ASSESSMENT OF PRESCRIBING PATTERN AND COMMON ADVERSE DRUG REACTIONS IN PATIENTS RECEIVING CHEMOTHERAPY FOR BREAST AND STOMACH CANCER

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ABSTRACT

Background: Cancer affected many communities all over the world makes the disease second leading cause of death. Recent statistics report states that globally one among co-deaths are due to cancer. **Objectives:** The main objectives of the study was to assess the prescribing pattern and common adverse drug reactions in patients receiving chemotherapy for breast and stomach cancer. **Materials and Methods**: Study was carried out at oncology department, Mysore Medical College Of Research Institute and Associated Hospitals; KR Hospital, Mysore, India, from July 2020 to October 2020. A total of 101 patients were enrolled in the study as per inclusion and exclusion criteria. Patient's demographic data were collected by using data collection form and adverse drug reactions were assessed by Naranjo Causality assessment scale, Hardwig Scale. **Result**: Out of 101 candidates, females show dominance over male and majority of the patients were in the age group 41-50years. Candidates with breast cancer(86) were more in number to that of candidates stomach cancer(15). The frequently assessed ADR's were nausea, vomiting, anemia and alopecia respectively. Doxorubicin+Cyclophosphamide was the most commonly used chemotherapy drug for breast cancer and Docetaxel+cisplatin for stomach cancer. **Conclusion**: The study was conducted to analyze the adverse drug reaction among cancer patients. A decline in disease can be obtained by giving awareness and proper education about the disease in the population.

KEYWORDS: Adverse drug reactions (ADR's).

INTRODUCTION

Cancer can result from abnormal proliferation of any of the different kinds of cells in the body. Tumor or mass of cells, formed of these abnormal cells may remain within the tissue in which, or it may begin to invade nearby tissues.[1] An invasive tumor is said to be malignant, and cells shed into the blood or lymph from a malignant tumor are likely to establish new tumors throughout the body. Tumors threaten an individual's life when their growth disrupts other tissues and organs.[8] Chemotherapy is recognized as one of the major treatment for different types of cancer, chemotherapy is the use of cytotoxic drugs to destroy cancer cells. It usually works by keeping the cancer cells from growing, dividing and making more cells. It may be used before surgery to shrink a tumor or after surgery to destroy any cancer cells that remains and to prevent the reoccurrence of cancer.[8]

Prescription pattern is a method of analysis of prescription use of different drugs. It is used to analyze the anticancer drugs and class of drugs being used for the treatment. It used to measure the safety and efficacy of the ongoing treatment. Adverse drug reactions in chemotherapy is any response to drug used for the treatment which can be noxious or unintended and occurs at normal doses for prophylaxis and treatment of the cancer.[7] Based on the evidences antineoplastic drugs account for most of ADRs compared to all other class of drugs. Detection of ADR's may help in minimizing the harm either by modifying the drug dosages regimen or by changing the target drug with a suitable alternative.

METHODS AND METHODOLOGY

This is a hospital based observational study. It was conducted at Mysore Medical College and research Institute and Associated Hospitals(KR Hospital): Mysore. The study was carried out at Oncology department among breast and stomach cancer patients who are undergoing chemotherapy as healthcare. The study duration was a period of three months from July 2020 to October 2020. The data were collected from the patient's medication history and their bystanders respectively after getting informed consent. The

department of oncology comprise of doctors specialized in cancer disease and for pharmacist. Nursing students are also available for the services. During the study period we attended 101 patients who are above 18 years old. Patients who are not willing for the study, incomplete information and people who are below 18 and above 80years are excluded from the study.

Importance of the study was explained to the participants and informed consent was taken from the patients or their bystanders. ADR probability was assessed by Naranjo Causality Assessment scale and Hartwig Scale used to monitor the severity of ADR and this was filled by patient itself and recorded the same. The data collected from the patients using questionnaire and data collection form are statistically analyzed by using SPSS.

RESULTS
Demographic details
Table 1: Gender Distribution of the Study.

Si No:	Gender	Frequency	Percentage
1	Male	17	16.8%
2	Female	84	83.2%
	Total	101	100%

Table 2: Type of Cancer.

Si No:	Type of Cancer	Gender	Frequency	Percentage
1	Breast cancer	Female Male	80	93%
			6	7.0%
		Total	86	100%
2	Stomach cancer	Female Male	4	26.7%
			11	73.3%
		Total	15	100%

Table 3: Age Categorization in the study population.

Si No:	Age Categorization	Frequency	Percentage
1	21-30	6	5.9%
2	31-40	17	16.8%
3	41-50	36	35.6%
4	51-60	27	26.7%
5	61-70	9	8.9%
6	71-80	6	5.9%
	Total	101	100%

PRESCRIPTION PATTERN
Table 4: Prescription Pattern for Breast Cancer.

Si No:	Prescription Pattern	Frequency	Percentage
1	Doxorubicin+Cyclophosphamide	45	52.33%
2	Trastuzumab+Docetaxel+Zoledronic acid	3	3.52%
3	Doxorubicin+Cyclophosphamide+Docetaxel	15	17.44%
4	Doxorubicin+Cyclophosphamide+Paclitaxel	9	10.46%
5	Cyclosphosphamide+Docetaxel	1	1.16%
6	Carboplatin+Gemcitabin	2	2.32%
7	Doxorubicin+Cyclophosphamide+Docetaxel+Gemc itabin+5-Flurouracil	6	6.97%
8	Trastuzumab	1	1.16%
9	Doxorubicin+Cyclophosphamide+Docetaxel+Trast uzumab	2	2.32%
10	Doxorubicin+Cyclophosphamide+5-Flurouracil	2	2.32%
	Total	86	100%

Table 5: Prescription Pattern for Stomach Cancer.

Si No:	Prescription Pattern	Frequency	Percentage
1	Epirubicin+Oxaliplatin	6	40%
2	Docetaxel+Cisplatin	7	46.67%
3	Doxorubicin+Cyclophosphamide+5-Flurouracil	2	13.33%
	Total	15	100%

ADVERSE DRUG REACTIONS
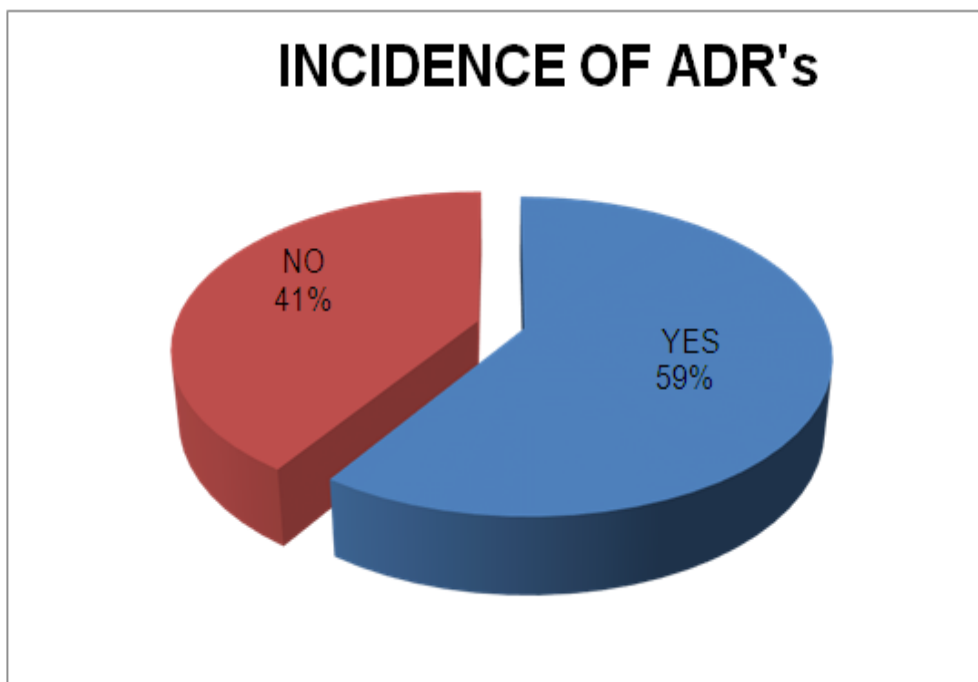
Table 6: Suspected Adverse Drug Reactions.

Si No:	Suspected ADR	Frequency	Percentage
1	Alopecia	22	18.33%
2	Nausea & Vomiting	31	25.83%
3	Burning Sensation & Dizziness	2	1.67%
4	Gastritis	5	4.17%
5	Diarrhoea	5	4.17%
6	Decreased Appetite	2	1.67%
7	Rashes	4	3.33%
8	Headache	4	3.33%
9	Febrile Neutropenia	5	4.17%
10	Lymphocytopenia	10	8.33%
11	Constipation	2	1.67%
12	Thrombocytopenia	5	4.16%
13	Anemia	23	19.17%
	Total	120	100%

Table 7: Suspected Medication.

Si No:	Suspected Medication	Frequency	Percentage
1	Doxorubicin	7	11.66%
2	Cyclophosphamide	22	36.66%
3	Docetaxel	8	13.33%
4	Paclitaxel	6	10%
5	Carboplatin	1	1.67%
6	Gemcitabine	3	5%
7	Cisplatin	1	1.67%
8	Oxaliplatin	3	5%

9	5-Flurouracil	4	6.67%
10	Trastuzumab	4	6.67%
11	Epirubicin	1	1.67%
	Total	60	100%

Table 8: Naranjo Causality Assessment of ADR.

Si No:	Naranjo Assessment Scale	Frequency	Percentage
1	Definite	2	3.33%
2	Probable	9	15%
3	Possible	49	81.67%
	Total	60	100%

Table 9: Hartwig Severity Assessment Scale.

Si No:	Severity	Frequency	Percentage
1	Mild	25	41.67%
2	Moderate	30	50%
3	Severe	5	8.33%
	Total	60	100%

Table 1 Shows greater dominance of females over males in the study population. Among 101patients included in the study 84 (83.2%) were females and 17 (16.8%) were males.

Table 2 Among 101 patients 86 (85.1%) were diagnosed with breast cancer out of which females were 80 (93%), males 6 (7%) and 15 (14.9%) were having stomach cancer in that female 4, male 11.

Table 3 Point out that 35.6% of the cancer patients are in the age group of 41-50years and least were in age group of 21-30years, 71-80 years respectively.

Table 4 Shows a clear picture regarding the different chemo-drugs used in the treatment of breast cancer. Doxorubin+Cyclophosphamide (52.33%) was the most commonly prescribed regimen.

Table 5 out of the 15 stomach cancer patients 7 (46.67%) patients were prescribed with Docetaxel+Cisplatin regimen.

Table 6 It is understood that the most commonly reported ADR is Nausea & Vomiting 25.83% followed by Anemia (19.17%), Alopecia (18.33%) respectively.

Table 7 Among the study population the mostly suspected drug causing ADR is Cyclophosphamide (36.66%)

Table 8 Among 120 ADR's found in the study population, the Naranjo scale assessment provides 81.67% of ADR's are possible, 15% are probable and 3.33% are definite.

Table 9 Shows that out of 120 ADR's, 50% of ADR's were moderate, 41.67% mild and 8.33% were severe.

DISCUSSION
The study was carried out to assess the prescription pattern and common adverse drug reactions in patients receiving chemotherapy for breast and stomach cancer. The study was carried out in the oncology department, Mysore Medical College and Research Institute and Associated Hospitals (KR Hospital) over a period of 3 months from July 2020 to October 2020.

DEMOGRAPHICS
Out of all 101 patients reviewed, it was seen that majority of the patients were females (83.2%) over the males (16.8%). Maximum of the patients belonged to the age group 41-50 years and the least age group was 21-30years respectively. It was also found that out of 86 patients diagnosed with breast cancer 93% of the subjects were females while stomach cancer was detected in 73.3% of male patients. This study was supported by the study conducted by **Manichavasagam et al.**[1] His study Stated 54.5% were females out of the total patients analyzed, he also figured out that least affected age group was 18-30.In his study he stated breast cancer to be more prevalent cancer among the women while stomach cancer was also found prevailing after lung cancer.

PRESCRIPTION PATTERN
It was recorded that out of 101 subjects taken for the study, 85.1% of the patients has chemotherapy for breast cancer followed by stomach cancer 14.9%. As shown in **table: 4** The most frequently used drug regimen for breast cancer in the above study comprised of Doxorubicin +Cyclophosphamide which was 52.3%, while the least given drug was trastuzumab (1.16%). this result was comparable with a study conducted by **Adhikari et al**[2] where he documented cyclophosphamide(20%) to be most commonly used drug for the breast cancer chemotherapy. the study also stated doxorubicin(12%) was second most established drug after docetaxel used for chemotherapy.

Table: 5 suggest that out of 14.9% of patients treated for stomach cancer, the most frequently used drug regimen was Docetaxel+cisplatin (46.6%). Docetaxel as Single – agentdrug shows 17- 24% more response rate in chemotherapy and pretreated patients. It was also seen that combination of docetaxel with cisplatin and 5-FU was also found much effective in maintaining the survival rate and quality of life of the patients.[3]

ADVERSE DRUG REACTIONS
As of **table:6** the most common adverse drug reactions experienced among chemotherapy patients was Nausea and vomiting which was reported to 25.3% of the patients, followed by anemia 19.1%. while 18.3% of the patients also experienced Alopecia. Constipation and Dizziness was found to be the least reported adverse drug reactions. This can be strengthened by the results of **chopra.d et al[4]** where she stated that 25.5% had Nausea and Vomiting and 20.5% patients had alopecia. As mentioned in **table: 7**cyclophosphamide was most likely to be causing the adverse drug reactions for 36.6% of the patients followed by docetaxel (13.3%) and doxorubicin (11.6%). This study was concurrent to study conducted by **Saini.VK et al[5]** where he found that 85.4% of the patients treated with cyclophosphamide had experienced one or the other adverse drug reactions.

CONCLUSION
Cancer is one of the leading causes of death in both developed and developing countries. Cancer cells are formed due to abnormal growth of normal cells because of mutation of DNA. Among the different types of cancers, breast cancer is most prevalent among the woman.[9] The current study explores the demographic characteristics. The ratio of male and females were also monitored in the study. Prescription pattern for breast and stomach cancer along with the common adverse drug reactions were monitored during the study.

In our study female patients were more in number when compared with males also majority of the patients belongs to the age group of 41-50 years.

The study comprises of breast and stomach cancer patients, commonly prescribed drug for breast cancer was Doxorubicin+Cyclophosphamide and for stomach cancer Docetaxel+Cisplatin.

Doxorubicin+Cyclophosphamide are mainly prescribed for breast cancer because Doxorubicin stops damaged cancer cells from continuing to grow, while Cyclophosphamide stops cancer cells from reproducing.

About 60 patients were reported with ADR during the study in which 51 are females and 9 are male patients. The most common ADR is nausea & vomiting, Cyclophosphamide is the major drug contributing to ADR. Hartwigs severity scale was used to categorize severity of ADR and most were found to be moderate & mild. Naranjo causality Assessment provides all the reported ADR's come under probable and possible.

ADR's are associated with considerable morbidity, mortality and high medical cost. Most of the ADR's with drugs are unreported due to unawareness of healthcare professionals, lack of time to report and a dearth of sufficient staff in the hospital. Hence it is necessary to recogonize the pattern of ADR's occurring with anticancer drugs so as to enhance the quality of life and to reduce the cost of ADR related hospitalization among cancer patients.

REFERENCES
1. Manichavasagam M, et al. Prescribing Pattern of Anticancer Drugs in a Medical Oncology Department of a Tertiary Care Teaching Hospital. Ann Med Health Sci Res., 2017; 7: 1-3.
2. Adhikari A, Chakraborty D, Indu R, Bhattacharya S, Ray M, Mukherjee R. DRUG PRESCRIPTION PATTERN OF BREAST CANCER PATIENTS IN A TERTIARY CARE HOSPITAL IN WEST BENGAL: A CROSS-SECTIONAL AND QUESTIONNAIRE-BASED STUDY. Asian J Pharm Clin Res [Internet]. 2018 Mar. 1 [cited 2020 Oct. 30]; 11(3): 398-01. Available from: https://innovareacademics.in/journals/index.php/ajpcr/article/view/23180
3. Docetaxel in the treatment of gastric cancer Peter C Thuss-Patience, Albrecht Kretzschmar, and Peter Reichardt Future Oncology, 2006 2:5, 603-620.
4. Chopra D, Rehan HS, Sharma V, Mishra R. Chemotherapy-induced adverse drug reactions in oncology patients: A prospective observational survey. *Indian J Med Paediatr Oncol*., 2016; 37(1): 42-46. doi:10.4103/0971-5851.177015
5. Saini VK, Sewal RK, Ahmad Y, Medhi B. Prospective Observational Study of Adverse Drug Reactions of Anticancer Drugs Used in Cancer Treatment in a Tertiary Care Hospital. *Indian J Pharm Sci*., 2015; 77(6): 687-693. doi:10.4103/0250-474x.174990
6. Cooper GM. The Cell: A Molecular Approach. 2nd edition. Sunderland (MA): Sinauer Associates; 2000. The Development and Causes of Cancer as of 29/10/2020. Available from: https://www.ncbi.nlm.nih.gov/books/NBK9963/
7. Behera SK, Kishtapati CR, Gunaseelan V, Dubashi B, Chandrasekaran A, Selvarajan S. Chemotherapy Induced Adverse Drug Reactions in Cancer Patients in a Tertiary Care Hospital in South India. J Young Pharm., 2017; 9(4): 593-7.
8. www.cancer.net/navigating-cancer-care/how-cancer-treated/chemotherapy/understanding- chemotherapy as of 29/10/2020 https://www.cancer.net/navigating-cancer-care/how-cancer-treated/chemotherapy/understanding-chemotherapy https://www.jyoungpharm.org/sites/default/files/10.5530jyp.2017.9.113_0.pdf
9. Reddy D, kalyani G, Pradeep K, Asif M, Kartheek

D, Gangabhavani M. The survey of cancer patients in the region of Guntur: Based on hospital registry. Int J Pharm Pharm Sci., 2017; 9: 288- 32.