

Drug Therapy Evaluation For Patients With Breast Cancer In Private Hospital

^[1*]Anandkumar S, ^[2]Manikandhan C, ^[3]Sureshkumar P

^[1]Department of Pharmacy Practice, Sri Shanmugha College of Pharmacy, Sankari, Tamilnadu, India.

^[2]Department of Pharmacology, Sri Shanmugha College of Pharmacy, Sankari, Tamilnadu, India.

^[3]Department of Pharmaceutics, Sri Shanmugha College of Pharmacy, Sankari, Tamilnadu, India.

*Corresponding Author

Dr. S. Anandkumar, M.Pharm., Ph.D.,
Professor, Department of Pharmacy Practice,
Sri Shanmugha College of Pharmacy,
Pullipalayam, Morur (Po),
Sankari (TK), Salem (Dt), Tamil Nadu, Pin-637 304.
Ph: +91 9942541867
E-mail: sakumar0307@gmail.com.

Abstract: The study aims to evaluate the drug therapy in breast cancer patients in a tertiary care teaching hospital. A prospective observational study was carried out for 6 months among breast cancer inpatients of either sex, with age ≥ 18 years with or without co-morbidities. Demographics of the patients, co-morbidities, chemotherapeutic drug regimens used, ADRs associated with chemotherapy and severity of pain were recorded. A total of 77 breast cancer cases were collected, among them 75 were females and 2 was male. Nine chemotherapeutic drug regimens (8 drug combinations+1 single drug regimen) were prescribed, out of which the most commonly used chemotherapy single drug regimen was Inj. Docetaxel (47.3%) and combination regimen was Inj. Cyclophosphamide + Inj. Doxorubicin (30%). Most frequent adverse effects seen in patients receiving chemotherapy was alopecia (96.4%) followed by nausea (85.4%) and vomiting (76.4%). The adjuvant therapy included anti-emetics (5-HT₃ antagonist), corticosteroids, H₂ antagonists, antihistamines, and antipyretics.

Keywords: Breast Cancer, Chemotherapy, Adverse drug reaction.

1. Introduction

Breast cancer is the most common cancer in women worldwide, and it accounts for the second most common cancer overall with nearly 1.7 million new cases diagnosed in 2012. This represents about 12% of all new cases and 25% of all cancers in women. Worldwide it is the fifth most common cause of death from cancer in women.¹ Breast cancer has ranked number one cancer among Indian females with age adjusted rate as high as 25.8 per 100,000 women and mortality 12.7 per 100,000 women. Breast cancer projection for India during time periods 2020 suggests the number to go as high as 1797900.²

The growth of cancerous cells in the breast is what causes breast cancer. The lining of the breast ducts or milk glands is where the cancerous cells start. Breast cancer risk factors include ageing (80% of cases are seen in women over 50), family history, and BRCA1 and BRCA2 gene mutations. Breast cancer history, abnormal breast biopsies, menstruation before the age of 12 or menopause after the age of 55, not having children or having children after the age of 30, drinking alcohol twice a day or more, obesity, high-fat diets, radiation exposure to the breast (for example, during treatment for another cancer), and postmenopausal hormone replacement therapy (HRT) with a combination of oestrogen and progesterone drugs are all considered risk factors. The principles of the third stage include the main tumor's size and extension (T1-4), the presence and amount of lymph node involvement (N1-3), and the existence or absence of distant metastases (M0-1).^{3,4}

2. Aims And Objectives

The study's primary goal is to assess the use of medication in patients with breast cancer in tertiary care teaching hospitals. The goals are to analyse the drug prescription pattern for breast cancer and any co-morbid conditions that may exist; to evaluate adverse drug reactions related to medication therapy using Naranjo's Causality Assessment Scale; to analyse the grading and staging of breast cancer; and to evaluate the severity of pain using the Wong-baker FACES pain rating scale and the brief pain inventory scale.

3. Methodology

A six-month prospective observational study was conducted among the inpatients of the Erode Cancer Centre Erode, a 50-bed oncology hospital. The hospital serves both rural and urban residents. The majority of the patients are from lower and middle-class backgrounds. All female and male patients with breast cancer who were at least 18 years old and willing to provide consent were included in the trial. The study excluded individuals with other cancer kinds, psychiatric patients, those in their pediatric years, and newborns.

Every day for six days a week, the oncology ward was visited, and data about the patient's demographics and medication usage was entered on a semi-structured form. Patients and/or caregivers were asked for their informed consent before being handed a patient information leaflet. To obtain the essential patient data, a properly developed data collection form was utilized to gather information from the medical file and through patient interviews. A validated questionnaire will be used to expand clinical pharmacy services in patient care. Using Naranjo's Causality Assessment Scale, the reverse medication reaction brought on by chemotherapy was evaluated.

4. Results

Among the 77 patients studied, 65 received chemotherapy, one received radiation therapy, and one received surgical operation.

Demographics

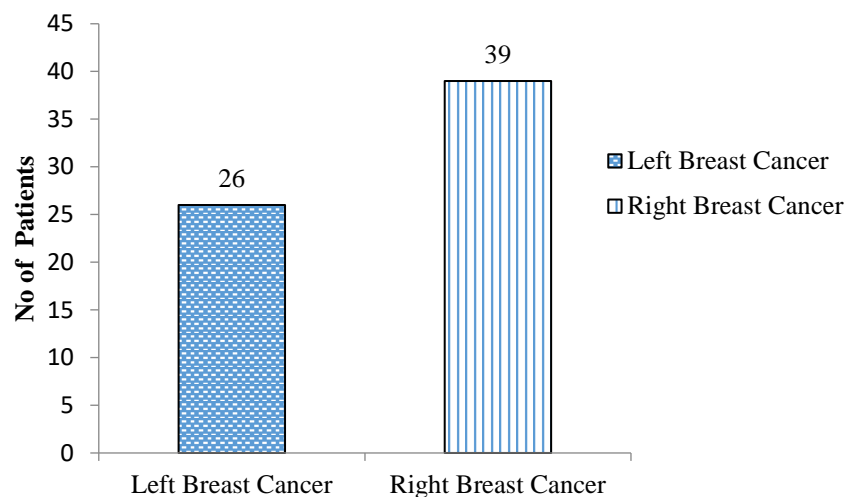
There were 75 (97.4%) females and 2 (2.5%) males among the 77 patients investigated. The patient's mean age was 49.3 ± 11.27 years, with a minimum age of 35 years and a maximum age of 74 years. There were 61 (79.2%) from rural areas and 16 (20.7%) from city. When the patient's educational status was considered, just 9 (11.6%) were well educated, whereas 68 (88.3%) were moderately educated.

Personal History

5 (6.4%) of the patients were alcoholics, whereas 2 (2.5%) were smokers). Out of 75 female patients, 42 (56%) were premenopausal and 33 (44%) were postmenopausal. According to marital status, 57 (76%) were married, 5 (6.6%) were unmarried, and 6 (8%) were widowed 3 (4%) of the 6 (8%) female breast cancer patients were nulliparous.

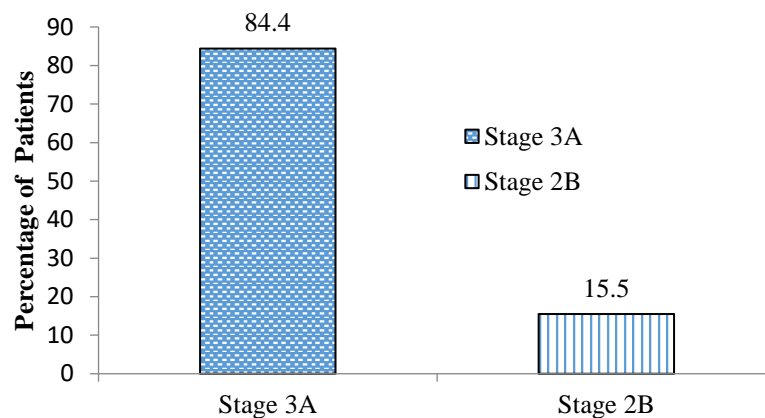
Disease Status

Among the 77 patients, 26 (33.7%) had left breast cancer, 39 (50.6%) had right breast cancer, and 12 (15.5 %) had bilateral breast cancer. According to AJCC staging, the majority of the patients were detected in stage 3A (65), with 12 individuals in stage 2B. The biggest number of patients were discovered in grade 2 (57), followed by 20 individuals in grade 1 (**Figure 1, 2**).



Disease Status of the Patients

Fig 1: Disease Status of the Patients



Stages of Cancer

Fig 2: Stages of Cancer

Out of 77 patients, 29 (37.6%) had modified radical mastectomy, 2 (2.5 %) had a lumpectomy, and 1 (1.2%) had an excision operation. Out of 77 breast cancer patients, 9 developed liver metastases (11.6 %) and 7(9.09%) had diabetes with hypertension. Among the 77 patients who got chemotherapy, the majority (22.2%) came for cycle 1 and the minority (7.2%) came for cycle 2.

Drug Regimen

Most of the patients receiving Cyclophosphamide+Adriamycin + Doxorubicin 89.9% and Docetaxel + Doxorubicin 3.3% combo therapy. Furthermore, the 5 Flurouracil +Cyclophosphamide were 3.2%, Cyclophosphamide +Docetaxel+ Adrimycin were 3.6% **(Figure 3).**

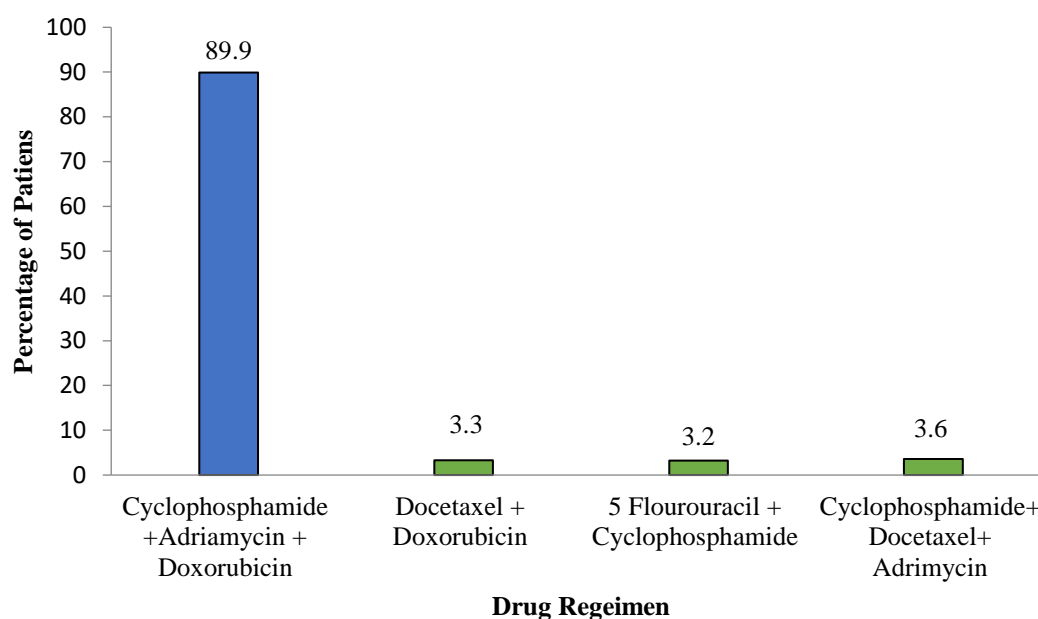


Fig 3: Drug Regimen of Cancer Patients

All of the 77 patients who received chemotherapy got antiemetics (Ondansetron), Corticosteroids (dexamethasone), and H2 antagonists (ranitidine) as medications to treat chemotherapy-induced adverse events. Some patients were given antipsychotics and antihistamines. Prepitant, a neurokinin-1 receptor antagonist, was given to two patients (5.2%) to relieve chemotherapy-induced nausea. Among the eight individuals who experienced pain, the most commonly utilized painkiller (50%) was a combination of acetaminophen and tramadol.

Adverse Drug Reaction

During the study period, 15 ADRs were observed in 77 patients. Alopecia (96.4%) was the most prevalent ADR recorded, followed by nausea (85.4%), Vomiting (70.58%), Drowsiness (31.2%), Nail discoloration (16.25%), Fatigue (22.1%), Mouth Ulcer (5.88%), Anorexia (16.2), Anemia (12.6%), Headache 11.6%, Diarrhoea 12.2%, Skin discoloration (5.88%), Anxiety (52.3%). Based on their causative relationship, the reported ADRs in patients receiving single and multi-drug chemotherapeutic treatments were further classified as definite, possible, likely, and questionable. According to Naranjo's Causality Assessment Scale, the majority of ADRs were classified as definite.

The most common adverse reaction reported in patients undergoing Cyclophosphamide+Doxorubicin combination therapy and Docetaxel monotherapy was nausea, with percentages of 88.23% and 92.30%, respectively. Both of the two patients taking Cyclophosphamide+5-Flourouracil + Methotrexate drug regimen were reported to experience tiredness and baldness. Patients on Cyclophosphamide + Adriamycin + Doxorubicin and Docetaxel + Doxorubicin combo therapy experienced nausea and vomiting. Furthermore, the Docetaxel+Doxorubicin medication regimen was associated with sleepiness and baldness. Alopecia, diarrhoea, anxiety, constipation, and fever were reported in patients receiving 5 Flourouracil + Cyclophosphamide combination therapy, whereas nausea, vomiting, alopecia, while individuals getting Cyclophosphamide + Docetaxel + Adrimycin combination therapy had nausea, vomiting, alopecia, and anemia (**Figure 4**).

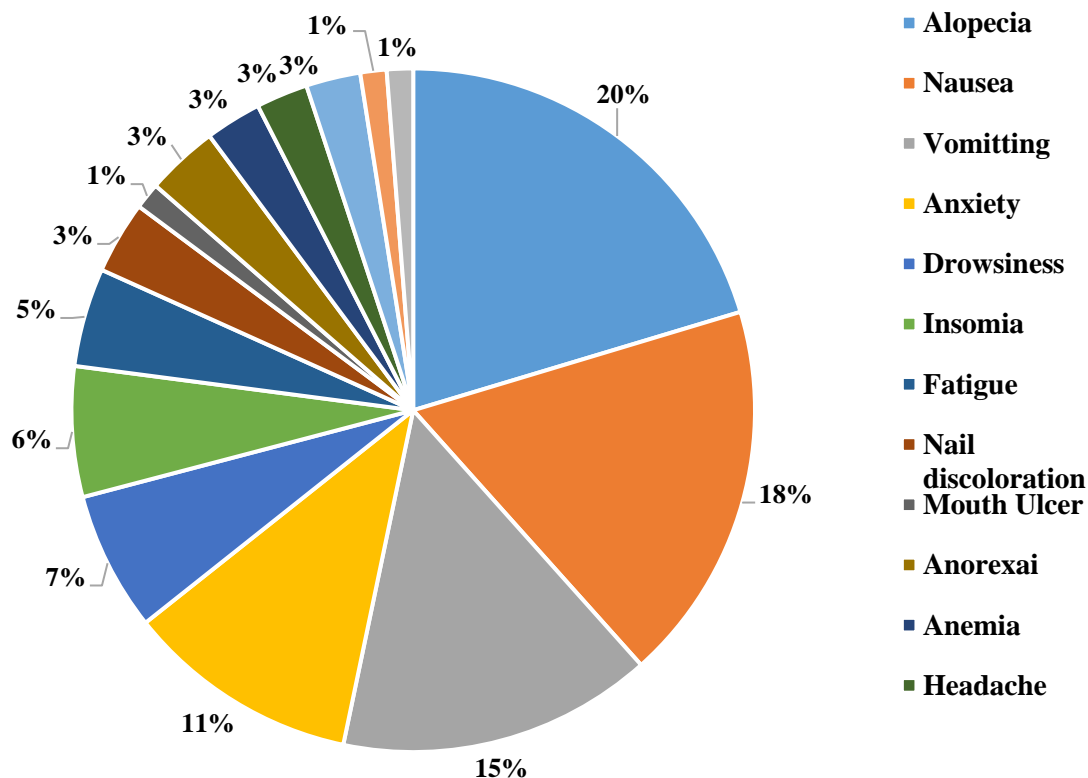


Fig 4: ADR among Anti-Cancer Utilized patients

5. Discussion

Breast cancer is the most common type of cancer among Indian women. Previously, cervical cancer was the most common cancer in Indian women, but breast cancer has recently surpassed cervical cancer as the primary cause of cancer death.² A total of 77 individuals with breast cancer were enrolled in the study, with (97.4%) being females and (2.5 %) being males. The majority of patients (49.3%) are between the ages of 41 and 50, which is similar to the findings of Agarwal G et al.³

In Asia, the prevalence of breast cancer is highest among women in their forties. Almost 9 (11.6%) of the 77 patients were alcoholics, and 3 (3.8%) were smokers. According to a study conducted by Hamajima N et al.⁴ the relative risk of breast cancer increased with increasing alcohol intake, both in neversmokers and in ever-smokers, but among those who drank no alcohol, ever-smokers, and current smokers were not at an increased risk of breast cancer compared to never smokers. There were 61 (79.2%) from rural areas and 16 (20.7%) from city, owing to a lack of health education. In contrast to our findings, Nagrani RT et al.⁵ found that living in rural areas reduces the risk of breast cancer.

Ali R et al.⁶ discovered in a contrast study that patients If they were widowed, divorced, or single, they were more likely to be diagnosed with a later stage of cancer. They were also found to have symptoms that lasted longer than married women. This could be owing to the ability of married women must rely on their husbands for household management support. Husbands are also a source of income. support, giving these women a greater voice opportunity to seek medical treatment as opposed to widower or divorced ladies on their own maintaining a home Earnings or work. Our study included 16 nulliparous women (21.3%) and 59 (78.6%) parous women. However, according to MacMahon B et al.⁷, women who had their first child after the age of 35

had risks that were roughly 20% higher than those who were nulliparous. Only 9 (11.6%) of the 77 breast cancer patients studied were highly educated, while 19 (24.6%) were uneducated, according to a study done by Ali R et al.⁶, which found that women with higher education levels were diagnosed at earlier stages of cancer than women with lower education levels. Perhaps a higher level of education among women in South India makes them more aware of the hazards linked with cancer symptoms, making them more willing to seek treatment. The majority of the patients had a lump in their throat. 39 (50.6%) individuals had right breast cancer, whereas 26 (33.7%) had left breast cancer. Three instances (15.5%) had breast cancer on both sides. According to a study conducted by According to Hussain MA et al.⁸ the prevalence of breast carcinoma was more on the upper outer quadrant on the left side in agreement with earlier studies and the study by According to Seymour I et al.⁹, the probable explanations are that the left breast is larger and the upper outer quadrant is larger has a higher volume of breast tissue than the average woman.

The American Joint Committee on Cancer divided breast cancer into four major stages based on the extent and size of the primary tumour (T1-4), the existence and extent of lymph node involvement (N1-3), and the presence or absence of distant metastasis (M0-1).⁴ Nearly 65 patients (84.4%) were diagnosed with stage 3 breast cancer and 12 patients (15.5%) were diagnosed with stage 2.

Modified radical mastectomy was performed on 77 individuals. 29 (37.6%) had modified radical mastectomy, 2 (2.5 %) had a lumpectomy, and 1 (1.8%) had an excision operation. Out of 77 breast cancer patients, 9 developed liver metastases (11.6 %) and 7(9.09%) had diabetes with hypertension.

According to a study conducted by M. Extermann et al.¹¹ investigated the risk and behavior of older patients. Co-morbidities and cancer can both have a significant impact their related treatment.

Out of 77 patients, 75 had chemotherapy, one received radiation therapy, and one received surgery. The majority of patients (19.2%) were on their first cycle of chemotherapy, followed by 15.4% in cycle 8, 13.5% in cycle 4, 14.7% in cycles 3 and 6, 10.1% in cycles 5 and 7, and 9.2% in cycle 2.

The most commonly prescribed chemotherapy drug regimen in our study population was Inj. Docetaxel 26 (47.3%). This was supported by the study done by Chevallier B et al.¹² which suggests that Docetaxel has major anti-tumor activity when used as a single cytotoxic agent as first-line chemotherapy in advanced breast cancer. The most commonly prescribed chemotherapy drug combination was inj Cyclophosphamide + Adriamycin + Doxorubicin 89.9%, Docetaxel + Doxorubicin 3.3%, 5 Fluorouracil + Cyclophosphamide 3.2%, Cyclophosphamide+ Docetaxel+ Adrimycin 3.6% and most of the patients were in the age group of 41 to 50 years.

Premedication usually comprises of two or more medicines. Given to patients before to chemotherapy to prevent nausea, vomiting, and other hypersensitive reactions. According to the study, nearly all of the individuals (n=55) who had Ondansetron was given to patients who had undergone chemotherapy. Dexamethasone (corticosteroid) with 5-HT3 antagonist which is consistent with the findings of Sakata Y et al.¹⁶ indicates that corticosteroids have an effective antiemetic effect in chemotherapy patients. According to John PA et al.¹⁷'s meta-analysis, Dexamethasone is beneficial in avoiding emesis in both children and adults. Cancer has two stages: acute and delayed.

Another study, conducted by Hajdenberg J et al.¹⁵, found that the combination of Palonosetron (5-HT3 antagonist) and Dexamethasone infused as premedication in patients receiving emetogenic chemotherapy was effective and safe in preventing acute and delayed chemotherapy-induced nausea and vomiting. In order to avoid the stomach irritation caused by most chemotherapeutic medicines, 55 chemotherapy patients were given injections of ranitidine. According to Warr GD et al.¹⁶, aprepitant (neurokinin1 receptor antagonist) was the most commonly used antiemetic drug against cyclophosphamide and anthracyclines. Our research found a similar pattern of treatment, with 2 (5.2%) patients receiving Aprepitant while on cyclophosphamide drug therapy.

As supporting medications, some patients were given antipsychotics (19%), analgesics (13.54%), antihistamines (52.1%), PPIs (5.5%), antibiotics (5.5%), vitamin supplements (6.5%), probiotics (3.8%), and hypnotics (2.8%). They are mostly used to address the negative effects of chemotherapy. Antihypertensive medicines (Amlodipine, Telmisartan), oral hypoglycemic drugs (Pioglitazone + Metformin + Glimepiride, Metformin + Glimepiride, Metformin, Glyciphage), and levothyroxine were given to patients with comorbidities. In our study, 5 (8.7%) patients had bone metastasis and received Inj. Zoledronic acid, which is

supported by a study conducted by Kohno N et al.¹⁷ that found Zoledronic acid significantly reduced skeletal complications compared to placebo across multiple end points in Japanese women with bone metastasis from breast cancer.

Although pain is the most prevalent subjective sensation in cancer patients, it is not a common early breast cancer symptom, however the tumour can produce pain as it presses into neighboring healthy tissues. Only eight individuals in this trial complained of pain, and they were given analgesics for it. Acetaminophen + Tramadol was the most usually recommended analgesic (32%), followed by Diclofenac + Tramadol (19 %) and Acetaminophen + Aceclofenac (21%). According to a study conducted by Ramalakshmi S et al.,¹⁸, acetaminophen was provided as analgesics for mild pain in 8% of the patients, ibuprofen in 10% of the patients, and aspirin in 5% of the patients, while morphine sulphate was given to 5% of the patients for severe pain.

An adverse medication reaction is defined by the World Health Organisation. ADR is defined as "a noxious and unintended response to a drug that occurs at normal doses." in humans for the prevention, diagnosis, or treatment of sickness, or for modifying physiological function." Potential challenges are encountered in all therapy practices. overcome by a system established by many countries worldwide by recording ADRs and these Databases contain information and statistics on these difficulties. It is necessary to have appropriate standardized ADRs should be measured precisely using scales.

There are various scales available for assessing harmful medication effects responses caused by the usage of several medicinal agents Naranjo's Causality, WHO Assessment Scale of Evaluation, Modified Hartwig and Siegel Scale Schumock and Thornton scales, for example. ADR severity is measured. All 77 breast cancer patients who received chemotherapy suffered at least one or more ADRs. The most common adverse effects seen in chemotherapy patients were alopecia (n=53, 96.4%), nausea (n=47, 85.4%), and vomiting (n=42, 76.4%). According to the Anjum F et al.²² study, the most common adverse effects seen in patients as a result of adjuvant chemotherapy were anemia/neutropenia (n = 764, 94.20%), alopecia (n = 763, 94.08%), fatigue/anorexia (n=743, 91.61%), and vomiting/nausea (n=799, 98.52%). The majority of patients reported nausea, vomiting, alopecia, and anaemia as a result of their single and combination chemotherapy treatment regimens.

The World Health Organization describes pain as "an unpleasant sensation." unpleasant physical or emotional experience linked to actual or potential tissue injury, as detailed in terms of such harm." Although pain is not a typical occurrence, 8 out of 77 patients had a breast cancer symptom they had gotten treatment for acute pain analgesics. The Brief Pain Inventory (BPI) analyses pain in a short period of time. The degree of pain and its impact on performance.

It also aids in determining the sort of pain the patient is experiencing. Using BPI, we determined that the majority of patients (n=5, 62.5%) had piercing pain in our study. The Wong Baker FACES Pain Rating Scale is a pain scale that depicts a succession of faces ranging from a smiling face at 0 representing "no hurt" to a sobbing face at 10 representing "worst hurt." The patient selects the face that best matches their level of discomfort based on the faces and descriptions. The Wong-Baker FACES Pain Rating Scale was employed in this study to rate pain, with 36 (63.2%) patients receiving a score of 2 indicating 'hurts a little bit' and 16 (28%) receiving a score of 0 indicating no hurt.

6. Conclusion

According to the findings of this study, 'Docetaxel' is the most commonly used medication regimen in chemotherapy, followed by 'Cyclophosphamide' with 'Doxorubicin'. Anti-emetics (5HT3 antagonists), corticosteroids, and H2 antagonists are the most commonly utilized medication regimen for adjuvant therapy, followed by antihistamines and antipyretics. Alopecia was the most prevalent ADR found, followed by nausea and vomiting. Only a few number of patients experienced pain. Early detection of breast cancer patients, as well as regular medical check-ups for individuals with a family history of breast cancer, can help improve the survival rate of breast cancer patients. The majority of the patients were from rural areas and had low socioeconomic level.

References

- [1] <http://www.wcrf.org/int/cancer-facts-figures/dataspecific-cancers/breast-cancer> statistics (World cancer research fund international [internet]. 22 Bedford Square, London WCB HH: Breast cancer statics. Accessed on 18/09/2017).
- [2] Malvia S, Bagadi SA, Uma SD, Saxena S. Epidemiology of breast cancer in Indian women, *Asia P J ClinOncol*, 13 (4), 2017 Aug, 289-95.
- [3] Agarwal G, Pradeep P.V, Aggarwal V, Yip CH, Cheung PSY. Spectrum of breast cancer in Asian women, *World J Surg*, 31 (5), 2007, 1031-40.
- [4] Llongueras S, Hamajima SD, Hirose N, Tajima K, Rohan K, Calle T, Heath EE, Jr. CW. Alcohol, tobacco and breast cancer- collaborative reanalysis of individual data from 53 epidemiological studies, including 58,515 women with breast cancer and 95,067 women without the disease, *Br J Cancer*, 87 (11), 2002 Nov, 1234-45.
- [5] Nagrani RT, Budukh A, Koyande S, Panse NS, Mhatre SS, Bhadwe R. Rural urban differences in breast cancer in India. *Indian J Cancer*, 51 (3), 2014 Sep, 277-81.
- [6] Ali R, Mathew A, Rajan B. Effects of socio-economic and demographic factors in delayed reporting and late-stage presentation among patients with breast cancer in a major cancer hospital in South India, *Asian Pac J Cancer Prev*, 9 (4), 2008, 703-7.
- [7] Macmahon B, Cole P, Lin T M, Lowe CR, Mirra AP, Ravnihar B, Salber EJ, Valaoras VG, Yuasa S. Age at first birth and breast cancer risk, *Bull. WldHlth Org*, 43, 1970, 209-21.
- [8] Hussain MA, Ali S, Tyagi SP, Reza H. Incidence of cancer breast at Aligarh, *J Indian Med Assoc*, 92, 1994, 296-7.
- [9] Schwartz SI, Principles of Surgery. 7th ed. United States of America: McGraw hill professional publication, 1999, 564.
- [10] Extermann M, Interaction between comorbidity and cancer, *Cancer Control*, 14 (1), 2007, 13-22.
- [11] Chevallier B, Fumoleau P, Kerbrat P, Dieras V, Roche H, Krakowski I, Azli N, Bayssas M, Lentz MA, Van GM. Docetaxel is a major cytotoxic drug for the treatment of advanced breast cancer: a phase II trial of the clinical screening cooperative group of the European organization for research and treatment of cancer, *J ClinOncol*, 13 (2), 1995 Feb, 314-22.
- [12] Sakata Y, Komatsubara S, Watanabe M, Mineyama H, Abe N. Antiemetic efficacy of high dose hydrocortisone in patient receiving cisplatin therapy. *Hinyokika Kiyo*, 32 (12), 1986 Dec, 1799-812.
- [13] Loannidis JP, Hesketh PJ, Lau J. Contribution of dexamethasone to control of chemotherapy-Induced nausea and vomiting: A meta-analysis of randomized evidence, *J ClinOncol*, 18 (19), 2000 Oct 1, 3409-22.
- [14] Hajdenberg J, Grote T, Yee L, Arevalo AR, Latier LA. Infusion of palonosetron plus dexamethasone for prevention of chemotherapy induced nausea vomiting, *J Support Oncol*, 4 (9), 2006 Oct, 467-71.
- [15] Warr DG, Hesketh PJ, Gralla RJ, Muss HB, Herrstedt J, Eisenberg PD, Raftopoulos H, Grunberg SM, Gabriel M, Rodgers A, Bohidar N, Klinger G, Hustard CM, Horgan KJ, Skobieranda F. Efficacy and tolerability of aprepitant for the prevention of chemotherapy-induced nausea and vomiting in patients with breast cancer after moderately emetogenic chemotherapy, *J ClinOncol*, 23 (12), 2005 Apr 20, 2822-30.
- [16] Kohno N, Aogi K, Minami H, Nakamura S, Asaga T, Watanabe YIT, Goessi C, Ohashi Y, Takashima S. Zoledronic acid significantly reduces skeletal complications compared with placebo in Japanese women with bone metastases from breast cancer: a randomized, placebo-controlled trial, *J ClinOncol*, 23, 2005, 3314-21.
- [17] Ramalakshmi S, Ramesh A, Sahini K, Babu KS, Kousalya K, Saranya P. A study on prescribing trends of supportive care drugs used in cancer chemotherapy in tertiary care teaching hospital, *Ind J of Pharm Pract*, 6 (3), 2013, 36-9.