



**ORIGINAL RESEARCH ARTICLE**

**STUDY OF PATTERN OF ADVERSE DRUG REACTION DUE TO CANCER CHEMOTHERAPY AND THEIR MANAGEMENT IN HOSPITALIZED PATIENT IN BP KOIRALA MEMORIAL CANCER HOSPITAL**

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**ABSTRACT**

Adverse Drug Reactions (ADRs) are a global problem adding to the economic burden of the society. Anti-cancer drugs are prone to cause ADRs and there is lack of pharmacovigilance data on such type drugs. Therefore, the present study was undertaken to monitor suspected ADRs in the cancer chemotherapy with its management in B.P. Koirala Memorial Cancer Hospital (BPKMCH). The study was done in the inpatient department of BPKMCH from May, 2014 to July, 2014, among the patients receiving chemotherapy. It was a hospital based prospective observational study. Most commonly occurring cancer were lung (16%), ovary (15%), cervix (11%), breast, blood, and throat (9%). Most frequently used drugs for cancer chemotherapy were paclitaxel (25%), cyclophosphamide (18%), vincristine (9%), cisplatin (11%) and adriamycin (6%). Most common ADRs experienced were nausea & vomiting (85.45%), loss of appetite (72.72%), mucositis (65.45%), pain (63.63%), loss of breath (40%), constipation (52.72%) and polyneuropathy (58.18%).

**Key words:** ADR, Cancer, Chemotherapy, Chemotherapeutic agents, management.

**INTRODUCTION**

In Nepal, and many other developing countries, cancer is traditionally believed to be a disease of death. In the medical profession, cancers are believed to be primarily an environmental disease. About 5-10% of cancers occur due to genetics, the rest are due to environmental factors such as food habit, lifestyle and environment. The frequency of cancer appears to be increasing, especially in developing countries including Nepal, leading to a serious impact on quality of life and survival of patients. Cancer has become the leading cause of death worldwide in economically developed countries, and the second highest cause of death in developing countries. The exact prevalence rate of cancer is not known for Nepal because the cancer registry system is very poor, and a population-based national cancer registry system does not exist in Nepal. However, some hospital-based and local population-based data of cancer treatment are available. In 2005 there were 4397 cancer cases reported from 7 major hospitals dealing with cancer patients. B. P. Koirala Memorial Cancer hospital, Bharatpur has the highest number of cancer patients, visiting from most districts of Nepal and some neighboring parts of India. In 2010, the total number of out-patients registered in BPKMCH was 87,042. Among them 17.31% were diagnosed as cancer patients, and 5442 patients were admitted for cancer treatment. Being a largest hospital, large numbers of people are receiving treatment in this hospital. Various chemotherapeutic agents are used for the treatment of cancer. These Chemotherapeutic agents kill

cancer as well as normal cells because of which patient are experiencing several numbers of side effects during and after the course of chemotherapy. So these side effects must be managed, to avoid serious effects and patient non compliance. The side effects of chemotherapy plays role in worsening health related quality of life (HRQL) of patients, diminishing the physical activity resulting in limited treatment and increased morbidity.<sup>1,2</sup> In recent years, targeted therapy has considerably increased the survival rate in patients affected. These types of newer interventions in the field of treatment of cancer show more side effects.<sup>3</sup> ADR reporting and its management will enhance the effectiveness of the therapy and reduce the side effects which ultimately reduces the rate of mortality. Previous researches conducted in various countries by several doctors, Pharmacists and Chemists include only the pattern of ADRs, but our research has been focused in ADR pattern as well as the approaches made for their management.

**MATERIALS AND METHODS**

This is the hospital based prospective study. Patient profiles were used as data collection tools. They were taken as major material used in this research in which demographic records, associated illness, diet history, smoking history, chemotherapeutic agents, their adverse events and interventions to manage these adverse events were recorded. The study was conducted from March, 2014 to August, 2014. Total 55 patients were enrolled. The

patients admitted in the inward patient department, treated with anti-neoplastic drugs during the study period were included in the study. The patients with other co-morbid diseases were excluded from the study.

**RESULTS**

Statistical analysis in this study was carried out for various parameters like age, gender, risk factors, site of cancer, use of chemotherapeutic agent, side effect caused by these agents, drugs used to manage these side effects etc. Out of total patient studied maximum number of 21 patients of age group 31- 45 followed by age group of 46 - 60. The percentage of male and female population was 47 and 53 respectively. Cancer is more prone in female than in male.

**Table 1: Distribution of sociodemographic characteristics**

Characteristic		Frequency	Percentage
Age	0-15	5	9
	15-30	7	13
	30 -45	21	38
	45 -60	16	29
	>60	6	11
Marital Status	Married	44	80
	Unmarried	7	13
	Widow	4	7
Socioeconomic Status	Upper	1	2
	Upper Middle	9	20
	Lower Middle	4	9
	Upper Lower	29	64
	Lower	2	5
Risk Factor	Smokers	18	23
	Alcohol	15	19
	Tobacco	15	29
	Other	31	39
Dietary Habits	Vegetarian	4	7
	Lactovegetarian	7	13
	Non vegetarian	44	80

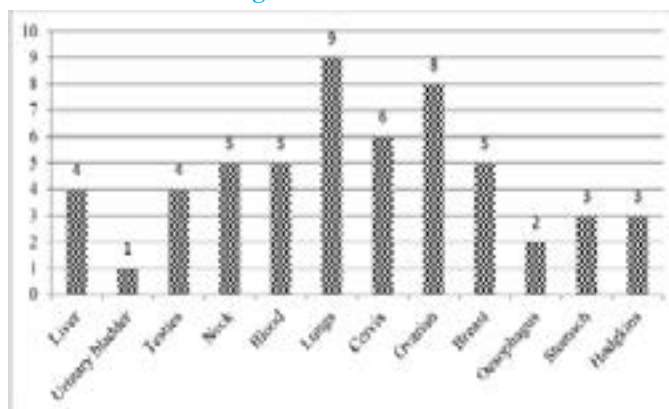
The most common cancer in our study is found to be lung cancer followed by ovarian cancer.

**Table 2: Site of cancer**

Site of cancer	No. of patients	Percent
Liver	4	7
Urinary bladder	1	2
Testis	4	7
Neck	5	9
Blood	5	9
Lungs	9	16
Cervix	6	11

Ovarian	8	15
Breast	5	9
Esophagus	2	4
Stomach	3	6
Hodgkin's	3	5
<b>Total</b>	<b>55</b>	<b>100%</b>

**Fig. 1: Site of cancer**

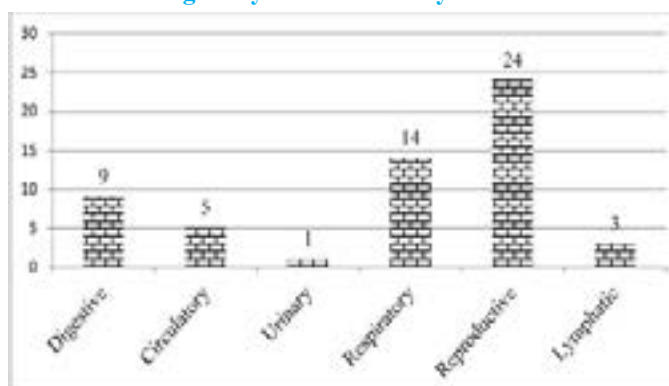


The detail of system affected by cancer is given in figure below. In this study, it was seen that reproductive system (43%) was affected highest number of patients followed by respiratory system (25%).

**Table 3: System affected by cancer**

System Involved	No. of patients	Percent
Digestive	9	16
Circulatory	5	9
Urinary	1	2
Respiratory	14	25
Reproductive	24	43
Lymphatic	3	5
<b>Total</b>	<b>55</b>	<b>100</b>

**Fig. 2. System affected by cancer**

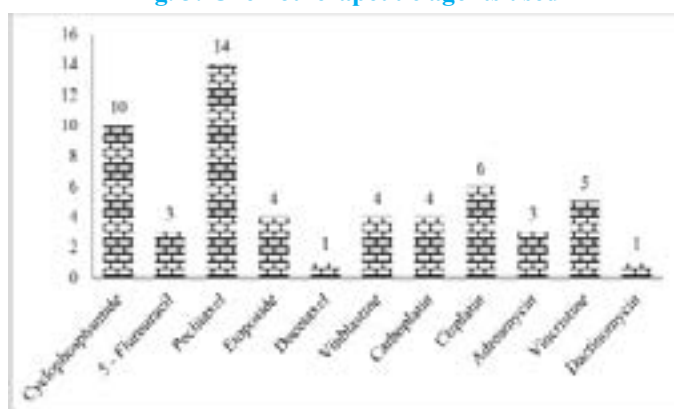


In our study, the most commonly used chemotherapeutic agent was Paclitaxel (25%) followed by Cyclophosphamide (18%) and the most rarely used chemotherapeutic agents were Docetaxel (2%) and Dactinomycin (2%).

**Table 4: Chemotherapeutic agent used**

Chemotherapeutic agent	No. of patients	Percent
Cyclophosphamide	10	18
5-Fluorouracil	3	6
Paclitaxel	14	25
Etoposide	4	7
Docetaxel	1	2
Vinblastine	4	7
Carboplatin	4	7
Cisplatin	6	11
Adreamycin	3	6
Vincristine	5	9
Dactinomycin	1	2

**Fig. 3: Chemotherapeutic agents used**

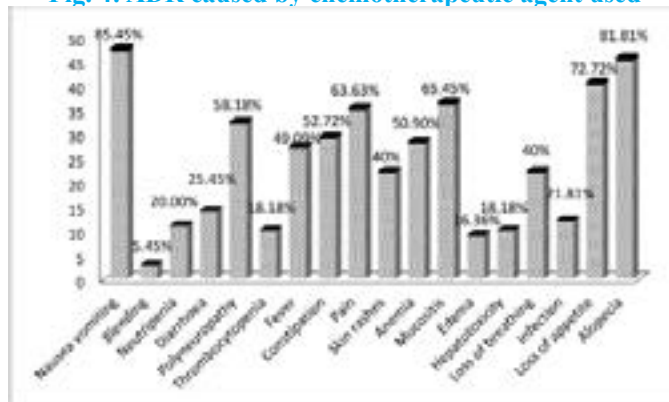


Nausea and Vomiting (85.45%) is the most common adverse events seen, followed by alopecia (81.81%).

**Table 5: ADR caused by chemotherapeutic agent used**

Adverse events	No. of patients	Percent
Nausea vomiting	47	85.45
Bleeding	3	5.45
Neutropenia	11	20.00
Diarrhoea	14	25.45
Polyneuropathy	32	58.18
Thrombocytopenia	10	18.18
Fever	27	49.09
Constipation	29	52.72
Pain	35	63.63
Skin rashes	22	40
Anemia	28	50.90
Mucositis	36	65.45
Edema	9	16.36
Hepatotoxicity	10	18.18
Loss of breathing	22	40
Infection	12	21.81
Loss of appetite	40	72.72
Alopecia	45	81.81

**Fig. 4: ADR caused by chemotherapeutic agent used**



**DISCUSSION**

During the study, it has been found that age group of 30 - 45 (38%) was mostly affected by cancer followed by age group between 45- 60 (29%). The overall risk accumulation is combined with the tendency for cellular repair mechanisms to be highly effective in a person at the age of 30-45<sup>4</sup>. The occurrence of cancer is more in female (53%) as compared to male (47%). This may be because of the hormonal differences between the male and female. Certain hormones such as estrogen alone or estrogen along with progestin is found in higher amount in female because of which they are at high risk of cancer. Menopause may also be the cause of cancer in female. Treatment of certain diseases with hormone therapy may also increase risk of cancer in female<sup>5</sup>. Socioeconomic status was assessed using modified Kuppuswami scale. It was found that 64% were from upper lower, 20% were from upper middle, 9% were from lower middle, 5% were from lower and remaining 2% were from upper socioeconomic status. Lack of diet physical activities, eating habit, lack of high fibrous food, consumption of fatty, red meat, high salty and starchy food in middle class people may also result in cancer<sup>6</sup>. The occurrence of cancer is greater in non vegetarian (80%), than lacto-vegetarian (13%) and vegetarian (7%). From the study, lung cancer (16%) was found to be most common cancer. Plant based diets are generally considered to be cancer protective. According to Knize MG, specific plant foods such fruits and vegetables, plants constitutes fibers, antioxidants and other phytochemicals that helps in achieving and maintaining a healthy lifestyle with reduced risk of cancer. Consumption of meat, specially red and processed meats, increases risk of several type of cancer<sup>7</sup>. Ovarian (15%) is second most common cancer. Cervical cancer (11%) is also a common cancer. Breast, neck and blood cancer were seen in 5 (9%) patient each. Similarly, liver and testis cancer were seen in 4 (7%) patients each. Stomach cancer (6%), Hodgkin’s lymphoma (5%), esophageal cancer (4%) and urinary bladder cancer (2%) were seen in patients. Smoking and tobacco use was found to be the major risk factor as the cause several cancers, especially lung cancer. Chemicals in tobacco and smoke are carcinogens, these are the substances which can damage cells and lead to cancer. The risk of lung cancer depends more on the length of time a person has smoked. Non smokers have a low risk of developing lung cancer. People who work with radioactive materials, asbestos, nickel and chromium have an increased risk. Air pollution may also be the

minor risk factor for lung cancer<sup>8</sup>. These results shows that the most common system affected by cancer was reproductive system (43%) followed by respiratory system (25%). Paclitaxel (25%) was the most common anti neoplastic agent used. Cyclophosphamide (18%), Cisplatin (11%), Vincristine (9%) were also highly used. Etoposide, Vinblastine and Carboplatin were used in 7% of patients each. Similarly, 5- Fluorouracil and Adreameycin were also used in 6% patients each. Dactinomycin and Doccetaxel were used in 2% of patients each. Paclitaxel is mostly used in the treatment of several types of cancer, either alone or in combination because of its effectiveness in wide range of tumors. In lung cancer, paclitaxel is given as 24 hour infusion, this combination has comparable efficacy to standard combination<sup>9</sup>.

In the study, Nausea and vomiting (85.45%) were found to be commonest ADRs in our patients. The most common mechanism of chemotherapy induced nausea and vomiting is through activation of chemoreceptor trigger zone. Since these are common problem associated with cancer chemotherapy, strategies are made to prevent and manage nausea and vomiting in patients undergoing chemotherapy<sup>10</sup>. Intravenous granisetron and ondansetron were mostly used for this purpose during chemotherapy and after receiving chemotherapy oral ondansetron or Domperidone or Metocloperamide were used. Alopecia (81.81%) was the second most common ADR. Next common ADR was found to be loss of appetite (72.72%). Since, patients receiving chemotherapy experience loss of appetite, the patient may feel weak. To manage this problem, use of appetizer was the most convenient method. Mucositis (somatitis) was seen in 65.45% of the patients, because of which patient may not eat and speak properly, for which use of chlorhexidine or povidone iodine gargle were mostly used. Sometimes vitamin B complex is used to treat weakness as well as mucositis. Patient with cancer and receiving chemotherapy suffers from pain. For the management of chemotherapy induced pain NSAIDs, tramadol or naproxen were mostly used. Polyneuropathy (58.18%) was also seen. Patients may have burning sensation, so they were advised to place ice pack in burning place. In case of polyneuropathy, oral methylcobalamin was prescribed to the patient. Constipation (55%) was another chemotherapy induced ADR. Patients were advised for diet control. Oral lactulose syrup was most commonly used drug to treat chemotherapy induced constipation. Because chemotherapy affects bone marrow, it causes anemia (50.90%), seen in our study. Anemia was managed by blood transfusion and erythropoietin mostly. Folic acid and iron polymaltose were also frequently used for the purpose<sup>10</sup>. Fever was also experienced by 49.59% of patients receiving chemotherapy. This problem was usually solved by using combination of paracetamol and ibuprofen. Sometimes intravenous paracetamol was also given. In severe cases, certain antibiotics (cefixime) and combination of codeine phosphate and paracetamol was also used. Patient receiving chemotherapy also experienced loss breathlessness (40%). Intravenous dexamethasone was most commonly used while receiving chemotherapy and later oral dexamethasone was used to treat this ADR<sup>11</sup>. Skin rashes (40%) was also a chemotherapy induced ADR, which was treated by using topical corticosteroids

(Fluticasone, Hydrocortisone, Clobetasone). Sometimes oral levocetirizine or fexofenadine was also used. Diarrhoea was experienced by 25.45% of patients. This ADR was mostly treated with oral or intravenous metronidazole. Sometimes loperamide tablet was also used. Chemotherapy also induced various infections (21.81%) for the management of which various antibacterial (levofloxacin, cefixime, vancomycin, amoxicillin + clavulanic acid) agents were used<sup>12</sup>. Next ADR was found to be neutropenia (20%). Usually various diet were prescribed for the management aspect, but in severe cases intravenous filgrastim was used. Other chemotherapy induced ADR were thrombocytopenia (18.18%), hepatotoxicity (18.18%), edema (16.36%) and bleeding (5.45%). For the management of hepatotoxicity, usually Liv 52 syrup or Amlycure DS\* Syrup/ Capsules were used. Oral prednisolone was used to treat edema and for treating bleeding, oral or intravenous tranexamic acid was mostly used<sup>13</sup>.

## CONCLUSION

Our study showed that the major cancer cases reported were lung cancer, ovarian cancer, cervical cancer, blood cancer, breast cancer and throat cancer. The female gender was found more prone to cancer than male with female and male ratio of 29:26. The increased risk of cancer cases concluded that the prevalence pattern of cancer is increasing day by day. With the increasing use of cancer cases, the use chemotherapeutic agent is also increasing. The most prescribed chemotherapeutic agents were Paclitaxel, Cyclophosphamide, Vincristine, Cisplatin and Etoposide. The most common ADR occurred with the use of chemotherapeutic agents were pain, nausea & vomiting, mucositis, loss of appetite, neutropnia etc. The most common drugs used for the management of ADRs were antiemetic, laxatives, appetizer, opioids & NSAIDs, mouth washes & gargles, etc. From the study we can conclude that most of the patients receiving chemotherapy experience some sort of adverse drug reaction, but most of the ADRs were found to be mild to the patients while some were life threatening. Pharmacist's interventions in assessing ADRs were found to be effective for the success of the therapy and for the patient compliance & adherence.

## FUTURE SCOPE OF THE STUDY

Pattern of adverse drug reaction occurring due to cancer chemotherapy and their management in hospitalized patient of BPKMCH were conducted and analyzed. The study was conducted only in hospitalized patient, while the patient receiving chemotherapy in day care centre may also experience similar type of ADRs. The study can be performed in the patients receiving chemotherapy in day care centre. Our study include pattern of ADR of as a whole chemotherapeutic agents. In future the ADR caused by an individual chemotherapeutic agent can be performed. Study can also be conducted regarding the dose of the drugs.

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