

EVALUATION OF CANCER PREVALENCE AND CYTOTOXIC MEDICATION PRESCRIBING IN CENTRAL REGION OF NEPAL

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ABSTRACT

In this study, our objective was to evaluate the cancer prevalence and inpatient prescribing pattern of cytotoxic medicines in one of the major tertiary care hospital for cancer treatment in central region of Nepal. A retrospective cross-sectional descriptive study was conducted. A modified data collection form was used to collect the information on patient demographics and prescribed drugs. Females were found to be more susceptible to cancer than males. 58 different types of cancer were observed with reproductive, respiratory and digestive cancers being prevalent. A total of 427 cytotoxic drugs were prescribed. The alkylating agent group of cytotoxics was the most frequently prescribed one (45.67%). The average number of drugs prescribed per prescription, cytotoxic drugs per prescription, antibiotics per prescription and other drugs per prescription were 10.77, 1.78, 0.37 and 8.99 respectively. The cytotoxic drugs were prescribed by brand names according to the hospital policy. The drugs prescribed from World Health Organization (WHO) model list of essential drugs and essential drug list of Nepal were 67.40% and 73.72% respectively. Percentage of encounters with antibiotics and injections prescribed were 31.25% and 100 % respectively.

Key words: *Cancer, Cytotoxic drugs, Nepal*

INTRODUCTION

Cancer is a multi-cellular disease which can arise from any cell types and organs with multi-factorial etiology [1]. Simply, cancer means the change in the body's cells that cause them to grow out of control [2]. It is a neoplastic disorder caused due to excessive proliferation of cells. Being a dreadful disease, it brings tremendous social distress, psychological suffering and hardship to the patients and relatives [3] and has become the important contributor to the global burden of disease [4]. Causes of cancer include factors such as tobacco, dietary factors, body mass and physical activity, and exposure in the workplace.

Cancer is the leading cause of death in economically developed countries and second leading cause of death in developing countries. In 2011, one out of four deaths in United States was due to cancer [5]. Due to advancements in health care systems, life expectancy of the individuals is increasing and so does the elderly population. As the chance of cancer incidence in elderly are high, the cancer prevalence may increase dramatically in years to come [6]. Due to this, cancer has become an important agenda in the health sector of every country.

For the treatment of cancer, various modalities like surgery, chemotherapy, radiation therapy, immunotherapy and monoclonal antibody therapy are used. The choice of therapy depends on the location and grade of the tumor, the stage of the disease, and the general state of the patient. Chemotherapy refers to the antineoplastic drugs used to treat cancer or the combination of these drugs into a cytotoxic standardized treatment regimen. The various types of chemotherapy include combined modality called combination chemotherapy. The fundamental principle of combination chemotherapy is that different drugs act through different cytotoxic mechanisms. Because of the ability of cytotoxic agents to kill cells, their actions are not specific to tumor cells only and also damage normal cells. As a result, they can produce significant side effects in patients or others exposed. Most cytotoxic drugs are potentially hazardous substances being mutagenic, teratogenic or carcinogenic. These substances may also cause secondary neoplasms in patients undergoing treatment. Extreme care must therefore be taken in handling and administering of such products. In Nepal, where the prevalence of cancer is high and the availability of treatment modalities is low, it is necessary to check and analyze the prescribing and usage patterns of cytotoxic drugs.

Drug utilization studies are most applicable and particularly focused on the most frequently used group of therapeutic drugs such as antibiotics, chemotherapy or those that constitute important therapeutic innovations [7]. The utilization of drugs is based on their prescribing pattern. The ultimate goal of this study was to explore the prevalence of cancer and evaluate the prescribing patterns of cytotoxic drugs in one of the major tertiary hospitals of Nepal.

MATERIALS AND METHODS

Study type

A retrospective cross-sectional study was conducted, which evaluated the prescription pattern and prevalence information of cancer of the year 2012.

Study site

The study was conducted in one of the major tertiary care hospitals for cancer treatment of Central region of Nepal. The collection of data was done from the in-patient medical record files of the year 2012. The patient records fulfilling the inclusion criteria were selected and evaluated for the prescribing patterns. The patients belonged to the medical wards and the permission to conduct the study was approved by the Hospital administration department.

Inclusion Criteria

The medical inpatients receiving the chemotherapy in Day Care and different wards were included. The medical inpatients to be included in the study had to be registered first in the hospital in the year 2012 and must also undergo chemotherapy of at least one chemo-cycle. The prescribing pattern in the first chemoplan treatment was studied.

Exclusion Criteria

The medical cancer outpatients and the ones receiving medical attention other than chemotherapy and of years other than 2012 were excluded. The patients undergoing treatment modes like radiation use and surgical removal of the cancer tumor were excluded from the study.

Data collection

The data were collected from the in-patient prescription records at the hospital. A modified data collection form was used to collect the information on patient demographics and information of prescribed drugs.

Operation Modality

The in-patient record files were obtained from the hospital and the information was filled in the form. The data collection was performed by all the members of the research group and was cross checked by one another for any missed information.

Sample Size

240 in-patient records of the year 2012 complied with the inclusion criteria. The prescription in the first chemoplan was included for the study. A total of 2766 in-patient records were filed in the year 2012 out of which 240 records met the inclusion criteria.

Ethical consideration

Ethical clearance was obtained prior to the initiation of the study from School of Health and Allied Sciences, Pokhara University.

Statistical Analysis

Results were analyzed using SPSS version 12.0.

RESULTS AND DISCUSSION

Sociodemography

Age Distribution of patients

The age wise distribution pattern of cancer patients is shown in Figure 1. The study revealed that majority of cancer cases was evident in the age groups between 40 to 70 yrs. The mean \pm standard deviation of the patient age was 51.8 ± 15.6 yrs. The age wise distribution of the patient showed that there was higher incidence of cancer in the age group of 60 to 70 years of age. The total incidence of the case constituted of 24.58% in this age group. The next susceptible age group of patient prone to cancer was 40 to 50 years. The graph also revealed that the incidence of cancer was least in the age group of less than 10 years. As we observe the bar graph, the cancer prevalence trend seems to increase with age. A correlation can be made with the increasing age and cancer prevalence. Ageing related processes may be responsible for increased cancer prevalence at increased age [8-11]. Several mechanisms have been proposed for explaining how vulnerability of cancer increases with age. Aging makes an organism susceptible to cancer due to hormonal balance disturbance, increase in number of loci of chronic proliferation, and the decline in the immune surveillance. Exposure to infectious agents and creation of pro-oncogenic tissue microenvironment with increasing age can promote the development of cancer [9, 11]. Figure 1 has revealed the cancer in the younger age to have lower occurrence. This can be attributed to more health consciousness by the younger generations [12].

Gender wise distribution of patients

The gender wise distribution pattern of cancer patients is shown in Table 1. On analyzing the distribution pattern of cancer patients according to gender, the data represented that cancer was more prevalent in females than males. The greater prevalence of cancer in females can be because of the involvement of their reproductive system such as the cervical cancer, ovarian cancer and breast cancer which occupy the major portion among all other forms of cancer [12]. These susceptible body parts cause greater incidence of cancer problems in the females. Another way of interpreting the increased incidence of cancer cases in females is the spare time they can utilize to make hospital visits. Nepalese female population is less employed than males. This means that the female population has free time to visit hospitals. The frequency of hospital visits by females is more than males, which provides greater chances of cancer diagnosis [13].

Table 1 Gender wise distribution of cancer patients

S.No.	Sex	Percentage
1	Male	39.58%
2	Female	60.42 %

Physiological system wise distribution of cancer patients

The distribution of cancer patients in various body systems is shown in Figure 2. In our study, it was observed that the cancer relating to the reproductive system had the highest percentage prevalence i.e. 38.32%. This was followed by respiratory cancer (28.75%) and the cancers of digestive system (18.75%). The greater incidence of the reproductive system cancer is due to greater female cases with involvement of female reproductive system. The various physiological and biochemical changes that occur in females with respect to age can be one of the main factors relating to increased cancer cases, especially that of the reproductive system. Breast cancer is due to abnormal female hormone levels in the body, which generally is seen in the later stages of life, especially after the menopause. The greater prevalence of cancers related to the respiratory system can also be due to the presence of brick bakeries in the area of data collection i.e. Bhaktapur. Bhaktapur area has many brick bakeries which contribute to the increased levels of air pollution. The workers at these local business sites are highly prone to respiratory cancers. Digestive cancer was the third most prevalent cancer case. The diet of the Nepalese people is rich in spices and fats. The recent trend of eating on the streets, great deal of junk foods and busy work schedules can greatly affect the incidence of digestive cancer cases. Nepalese have the common problem of gastritis due to unmanaged dietary schedules and feeding habits. Also the great increase in the consumption of processed and packaged food stuffs can be one of the major causes of fiber deficiency that affects the gastrointestinal functions.

Types of cancers observed

There were altogether 58 different types of cancer observed during the study period. The type of cancers observed with their corresponding number of patients is shown in Table 2. The cancers were found to be affecting every systems of the body revealing the non specific nature of the disease.

Table 2 Types of cancers observed

S.No.	Types of Cancer	No. of patients	S.No.	Types of Cancer	No. of patients
1.	Abdomen	2	30.	Nasopharyngeal	3
2.	Adenocarcinoma	1	31.	Neck cancer	1
3.	Alveolar soft tissue carcinoma	2	32.	Neuroblastoma	2
4.	Anaplastic astrocytoma	1	33.	NHL	9
5.	Breast cancer	41	34.	Oesophagus cancer	2
6.	Bronchogenic carcinoma	2	35.	Ovary cancer	10
7.	Buccal mucosa cancer	1	36.	Pancrea carcinoma	1
8.	Cervix	34	37.	Papillary carcinoma	1
9.	Clitoris	1	38.	Periapillary carcinoma	2
10.	Colon	12	39.	PGTD	2
11.	Conjunctival	1	40.	Plasma cell carcinoma	1
12.	Eining's sarcoma	1	41.	PNET	1
13.	Endometrium	3	42.	Prostate	1
14.	Epidermal	1	43.	Pyriiform fossa	1
15.	Esophagus	2	44.	Rectal	7
16.	Gall bladder	7	45.	Kidney	1
17.	Generalised lymphadenopathy	1	46.	Scalp	1
18.	Hodgkin's lymphoma	3	47.	Sinus	1
19.	Hypopharyngeal	2	48.	Small intestine	1
20.	Larynx	5	49.	Spindle cell neoplasm	1
21.	Lung cancer	43	50.	Stomach	5
22.	Mandibular gland cancer	1	51.	Supraglottis	4
23.	Mantle cell cancer	1	52.	Thyroid lobe	1
24.	Maxillary sinus cancer	1	53.	Upper lip	1
25.	Squamous cell carcinoma	1	54.	Urethra	1
26.	Mouth	1	55.	Urinary Bladder	2
27.	Multiple myeloma	1	56.	Vocal cord	1
28.	Nasal cavity	1	57.	Vulva	1
29.	Naso ethmoidal	1	58.	Hysterectomy with pelvic lymphadenopathy	1

Prescribing Patterns of Drugs
Anticancer drugs

Table 3 Prescribing patterns of cytotoxic drugs

Type	Group	Name	Number
Alkylating agents	Nitrogen mustards	Cyclophosphamide	55
		Ifosfamide	4
		Melphalan	1
	Triazines	Dacarbazine	3
	Platinum compounds	Carboplatin	38
		Cisplatin	86
		Oxaliplatin	8
Antimetabolites	Folate Antagonists	Methotrexate	5
		Leucovorin	12
	Pyrimidine pathway	Fluorouracil	54
		Cytarabine	1
		Gemcitabine	22
Cytotoxic antibiotics	Anthracyclines	Doxorubicin	42
		Epirubicin	16
	Others	Bleomycin	3
		Actinomycin	1
Plant derivatives	Taxanes	Paclitaxel	25
		Docetaxel	9
	Vinca alkaloids	Vincristine	17
		Vinblastine	4
	Camptothecins	Irinotecan	3
	Others	Etoposide	2
	Drug acting on hormonal milieus	Glucocorticoids	Prednisolone
		Total	427

The prescribing pattern of the cytotoxic drugs is shown in the Table 3. The prescribed drugs for the cancer patients included different cytotoxic drugs, antibiotics as well as other drugs that belonged to different therapeutic classes. There were altogether 427 cytotoxic drugs that were prescribed. The percentage of different classes of drugs prescribed in the cancer patients is presented in Figure 3. Alkylating agents constituted the major portion with drugs acting on hormonal milieu constituting the least.

In the present study, the encounter with the antibiotic prescribed was 31.25%. The antibiotics included here also included the cytotoxic antibiotics like doxorubicin, epirubicin, bleomycin, etc. The antibiotic prescription was remarkably less than that reported in Iran (61.9%) [14]. According to WHO, 15-25% of antibiotic encountered is expectable in the countries where an infectious disease is more prevalent [15]. However, this result is due to the fact that most of the antibiotics included the cytotoxic antibiotics that should be prescribed according to the respective regimen of cancer type. But if only the non cytotoxic antibiotics were analyzed, we found that the occurrence of these antibiotics per prescription was just 9.16% that falls within the limits as described by the WHO [15].

Supportive drugs

Cancer chemotherapy includes cytotoxic medicines accompanied by adjuvant and supplementing therapeutic measures. These additional medications other than the cytotoxic medicine are for reducing the side effect seen with the cancer chemotherapy. The average number of other drugs per prescription is presented in Table 4. In average, 5.7 different groups of drugs were prescribed in addition to the cytotoxic and antibiotic therapies.

Table 4 Average number of other drugs per prescription

S.No.	Drug Category	Average number per prescription
1.	Anti-emetics	1.67
2.	Rehydration Therapy	1.65
3.	Supplements	1.5
4.	Steroids	0.97
5.	Proton pump inhibitors	0.61
6.	H ₂ Antagonists	0.52
7.	Analgesics	0.20
8.	Miscellaneous	1.64

The study showed that the average number of anti-emetic drugs per prescription was 1.67. Anti-emetic drugs were used to reduce the nausea and vomiting associated with the cancer treatment via cancer chemotherapy. The number 1.67 signifies that more than one of the anti-emetic drugs per prescription were used for the management of chemotherapy induced vomiting. Single

molecule administration requires higher dosage for controlling vomiting, but the combination therapy requires less individual doses and is also more effective with lower side effects.

The average number of rehydration therapies per prescription was found to be 1.64. The rehydration therapy included the normal saline and Ringer's lactate solution. This was used to prepare required concentrations of the medication necessary for constant infusion. The cancer chemotherapy leads to the state of anorexia. This can cause severe depletion of essential nutrients required for normal body functioning. In our study there was prescription of 1.5 supplements given per prescription. The supplements include iron supplements, vitamin supplements and protein supplements.

The steroids, per prescription, were found to be 0.97. Mostly the chemotherapy included dexamethasone. Dexamethasone was used in the cancer chemotherapy in order to minimize the side effects of the chemotherapy which included nausea, vomiting and anorexia. Dexamethasone was used to alleviate nausea caused by chemotherapy medications, stimulate appetite, treat inflammation in the body, treat certain types of cancer (in conjugation with chemotherapy) and also decrease blood calcium levels (associated some bone cancer cases) [16].

Injections prescribed

From the 240 prescriptions, there were a total of 1612 injections out of 2585 total drugs prescribed. The injections prescribed were 62.36% of the total drugs prescribed. In this study, the percentage of prescription with cytotoxic injectables prescribed was found to be 100% and the percentage of prescription with injectables prescribed was found to be 100%. Although lower injection prescription is preferred and it should be as low as possible because the risk for spreading of infection through parenteral route can be avoided and cost incurred in therapy can also be minimized, but in case of cancer treatment and use of cytotoxic drugs, it cannot be applicable. It is because of the fact that most of the cytotoxic drugs should be given via parenteral route in a constant infusion rate. In addition to these, rehydration therapy should always be given through parenteral route.

WHO core drug use indicators

The overall findings for the WHO core drug use indicators are listed in Table 5. With regard to the average number of cytotoxic drugs per prescription, the value found in the present study was 1.78. However, in overall, the average number of drugs per prescription was found to be 10.77. The average number of cytotoxic drugs per prescription can be compared with the results from other studies carried out in Jordan (2.3) [17], Brazil (2.4) [18] and India (2.7) [19]. In similar studies conducted, the highest and lowest number of drugs per prescription values found was 3.8 in Nigeria and 1.3 in Ecuador and Tanzania [20]. In our study, the average number of overall drugs per prescription was found to be comparatively higher. This is because of the fact that for the treatment of cancer, other drugs like antiemetic drugs, proton pump inhibitors, antihistaminics, antacids, supplements, etc. should also be used in addition to cytotoxic drugs thus increasing the drug number per prescription.

Table 5 WHO core drug use indicators

WHO core drug prescribing indicators	Findings
Average number of cytotoxic drugs per prescription	1.78
Average number of antibiotics per prescription	0.37
Average number of other drugs per prescription	8.99
Average number of drugs per prescription	10.77
Percentage of encounters with an antibiotic prescribed	31.25%
Percentage of encounters with an cytotoxic injectables prescribed	100%
Percentage of encounters with an injection prescribed	100%
Percentage of drugs prescribed from EDL	73.50%
Percentage of drugs prescribed from WHO model list	67.27%

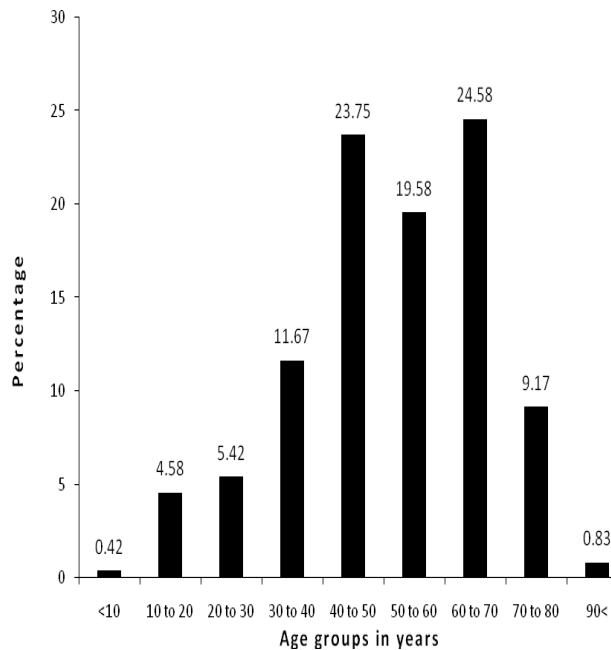


Figure 1 Age-wise distribution of cancer patients

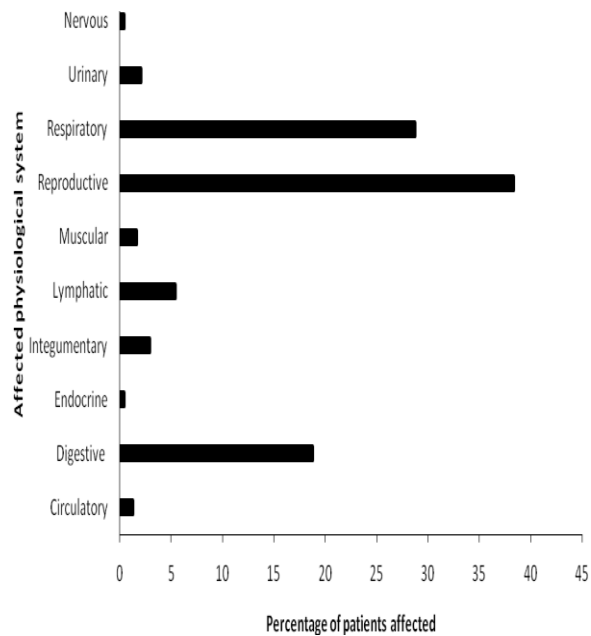


Figure 2 Physiological system wise distribution of cancer patients

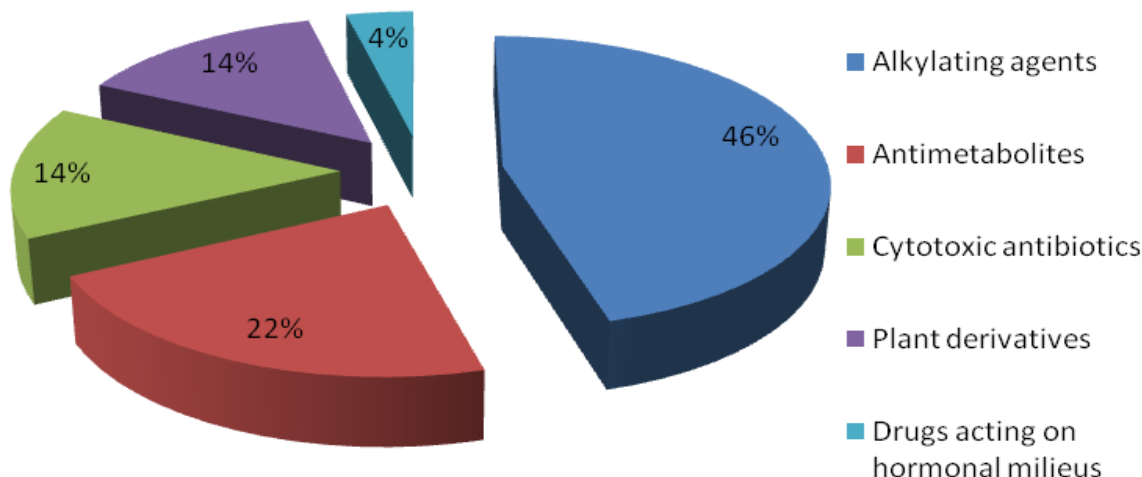


Figure 3 Groups of cytototoxic drugs prescribed

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