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STUDY OF ADVERSE DRUG REACTIONS TO CHEMOTHERAPEUTIC AGENTS AMONG CANCER PATIENTS IN A TERTIARY CARE HOSPITAL

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ABSTRACT
Objectives: To estimate the incidence of adverse drug reactions to chemotherapeutic agents in cancer patients. **Methods:** This cross sectional observational study was conducted between December 2016 and February 2017 in Medical oncology ward. Totally 94 cancer patients who fulfilled the criteria were included. A semi-structured proforma was used to record socio-demographic details, and the details of chemotherapy and adverse drug reactions. Causality assessment was done by using WHO-UMC scoring system. **Results:** Among 94 patients enrolled, 64% female and 36% male. Majority (62%) were in the age group of 51-60years, of lower socio-economic status (78%) and from rural areas (67%). The common types of cancer diagnosed were breast (24%), stomach (15%), ovary (14%), lung (12%), colorectal carcinoma (11%) and Gestational trophoblastic disease (3%). Around 59%, 24%, 14% of patients received two, three and single chemotherapeutic agents respectively. All patients had at least one adverse drug reaction, 31% had two or three adverse drug reactions, while 9% reported more than three adverse drug reactions. Most common cancer chemotherapeutic drugs used were 5-flurouracil(28%) and carboplatin(26%).The commonest adverse drug reaction was alopecia(45%), followed by dermatological reactions(19%), tingling sensation(17%), leucopenia(16%), nausea/vomiting(16%), anemia(13%) and thrombophlebitis(5%). Causality assessment revealed that all the adverse drug reactions were in probable category. **Conclusion:** All patients receiving chemotherapeutic drugs suffer at least one adverse drug reactions. Consistent monitoring of therapy is needed for early recognition of adverse drug reactions and prompt management.

KEYWORDS: Cancer, chemotherapy, adverse drug reactions (ADR).

INTRODUCTION
Carcinoma remains the leading cause of morbidity and mortality all over the world with its relative position varying with age and sex.[1] The incidence of cancer is around 70-90 per 1,00,000 population. In the year 2010, analysis of prevalence of cancer in developing country like India had shown estimated total cases to be around 2.5 million, with 8,00,000 new cases and 5,50,000 deaths occurring each year. Overall, cancers of lung, oesophagus, stomach, oral and pharyngeal cancers, mostly affect men. On the other hand, cervical and breast cancers are most common in women.[2]

Toxicity of the anticancer drugs is the major drawback in treatment of cancer, leading to poor treatment compliance, economical burden, prolonged hospital stay and at times mortality as well. Early detection and management of adverse effects is the cornerstone in the management of cancer patients treated with chemotherapeutic agents.[3]

In order to monitor the safety of drugs and to minimize the unwanted side effects 'The National Pharmacovigilance program' was started in India in 2010. As per the World Health Organisation (WHO), Pharmacovigilance (PV) is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse drug reactions or any drug-related problems.[4]

New processes, both at a regulatory and a scientific level are being developed with an aim of strengthening pharmacovigilance. On a regulatory level, these include conditional approval and risk management plans; on a scientific level, transparency and increased patient involvement are two important elements.[5] The success of the scheme depends upon the vigilance of health care professionals.[6] The common anticancer drugs used in our hospital were cisplatin, etoposide, paclitaxel, carboplatin, cyclophosphomide, adriamycin, 5-Flourouracil.

Paucity of data relating to drug safety monitoring in India led us to undertake this study where we tried to evaluate the pattern of ADRs occurring in cancer patients treated with chemotherapy in a tertiary care hospital in South India.

MATERIALS AND METHODS

Study design: Cross sectional descriptive observational study.
Study period: 3 months.
Study population: 94 patients.
Study centre: Department of Medical Oncology ward, Tirunelveli Medical College Hospital, Tirunelveli.

Inclusion criteria

- Age more than 18 years and less than 60 years irrespective of sex.
- Patients with any type of cancer.
- Patients receiving chemotherapy alone or chemotherapy and surgery or targeted therapy.

Exclusion criteria

- Patients receiving radiotherapy combined with chemotherapy.
- Patients who are not willing to give written informed consent.

Methodolgy

Cancer patients who were admitted for chemotherapy were assessed for emergence of adverse reactions both in clinical and laboratory parameters. The chemotherapy drug administered and number of cycles and other relevant details were recorded in a semistructured proforma. Socio-demographic data of the patients were recorded for each patient. The causality assessment for each adverse drug events were assessed by using WHO – UMC scoring. Study results were analysed statistically. Institutional ethical committee approval was obtained. Written informed consent was obtained from all patients in their own vernacular language.

RESULTS

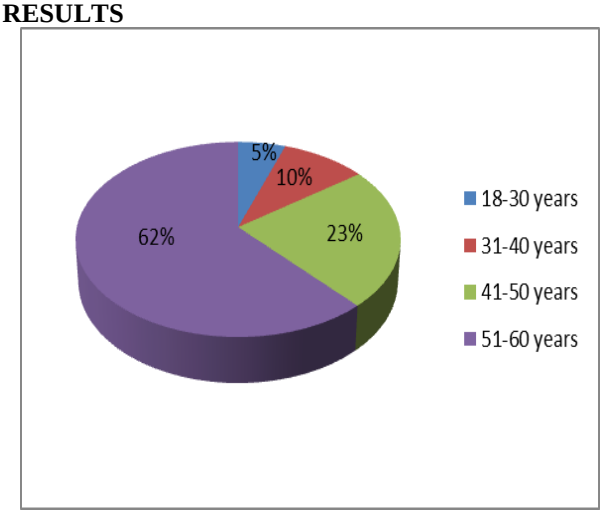

Figure. 1: In the present study majority of the cancer patients fall in the age group of 51-60 years(62%).

Age distribution of cancer patients

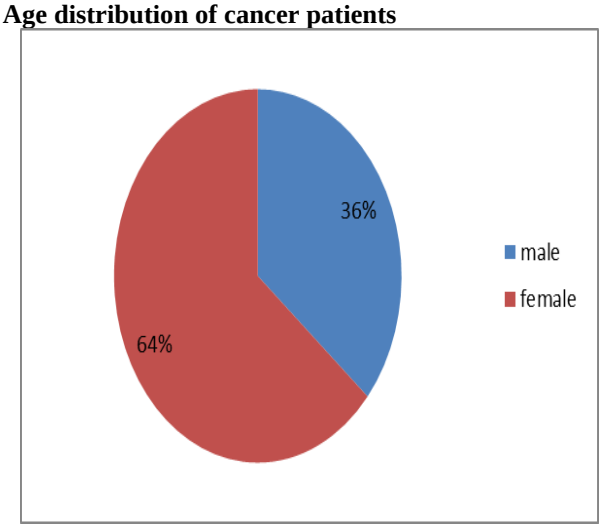

Figure. 2: Females (64%) dominated in the study population.

Sex distribution

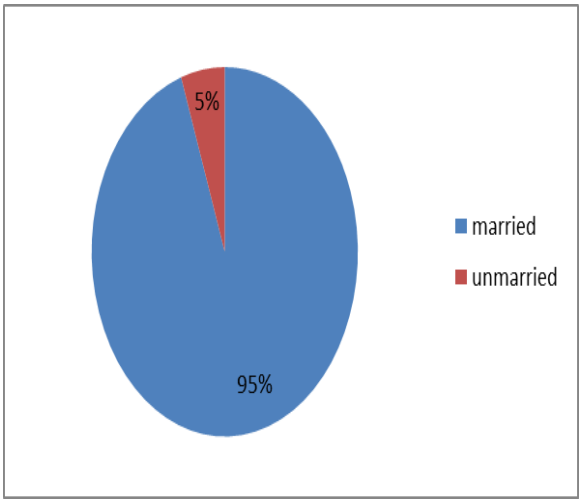

Figure. 3: 67% were from rural area and most of the study population were married (95%).

Marital status of study population

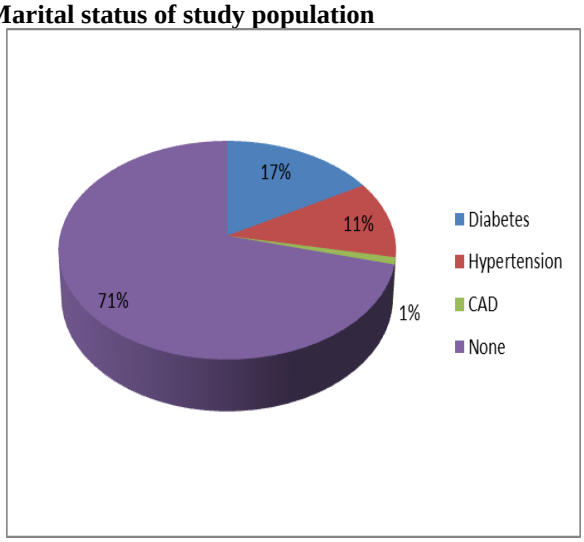

Figure. 4: Around 71% of patients did not have any medical co-morbidity.

Medical co-morbidities of study population

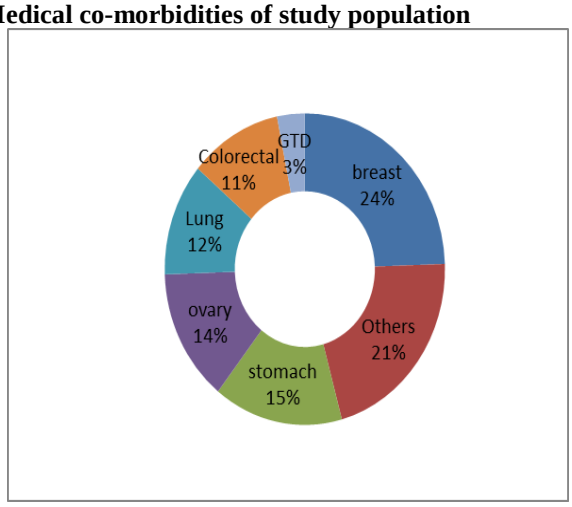

Figure.5: The most common organs involved in cancer were breast (24%), stomach (15%), ovary (14%), lung (12%), colorectal (11%), and gestational trophoblastic disease (3%).

Common types of cancer in percentage

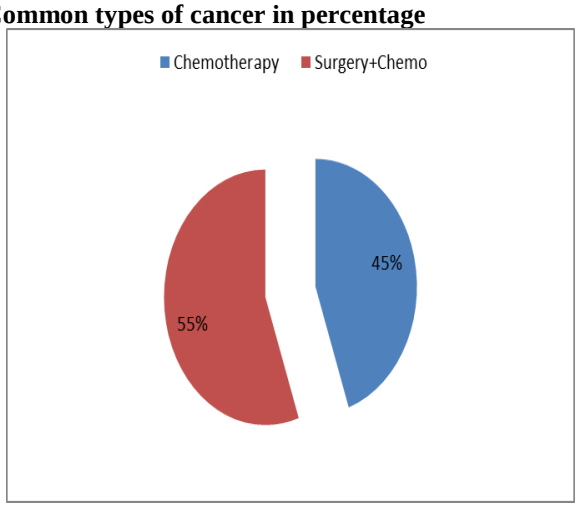

Figure.6: Around 55% of patients were treated with combined surgery and chemotherapy, remaining with chemotherapy alone.

Types of treatment received

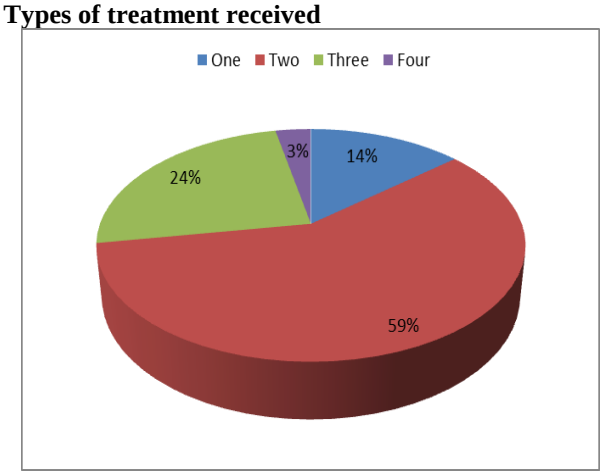

Figure. 7: Among the study population 59%, 24%, 14% of patients received two, three and one chemotherapeutic agents respectively.

No of chemotherapy drugs given to patients in percentage

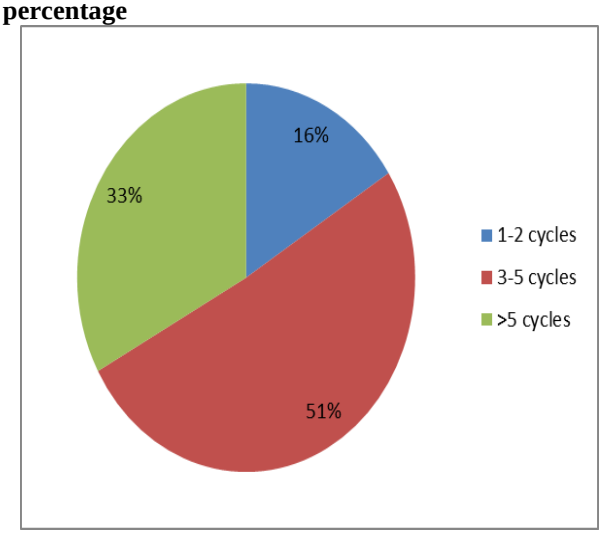

Figure.8: Half of the study population undergone 3-5 cycles of chemotherapy.

Chemotherapy cycles received

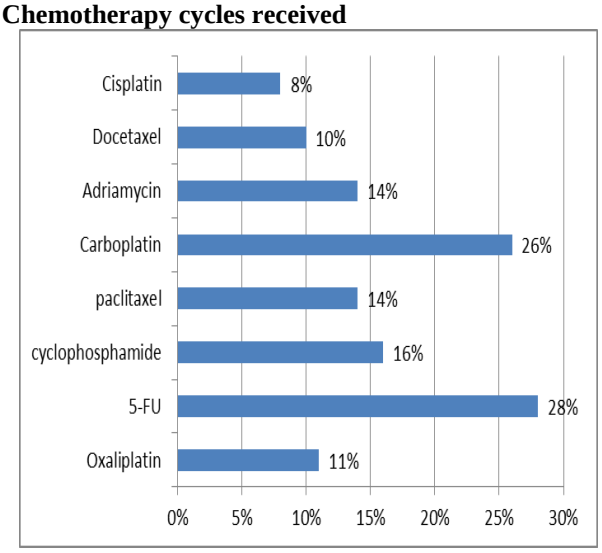

Figure.9: The commonly prescribed chemotherapeutic drugs were 5-Flurouracil (28%), carboplatin (26%), cyclophosphamide (16%), adriamycin (14%) followed by oxaliplatin, docetaxel and cisplatin.

Common chemotherapeutic drugs used

Alopecia (45%) was the most frequently reported ADR followed by other dermatological reactions (19%), tingling sensation (17%), leucopenia and nausea/vomiting (16% each), anemia (13%), thrombophlebitis (5%). ADRs were more frequent with 5-flurouracil, cyclophosphamide and carboplatin.

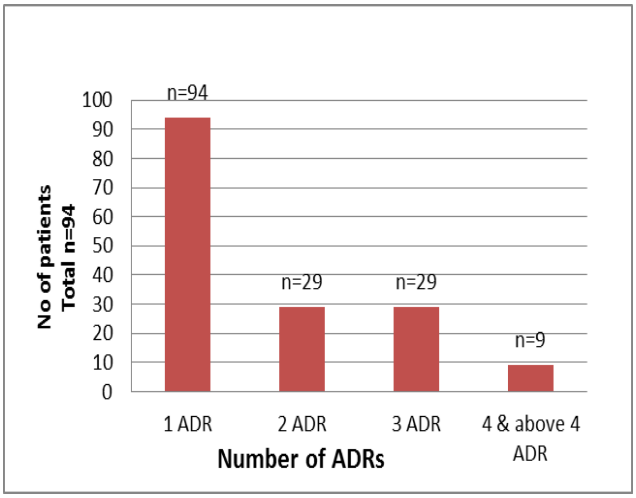

Figure. 10: All patients receiving chemotherapeutic drugs suffer at least one ADR

Number of adverse drug reactions

Table.1: Frequently reported adverse drug reactions and its causality assessment.

ADRs REPORTED	NO OF PATIENTS	PERCENTAGE	SUSPECTED DRUGS	CAUSALITY
Alopecia	48	45%	Adriamycin Paclitaxel Carboplatin Cyclophosphamide Docetaxel 5-FU	Probable
Dermatological (blackening of skin and nails, Oral mucosal ulcer, Skin rashes)	20	19%	Adriamycin Cyclophosphamide Docetaxel 5-FU	Probable
Tingling sensation and numbness	18	17%	Carboplatin Paclitaxel 5-FU Cyclophosphamide Oxaliplatin	Probable
Nausea and vomiting	17	16%	Oxaliplatin 5-FU Carboplatin Adriamycin Cyclophosphamide	Probable
Leucopenia	17	16%	5-FU Oxaliplatin Cisplatin	Probable
Anemia	13	13%	Carboplatin Cisplatin Etoposide 5-FU	Probable
Thrombophlebitis	6	5%	5-FU Docetaxel Carboplatin	Probable

DISCUSSION

The practice of cancer medicine has changed dramatically nowadays with treatment available for many previously fatal malignancies. Adjuvant chemotherapy has proven to extend life and prevent disease recurrence.[7] Despite these therapeutic successes, many of the anti cancer drugs possess narrow therapeutic index and a greater potential for causing adverse effects such as alopecia, nausea and vomiting, neutropenia/anemia/pancytopenia, constipation/diarrhoea and fatigue.[8]

The demographic profile of the present study shows that majority of females (64%) were found to have ADRs as

compared to males. This was consistent with other studies and the fact that women experience more adverse reactions to therapeutic drugs than men as a result of different pharmacokinetic and pharmacodynamic responses to drugs.[9,10] ADRs mostly occurred in the age group of 51 -60years, which was similar to that reported by other studies.[11] All patients had at least one ADR in our study.

In contrast to many studies, the most common ADRs found in this study were alopecia(45%) followed by dermatological reactions(19%), tingling sensation(17%), leucopenia(16%), and nausea and vomiting (16%). It was observed that majority of patients had received antiemetic as preventive therapy. This was consistent with findings of other studies done by Podder et al, Malik et al where also the majority of the cases received increased doses of antiemetic in order to manage ADR. Although both the newer targeted therapies and the traditional anticancer drugs are associated with toxicities of skin, hair, nails, and mucosa, accurate diagnosis and early recognition of potential reactions may reduce the significant morbidity, cosmetic disfigurement, and psychological distress.[12]

5-FU was reported as the most common drug responsible for ADRs, which was consistent with that reported by Poddar *et al*, whereas cisplatin was the most common drug causing ADRs in kirthi et al, Malik *et al* study.[13] The causality assessment revealed that most of the ADRs were "probable" category.

Enhanced use of preventative measures and early detection of drug toxicity has the potential to contribute to reduce the severity of ADRs. A comprehensive and effective pharmacovigilance need to be put into place to reduce the burden of ADRs and thereby further improve the benefit: harm ratio of the drugs.[14,15]

Limitation of the study

This study included only a limited number of patients in a single centre with small sample size. As most of the chemotherapy regimens were multidrug regimen, we could not ascertain the ADR for individual drugs.

CONCLUSION

All patients receiving chemotherapeutic drugs suffer at least one ADR. Pharmacovigilance offers a great deal in minimizing the ADRs by modifying the dose of the drugs and reduce the economic burden to the patient and to the society. Consistent monitoring of therapy is needed for early recognition of ADRs and to initiate prompt action.

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REFERENCES

1. Warnakulasuriya S. Global epidemiology of oral and oropharyngeal cancer, *Oral Oncol.*, 2009; 45(4): 309-16.
2. Most Prevalent Cancers in India, Available from: http://www.medindia.net/health_statistics/diseases/cancer
3. Amartya De. Monitoring of suspected adverse drug reactions in oncology unit of an urban multispecialty teaching hospital, International Journal of Research in Pharmaceutical and Biomedical Sciences, 2010; 1(2): 1-32.
4. World Health Organization. International Drug Monitoring: The Role of the Hospital. Geneva: World Health Organization, 1996.
5. Smitha K, BairykL, Vidyasagar MS et al., Adverse drug reaction profile of cancer patients on chemotherapy in a tertiary care hospital, International journal of Pharma and Bioscience, 2015; 6(2): 233-44.
6. Prasad A, Datta PP, Bhattacharya J, Pattanayak C, Chauhan AS, Panda P. Pattern of adverse drug reactions due to cancer chemotherapy in a tertiary care teaching hospital in Eastern India. J Pharmacovigilance, Feb 8, 2013; 1(2): 107.
7. Ejaz A, Casadaban L, Maker AV. Utilization and impact of adjuvant chemotherapy among patients with resected stage II colon cancer: a multi-institutional analysis. Journal of Surgical Research, Jul 31, 2017; 215: 12-20.
8. Wahlang JB, Laishram PD, Brahma DK, Sarkar C, Lahon J, Nongkynrih BS. Adverse drug reactions due to cancer chemotherapy in a tertiary care teaching hospital. Therapeutic advances in drug safety, Feb, 2017; 8(2): 61-6.
9. Poddar S, Sultana R. Pattern of adverse drug reactions due to cancer chemotherapy in tertiary care teaching hospital in Bangladesh. Dhaka Univ J Pharm Sci., 2009; 8: 11–6.
10. Kirthi C, Afzal A, Reddy M, Ali SA, Yerramilli A, Sharma S. A study on the adverse effects of anticancer drugs in an oncology center of a tertiary care hospital. Int J Pharm Pharm Sci., 2014; 6: 580–3.
11. Mallik S, Palaian S, Ojha P, Mishra P. Pattern of adverse drug reactions due to cancer chemotherapy in a tertiary care teaching hospital in Nepal. Pak J Pharm Sci., 2007; 20: 214–8.
12. Pavey RA, Kambil SM, Bhat RM. Dermatological adverse reactions to cancer chemotherapy. Indian Journal of Dermatology, Venereology, and Leprology, Jul 1, 2015; 81(4): 434.
13. Deepti Chopra, Harmeet S Rehan, Vibha Sharma, Chemotherapy induced adverse drug reactions in oncology patients ;A prospective observational study, Indian journal of medical and paediatric oncology, 2016; 37(1): 42-46.
14. Geer MI, Koul PA, Tanki SA, Shah MY. Frequency, types, severity, preventability and costs of adverse drug reactions at a tertiary care hospital. Journal of

pharmacological and toxicological methods, Oct 31, 2016; 81: 323-34.
15. Pirmohamed M, James S, Meakin S, Green C, Scott AK, Walley TJ, Farrar K, Park BK, Breckenridge AM. Adverse drug reactions as cause of admission to hospital: prospective analysis of 18 820 patients. Bmj, Jul 1, 2004; 329(7456): 15-9.