^2$, trastuzumab 440mg/$m^2$, docetaxel 100mg/$m^2$ every 3 weeks for 6 cycles.
- 6 cycles of paclitaxel 250mg/$m^2$, cyclophosphamide 600mg/$m^2$ and trastuzumab 440mg/$m^2$ administered every 3 weeks.

Chemotherapy regimen for breast cancer is given in cycles. On the first day of each cycle, patients will be receiving combination chemotherapy, and then no chemotherapy treatment for the next 20 days. At the end of 21 days, patients will be treated with the

second cycle of chemotherapy and so on. All patients were treated with combination chemotherapy in 4 to 8 cycles. A uniform hydration procedure was followed during the chemotherapy. Supportive care such as intravenous infusion, and drugs like ondansetron, dexamethasone, loperamide, T. Hyoscine, Levofloxacin, heparin and benzyl nicotinate ointment, lactulose and benzydamine gargles were given along with chemotherapy for anticipated side effects.

**Procedure:** Data collection form was designed to collect and record patient information from the case sheets. All case sheets of breast cancer patients receiving chemotherapy were collected from the hospital medical record room. Data collection was performed according to hospital regulations. The analysis of medical records including laboratory and other investigational reports sought data such as: patient identification, cancer classification, drugs used to treat cancer, time of chemotherapy treatment, presence of associated diseases and the frequency and severity of side effects induced by different chemotherapeutic regimens.

**RESULT**

Out of 150 patients, 149 (99.3%) patients were females and there was only one (0.66%) was male patient. Of 150 patients, 98 (65.3%) were in the age group 38-58, followed by, 34 (22.7%) were in the age group of 58- 78 years and 11 (7.3%) patients were in the age group of 18-38 years. The remaining 7 (5%) were in the age group of ≥ 78 years. Mean age was found to be 53.575 years. (Table & Figure 1)

**Table 1: Age wise distribution of patients (n =150)**

| Age | No. of patients (n= 150) | Female | Male | Percentage (%) |
|---|---|---|---|---|
| 18-38 | 11 | 11 | 0 | 7.3% |
| 38-58 | 98 | 98 | 0 | 65.3% |
| 58-78 | 34 | 33 | 1 | 22.7% |
| ≥ 78 | 7 | 7 | 0 | 4.7% |

A total of 90 (60%) were in the 3rd grade group and 45 (30%) were in the 2nd grade group of breast cancer. (Table & Figure 2).

**Table 2: Grade distribution of cancer patients ( n =150)**

| Grades of cancer | n = 150 | Percentage (%) |
|---|---|---|
| 1st Grade | 15 | 10% |
| 2nd Grade | 45 | 30% |
| 3rd Grade | 90 | 60% |

Among 150 patients, 101 (67.5%) patients were given with the drug docetaxel, 94 (62.5%) patients were given carboplatin, 105 (70%) patients were given trastuzumab, 49 (32.5%) patients were given paclitaxel, 56 (37.5%) patients were given cyclophosphamide and 45 (30%) were given doxorubicin. (Table & Figure 3).

**Table 3: Comparison of chemotherapeutic drugs (n=150)**

| Chemotherapeutic Drugs | Dose | ROA | No. of patients {N=150) | Percentage (%) |
|---|---|---|---|---|
| Docetaxel | 800mg | IV | 101 | 67.5% |
| Carboplatin | 450mg | IV | 94 | 62.5% |
| Trastuzumab | 440mg | IV | 105 | 70% |
| Paclitaxel | 250mg | IV | 49 | 32.5% |
| Cyclophosphamide | 700mg | IV | 56 | 37.5% |
| Doxorubicin | 80mg | IV | 45 | 30% |

Out of 150 prescriptions 94 (62.6%) patients were prescribed with 'docetaxel, carboplatin, trastuzumab 'regimen, followed by 45 (30%) patients with 'cyclophosphamide, doxorubicin, paclitaxel' regimen, 7 (4.6%) patients were prescribed with 'cyclophosphamide, trastuzumab, docetaxel' and only 4 (2.6 %) patients with 'paclitaxel, cyclophosphamide, trastuzumab' regimen. (Table & Figure 4)

**Table 4: Comparison of Treatment Regimen (n=150)**

| Drug regimen | No. of patients (n=150) | Percentage (%) |
|---|---|---|
| Docetaxel, Carboplatin, Trastuzumab | 94 | 62.6% |
| Cyclophosphamide, Doxorubicin, Paclitaxel | 45 | 30% |
| Cyclophosphamide, Trastuzumab, Docetaxel | 7 | 4.6% |
| Paclitaxel, Cyclophosphamide, Trastuzumab | 4 | 2.6% |

Out of 150 patients, 56 (37.5%) were found to overweight, 52 (35%) were normal followed by 38 (25%) obese patients overweight. Only 4 (2.5%) patients were found to be underweight, (table & figure 5)

**Table 5: BMI Categorization of patients (n= 150)**

| BMI | No. of patients (N=40) | Percentage (%) |
|---|---|---|
| Below 18.5 (underweight) | 4 | 2.5% |
| 18.5-24.9 (normal) | 52 | 35% |
| 25-29.9 (overweight) | 56 | 37.5% |
| Above 30 (obese) | 38 | 25% |

Among 150 patients, 120 breast cancer patients (80%) had lump in upper-outer quadrant region followed by 19(12.5%) in lower-outer quadrant region. 7 patients (5%) had lump in the lower-inner quadrant and 4 (2.5%) in upper-inner quadrant. (Table & Figure 6).

**Table 6: Quadrant Position of Lump in Breast Cancer (n=150)**

| Quadrant position | No. of patients (n=40) | Percentage (%) |
|---|---|---|
| Upper- outer quadrant | 120 | 80% |
| Upper- inner quadrant | 4 | 2.5% |
| Lower- outer quadrant | 19 | 12.5% |
| Lower – inner quadrant | 7 | 5% |

Out of 150 patients in the study, 67 (45%) have diabetes mellitus, 45 (30%) came with hypertension, 8(5%) with asthma, 15 (10%) with arthritis and 15 (10%) patients with no comorbidities. (Table & Figure7).

**Table 7: Distribution of comorbid conditions among breast cancer patients (n=150)**

| Comorbidities | No. of patients (n=150) | Percentage (%) |
|---|---|---|
| Hypertension | 45 | 30% |
| Diabetes Mellitus | 67 | 45% |
| Asthma | 8 | 5% |
| Arthritis | 15 | 10% |
| None | 15 | 10% |

Out of 150 patients included in the study, majority of the patients 41(27.5%) had nausea & vomiting, followed by diarrhea 26 (17.5%), fever 22(15%), and anorexia, 19 (12.5%) respectively. Other side effects commonly experienced by the study population are skin irritation and alopecia 11(7.5%), abdominal pain and constipation 8(5%). Only 4 (2.5%) patients had oral ulcers. (Table &Figure 8).

**Table 8: Chemotherapy-induced side-effects (n=150)**

| Side -effects | No of patients(n=150) | Percentage (%) |
|---|---|---|
| Nausea & Vomiting | 41 | 27.5% |
| Diarrhea | 26 | 17.5% |
| Anorexia | 19 | 12.5% |
| Abdominal Pain | 8 | 5% |
| Fever | 22 | 15% |
| Skin Irritation | 11 | 7.5% |
| Oral Ulcer | 4 | 2.5% |
| Constipation | 8 | 5% |
| Alopecia | 11 | 7.5% |

In our study, the most commonly seen side effect nausea and vomiting has occurred between the age group 18-38 and 38-58. Skin irritation was mostly seen in the age group 58-78. (Table & Figure 9).

**Table 9: Age wise distribution of side-effects(n=150)**

| Side-effects | 18-38 | 38-58 | 58-78 | ≥ 78 |
|---|---|---|---|---|
| Nausea & Vomiting | 7 | 34 | 0 | 0 |
| Diarrhea | 4 | 19 | 4 | 0 |
| Anorexia | 0 | 19 | 0 | 0 |
| Abdominal pain | 0 | 0 | 7 | 0 |
| Fever | 0 | 19 | 4 | 0 |
| Skin irritation | 0 | 0 | 11 | 0 |
| Oral ulcer | 0 | 0 | 4 | 0 |
| Constipation | 0 | 0 | 0 | 7 |
| Alopecia | 0 | 8 | 4 | 0 |

In the present study, out of 150 patients, most of the patients 94 (62.5%) had side effects with 'docetaxel, carboplatin, trastuzumab 'regimen whereas 45 (30%) patients had side effects with 'cyclophosphamide, doxorubicin, paclitaxel' regimen, followed by 7 (5%) patients with 'cyclophosphamide, trastuzumab, docetaxel' and 4 (2.5 %) patient with 'paclitaxel, cyclophosphamide, trastuzumab' regimen respectively.

**Table 10 Treatment regimen wise distribution of side effects.**

| Drug regimen | No. 0f side effects(N=150) | Percentage (%) |
|---|---|---|
| Docetaxel, Carboplatin, Trastuzumab | 94 | 62.5% |
| Cyclophosphamide, Doxorubicin, Paclitaxel | 45 | 30% |
| Cyclophosphamide, Trastuzumab, Docetaxel | 7 | 5% |
| Paclitaxel, Cyclophosphamide, Trastuzumab | 4 | 2.5% |

**Figure 1: Age wise distribution of patients (%) (n = 150)**

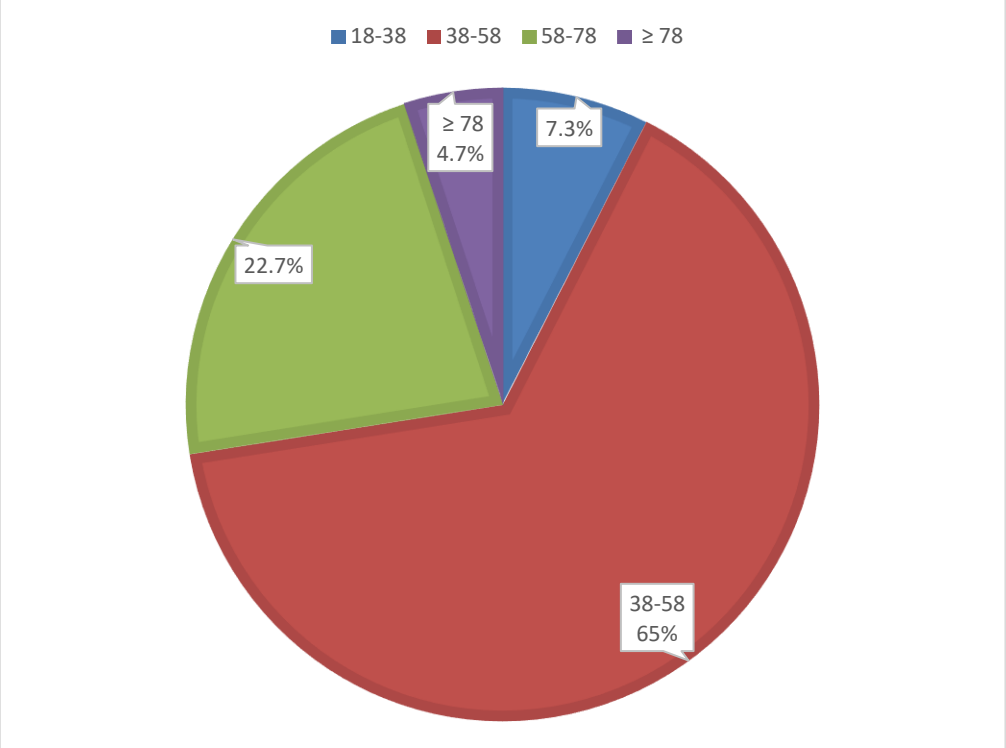


**Figure 2: Grade distribution of cancer patients ( n=150)**

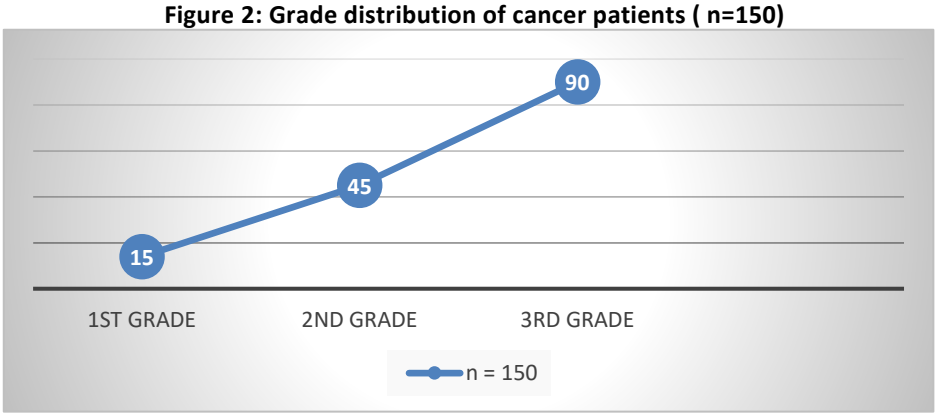



**Figure 3: Comparison of chemotherapeutic drugs (n = 150)**

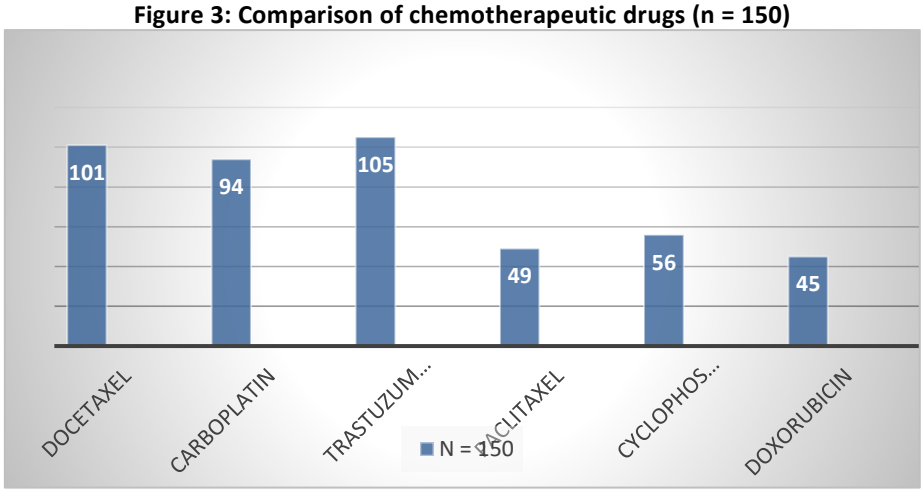



**Figure 4: Comparison of Treatment Regimen (n=150)**

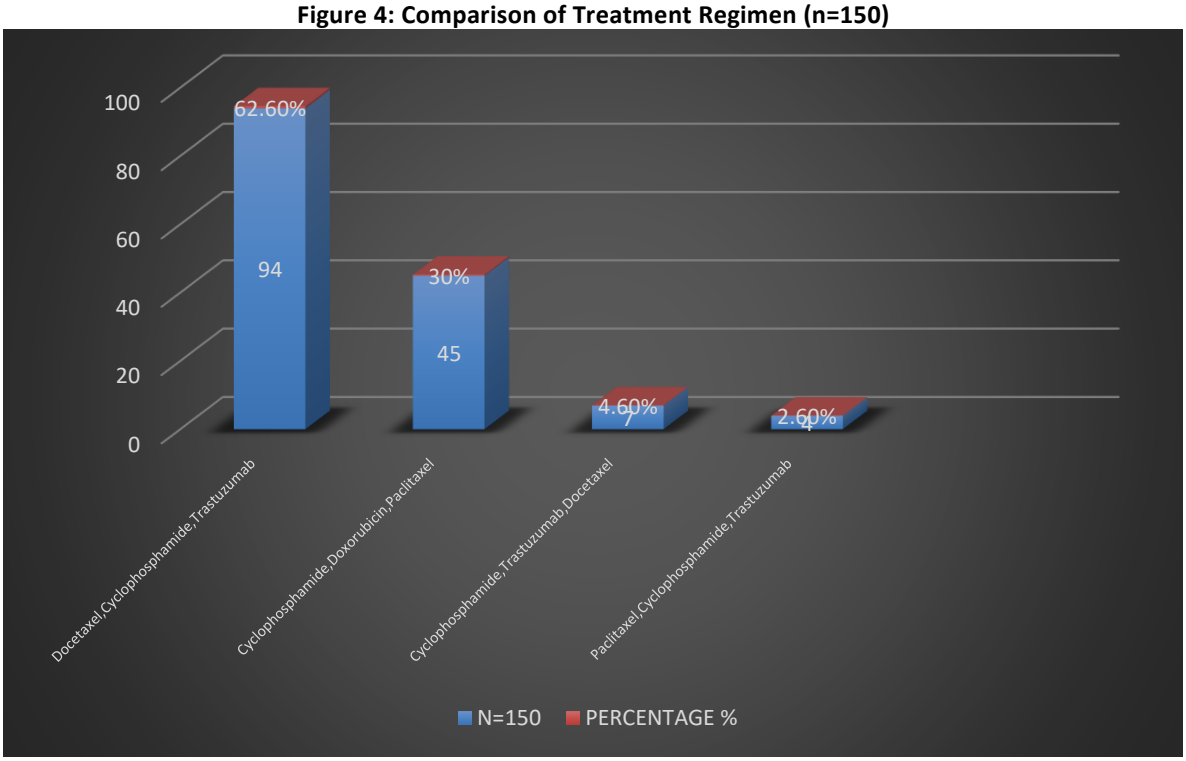


**Figure 5: BMI Categorization of patients (n=150)**

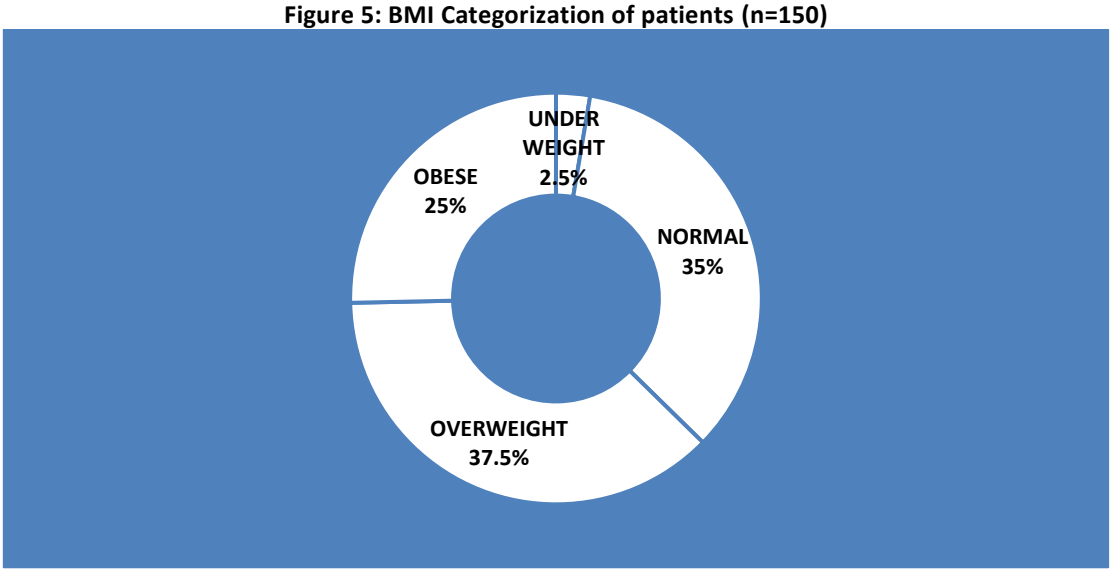



**Figure 6: Quadrant Position of Lump in Breast Cancer (n=150)**

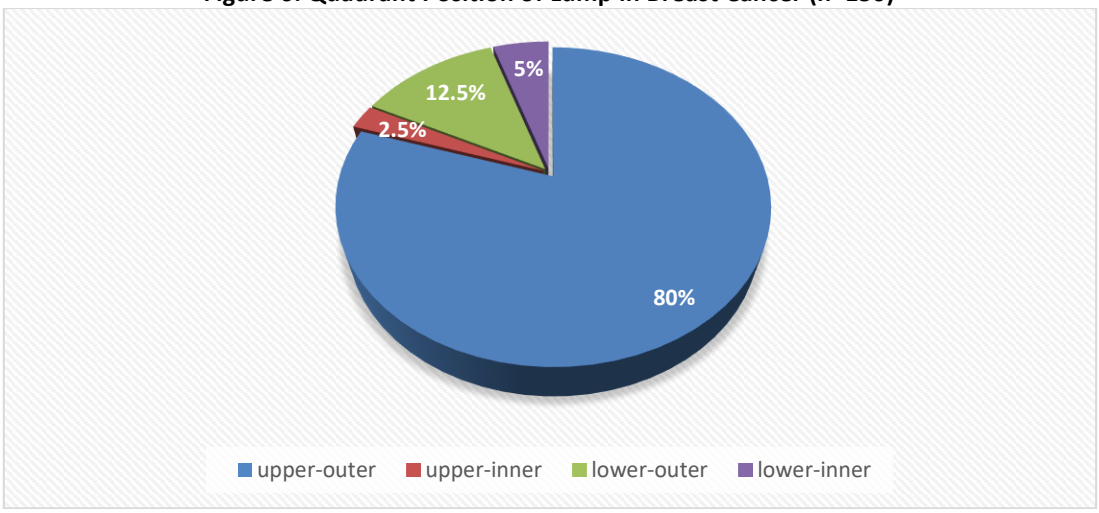



**Figure 7: Distribution of comorbid conditions among breast cancer patients (n=150)**

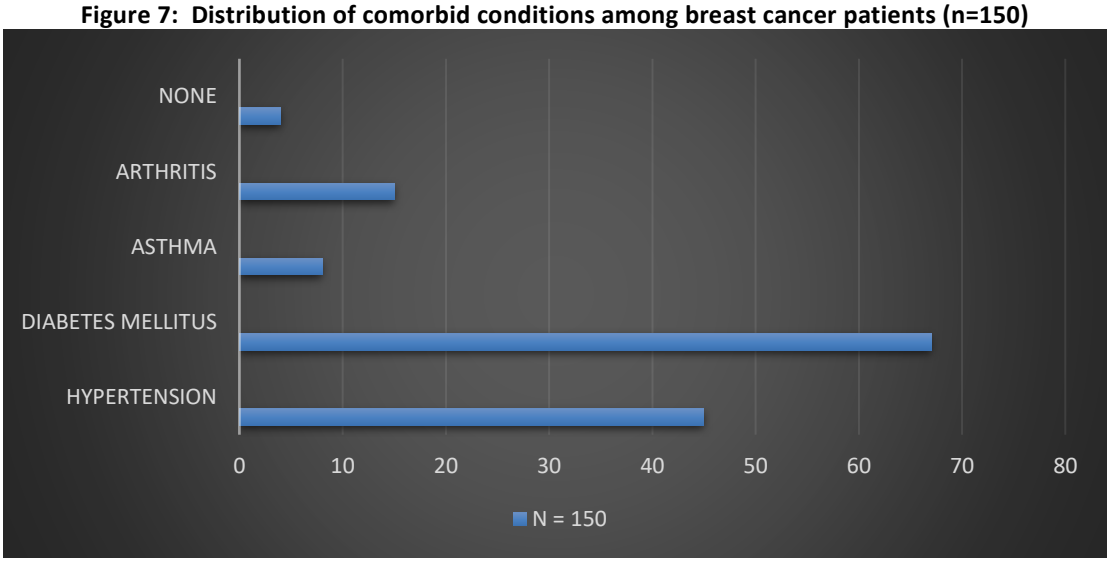


**Figure 8: Chemotherapy- induced side-effects (n=150)**

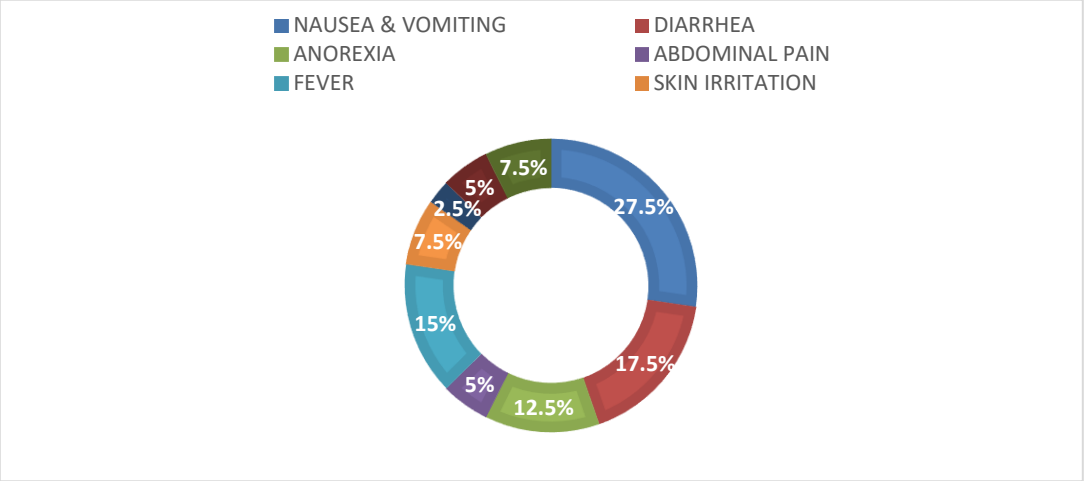



**Figure 9: Age wise distribution of side-effects (n=150)**

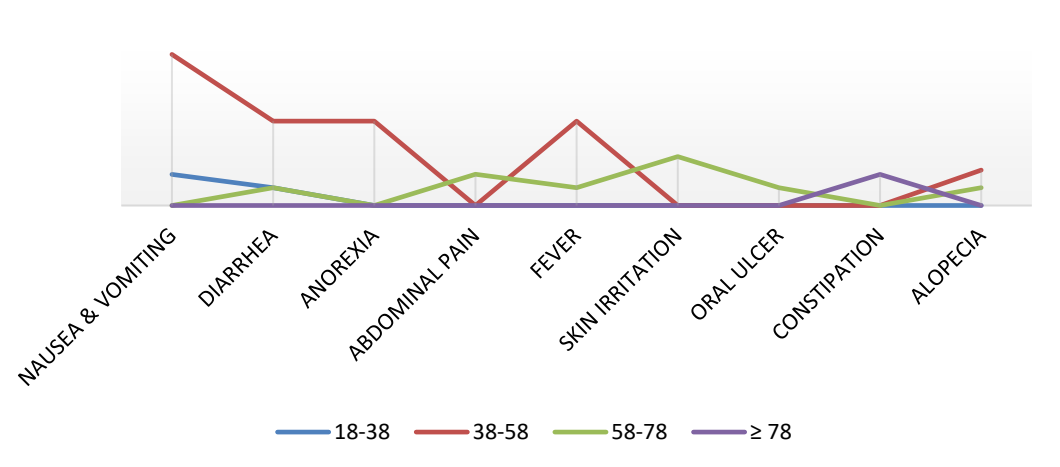
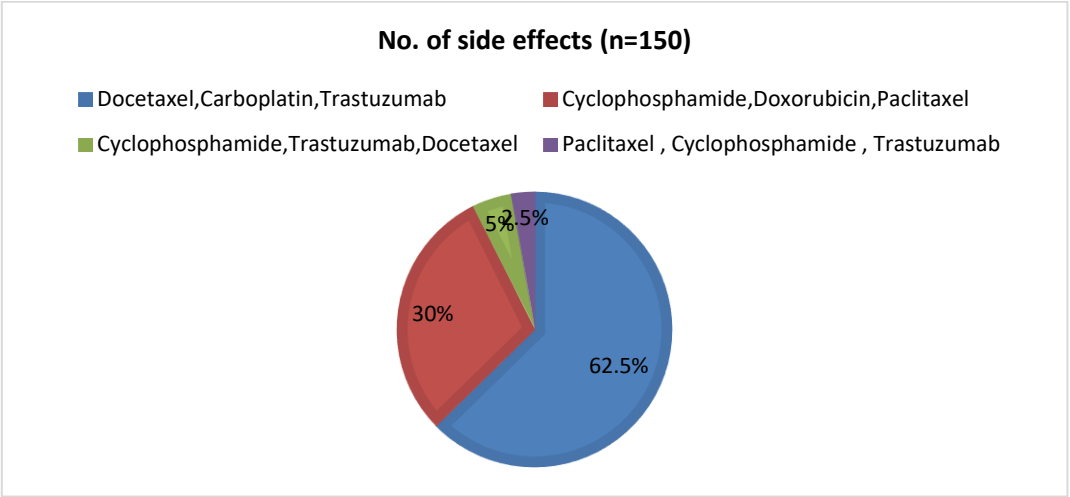



**Figure: 10 Treatment regimen wise distribution of side effects**




## DISCUSSION

The present study was conducted in the department of oncology of a tertiary care hospital, with the aim of identifying and evaluating the frequency and severity of chemotherapy induced side effects in breast cancer patients.

The study consisted of 150 breast cancer patients, in whom the analysis of the data collected revealed that, the patient age ranged from 33 to 83 years with

the median age 52 years. The mean age was found to be (53.575 years ± 13.25 years) and the lowest age of a patient with carcinoma breast was found to be 33 years.

Breast cancer in men is a rare disease. In this study, out of 150 study population 149 (99.3%) patients were females and only one male patient (0.66 %) was found to have breast cancer.

The grade of breast cancer can help predict how likely the cancer is to grow and tend to spread. In high grade breast cancer, (grade 3) the cells look very different to normal breast cells and are faster growing and spread more quickly and have a worse outlook (prognosis).

Several studies among Asian women suggest that higher BMI may be associated with an increased risk for breast cancer. In the present study, we have observed that more than 60% of the patients were above normal weight.

Our study also revealed that 80% (n=120) of patients had lump in the upper outer quadrant, followed by 12.5% (n=19) patients with lump in lower outer quadrant.

In this present study, 70% (n=105) of the cancer patients were prescribed with chemotherapeutic drug trastuzumab followed by docetaxel (67.5%) and carboplatin (62.5%).

According to our study, the most common treatment regimen given to 94 (62.6%) breast cancer patients was docetaxel, carboplatin and trastuzumab combination.

About 67 (45%) patients were reported with diabetes mellitus, followed by hypertension for 45 patients (30%), asthma for 8 (5%) patients and arthritis 15 (10%) patients at the time of cancer diagnosis. Among 150 study populations 15 patients were found to be without any co-morbidities.

A study conducted by *Michael J. Hassett et al (2020)* demonstrated, the association between chemotherapy related side effects and chemotherapy administration. In our study, we found that 27.5% (n=41) of patients were reported with nausea and vomiting as the major side effects followed by diarrhea (17.5%), fever (15%), anorexia, skin irritation, alopecia. abdominal pain, constipation, and oral ulcer as side effects. The results of the present analysis are in accordance with the study reports of *DevenderKodati et al (2019)* studies stated that breast cancer patients who received chemotherapy had statistically significantly greater odds of experiencing each of the above-mentioned chemotherapy-related side effects

Our present study shows majority of the side effects (65%) occurred at the age group of 38-58 years, which was quite like the study findings of *Astolfi et al (2013).* Tao et al studies also revealed that, patients with age above 35 show more side effects than that of the younger patients which is also similar to our present study.

A study conducted by *Stephan P. Bauersfeld et al (2018)* shows chemotherapy induced nausea and vomiting were the most seen side effect among study population (30%). In our study 27.5% of the study population experienced nausea and vomiting which is similar to the above study.

Among 150 patients included in the study, 37.5% (n=56) of patients had gastrointestinal side effects like diarrhea, abdominal pain, and Anorexia which can be attributed to cancer chemotherapy. This was similar to the study findings reported *by Christopher R. Frieseetal (2017).*

Fever occurs frequently in patients with chemotherapy-induced neutropenia. In the study conducted by *Fontanella C et al (2014),* Chemotherapy-induced neutropenic fever was observed in 15% of patients. In the present study 12.5% of the study population reported fever which is similar with above study findings and none of them had any severe infections.

Cutaneous Manifestations such as alopecia (5%), skin irritation/rashes (7.5%) were observed in the present study.

*Hyun Juyoon et al (2016)* demonstrated in their study that, most of the side effects were observed in 'docetaxel, carboplatin and trastuzumab', In the present study, since more than half of the patients (62.5%) were prescribed with 'docetaxel, carboplatin and trastuzumab' treatment regimen, according to our study , this combination regimen was associated with more side effects.

**CONCLUSION**

Chemotherapy-related side effects among breast cancer patients are worrisome. Our study had revealed some of the chemotherapy-related side effects commonly experienced by local breast cancer patients. Nausea and vomiting were the most commonly seen side effects and patients between the age group 38-58 were mostly affected with side effects of chemotherapy. It is important to provide more detailed information to patients about chemotherapy, along with potential side-effects prior to its commencement. Therefore, patients are better informed and understand the treatment that they are about to receive and the drug related side effects. We hope that by identifying and minimizing or preventing both short and longer-term toxicity from cancer chemotherapy, the treatments themselves will be better tolerated and more

effective, and the health and wellness of cancer survivors will be enhanced.

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