

# Drug Utilization Evaluation of Anticancer Drugs in a Charitable Hospital

## Abstract

**Background:** Evaluating the prescribing patterns of anticancer and supportive care drugs is necessary for ensuring effectiveness and patient's quality of life. **Aim:** This study aims to evaluate the prescribing patterns in patients receiving chemotherapy. **Settings and Design:** A prospective observational study was conducted in the Department of Medical Oncology at Justice K. S. Hegde Charitable Hospital. **Methods:** The study was conducted for 8 months from September 2017 to April 2018. Cancer patients who were above 18 years and are on chemotherapy along with supportive care medications were enrolled. **Statistical Analysis:** Data were analyzed using descriptive statistics. Continuous data were expressed as mean  $\pm$  standard deviation, and the nominal data were expressed as frequency and percentages. **Results:** Among 230 patients, majority of patients were in the age group of 45–60 years (47%), females (51.7%), Stage III (51.3%), solid tumor (85.5%), breast cancer (21.7%), doublet regimen (60.4%), who received doxorubicin and cyclophosphamide (36%) in breast cancer while paclitaxel and carboplatin (16.52%) were mostly prescribed among the different cancer types. The most commonly prescribed supportive care medications were dexamethasone (100%), ranitidine (100%), filgrastim (67.4%), tramadol and paracetamol (23.91%), and levofloxacin (9.56%). The percentage of drugs prescribed from the National List Essential Medicine and the World Health Organization (WHO) model list was 80.84% and 78.92%, respectively. **Conclusion:** According to the WHO core prescribing indicators, the average number of drugs per prescription was 9.63. Majority of the cancer patients were prescribed with paclitaxel and carboplatin (16.52%); dexamethasone and ranitidine (100%) were coadministered in all patients during their chemotherapy cycles.

**Keywords:** Cancer, chemotherapy, prescribing patterns, World Health Organization

## Introduction

Cancer is a group of disease, involving uncontrolled multiplication and spreading of abnormal forms of one's own body cells.<sup>[1]</sup> Mainly, there are two approaches for cancer treatment: local treatment approaches that include surgery and radiation and systemic treatment approaches that include chemotherapy and biological agents.<sup>[2]</sup>

Chemotherapy is a treatment option for majority of cancers. In chemotherapy, drugs are used to destroy cancer cells. There are different types of chemotherapy that includes adjuvant chemotherapy, neoadjuvant chemotherapy, induction chemotherapy, consolidation therapy, maintenance therapy, and palliative chemotherapy. In olden days, cancers were treated with single drug; but, nowadays, combination of drugs are given to overcome the cancer cell heterogeneity and

development of drug-resistant cells to kill total tumor cells.<sup>[1]</sup>

The chemotherapy-induced adverse effects may be uncomfortable; temporary or life-threatening adverse effects lead to reduction of doses of anticancer drugs, addition of supportive care drugs. Cancer supportive care involves the management of signs and symptoms or the management of chemotherapy-induced adverse effects.<sup>[3]</sup> This necessitates careful observation and evaluation of cancer chemotherapy, which in turn will help to optimize anticancer therapy with minimal toxicity and improved efficacy.

Prescribing pattern is an important tool in ascertaining the role of drugs. Prescription pattern is a process of analyzing the usage of drugs prescribed. Therefore, evaluating and monitoring the prescription patterns of anticancer drugs and supportive care drugs are necessary. The World Health Organization (WHO) developed core prescribing indicators which are meant

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to measure the characteristics related to polypharmacy, antibiotic use, drugs prescribed from WHO model list of essential medicines, and the National List Essential Medicine (NLEM).<sup>[4]</sup>

## Methods

### Study design and setting

A prospective observational study was conducted for 8 months from September 2017 to April 2018 in the Department of Medical Oncology at Justice K. S. Hegde Charitable Hospital, Mangaluru. Before the initiation of the study, ethical approval was obtained from the Institutional Ethics Committee (Ref. No: NGSMIPS/IEC/10/2017-18), Mangaluru.

### Sample size

The sample size was calculated based on the previously conducted study.<sup>[5]</sup> The minimum sample size required for conducting the study was 200.

### Study criteria

Cancer patients of either gender with age more than 18 years on chemotherapy along with supportive care medications were enrolled during the study period. Patients undergoing concurrent radiotherapy and not willing to participate in the study were excluded.

### Data collection

All the necessary details for the study were collected from the patient's medical record at inpatient department, and the medical records were reviewed on daily basis. All the enrolled patients were followed up to four cycles of chemotherapy. The information such as age, gender, past medical history, presence of comorbidities, type of cancer, stage of cancer, social habits, concurrent medications, and drug therapy was convened systematically and archived in the data collection form. All the drugs were classified as per the Anatomical Therapeutic Chemical classification (ATC code-level 1, WHO, 2016).<sup>[6]</sup> All the diseases were classified according to the International Statistical Classification of Diseases and related health problems (ICD 10, WHO, 2016).<sup>[7]</sup> In the present study, the WHO core drug prescribing indicators were used to determine the percentage of antibiotics and injectable prescribed, percentage of drugs prescribed from NLEM 2015, WHO model list of essential medicines (March 2017), and polypharmacy.<sup>[8-10]</sup>

### Data analysis

Prescribing patterns of chemotherapy were analyzed by collecting the details of drug usage including drug name, dose, indication, dosage form, frequency, duration, route of administration, chemotherapy cycles, and chemotherapy regimens and were recorded in the data collection form. Similarly, prescribing pattern of supportive drugs used

along with cancer chemotherapy was also recorded from the drug treatment chart and convened in the data collection form.

### Assessment of World Health Organization core drug prescribing indicators<sup>[8]</sup>

The following formulae were used for the assessment of the WHO core drug prescribing indicators:

The average number of cytotoxic drugs prescribed = Total number of cytotoxic drugs prescribed/total number of patients.

The average number of drugs prescribed = Total number of drugs prescribed/total number of patients.

Percentage of drugs prescribed by generic name = (Number of drugs prescribed by generic name/total number of drugs prescribed)  $\times$  100.

Percentage of encounters with injection prescribed = (Number of patients prescribed with injection/total number of patients)  $\times$  100.

Percentage of encounters with a cytotoxic injection prescribed = (Number of patients prescribed with a cytotoxic injections/total number of patients)  $\times$  100.

Percentage of encounters with antibiotic prescribed = (Number of patients prescribed with antibiotic/total number of patients)  $\times$  100.

Percentage of drugs prescribed from NLEM = (Number of drugs prescribed from NLEM/total number of drugs prescribed)  $\times$  100.

Percentage of drugs prescribed from WHO model list of essential medicines = (Number of drugs prescribed from WHO model list/total number of drugs prescribed)  $\times$  100.

## Results

A total of 230 patients with various types of cancer were enrolled in the study. Out of which, all the patients underwent four cycles of chemotherapy without any dropouts. In the agewise distribution, majority of patients were in 45–60 years (47%) compared to the other age groups. The mean age of the study population was  $52.17 \pm 13.15$  years. In genderwise distribution, majority of the patients were females (51.7%) when compared to males. Out of 230 patients, 75 patients had social habits, of which, majority of them were smokers (12.1%) followed by alcoholic patients (11.7%). Majority of the cancer patients was diagnosed with Stage III (51.3%), followed by Stage II (26.5%). There are different types of cancer which are commonly classified into solid and hematological tumors. Out of the solid tumors, breast cancer (21.7%) was most commonly observed followed by esophagus (10%). Among the hematological tumors, the most commonly observed cancer was non-Hodgkin's lymphoma (5.7%) followed by multiple myeloma (2.6%). Doublet regimen (60.4%) was

the most commonly prescribed chemotherapy followed by single regimen (19.1%). The demographic details of the study population are summarized in Table 1. Of 44 different cancer types, 36% of patients received doxorubicin and cyclophosphamide who had carcinoma of breast while paclitaxel and carboplatin (16.52%) were highly prescribed. The most commonly prescribed chemotherapy regimens among different cancer types are described in Table 2.

All patients received dexamethasone (100%), and the commonly prescribed antiemetics were palonosetron (81.3%) followed by ondansetron (66.5%). Out of 230 patients, 193 patients were prescribed with antibiotics to treat infections. Frequently prescribed antibiotics are levofloxacin (9.6%), sulfamethoxazole and trimethoprim (6.95%), ciprofloxacin (5.21%), and ofloxacin (5.21%). All the patients were prescribed with ranitidine (100%). Majority of the patients were prescribed with rabeprazole + domperidone (91.30%) followed by pantoprazole (34.78%), and 129 patients were prescribed with analgesics in which majority of them received tramadol + paracetamol (23.91%) followed by morphine (10%) and diclofenac and paracetamol (9.56%). In this study, 67.39% of the patients were prescribed filgrastim a granulocyte-colony stimulating factors for prophylaxis and treatment of chemotherapy-induced myelosuppression. Antihistamines were prescribed for majority of the patients in all the four cycles of chemotherapy. The most commonly prescribed supportive care medications are depicted in Table 3.

As per the WHO core drug prescribing indicators, the average number of drugs per prescription was 9.63. The percentage of antibiotics prescribed was 20.97%. The percentage of drugs prescribed from the NLEM and the WHO model list of essential medicines was 78.92% and 80.84%, respectively. The detailed WHO core drug prescribing indicators results are described in Table 4.

## Discussion

Alteration in chemotherapy regimen and supportive care medications is based on the variability of patients, demographic details, cancer types, and stages of cancer and depends on the expected toxicities, so it is necessary to evaluate the prescribing patterns of anticancer and supportive care drugs in cancer patients.

In this study, most of the patients were in the age group of 45–60 years (47%); this was in correspondence with the study carried out by Catic *et al.*<sup>[11]</sup> where 48% of patients were in the age group of 45–60 years. However, contradictory findings were also observed in a study conducted by Onwusah and Korubo<sup>[12]</sup> where 19.6% patients were in the age group of 61–70 years. Out of 230 patients, 51.7% were females and 48.3% were males. The study carried out by Manichavasagam *et al.* reported that females (54.57%) were predominant than the

**Table 1: Demographics of the study population**

Demographic details	Number of patients (%), (n=230)
Gender	
Male	111 (48.3)
Female	119 (51.7)
Age groups	
<30	15 (6.5)
30–45	45 (19.6)
45–60	108 (47)
60–75	56 (24.3)
>75	6 (2.6)
Comorbidities	
Hypertension	35 (15.2)
Diabetes mellitus	22 (9.6)
Asthma	13 (5.7)
CLD	2 (0.9)
IHD	4 (1.7)
CKD	1 (0.4)
No comorbidities	153 (66.5)
Social habits	
Smoking	28 (12.1)
Alcohol	27 (11.7)
Substance abuse	5 (2.1)
Both alcoholic and smoker	12 (5.2)
Alcoholic, smoker, and substance use	3 (1.3)
No social habits	155 (67.3)
Cancer stages	
Stage I	9 (3.9)
Stage II	61 (26.5)
Stage III	118 (51.3)
Stage IV	42 (18.3)
Solid malignancy	
Breast	50 (21.7)
Esophagus	23 (10)
Lung	17 (7.4)
Ovary	15 (6.5)
Buccal mucosa	10 (4.3)
Stomach	9 (3.9)
Colon	8 (3.5)
Rectum	7 (3.0)
Liver	5 (2.1)
Brain	4 (1.7)
Tongue	3 (1.3)
Leiomyosarcoma	3 (1.3)
Urothelial	3 (1.3)
Neuroblastoma	3 (1.3)
Others*	37 (16)
Hematological malignancy	
NHL	13 (5.7)
Multiple myeloma	6 (2.6)
Leukemia	4 (1.7)
HL	4 (1.7)
Follicular lymphoma	3 (1.3)
AML	2 (0.9)

*Contd...*



**Table 1: Demographics of the study population**

Demographic details	Number of patients (%), (n=230)
Myelodysplastic syndrome	1 (0.4)
Chemotherapy regimen	
Single regimen	44 (19.1)
Doublet regimen	139 (60.4)
Triplet regimen	35 (15.2)
Quadruple regimen	12 (5.2)

Others\* – Testis, Peritoneal, Supraglottis, Pyriform fossa, Ewing's sarcoma, Bone metastasis, Pancreas, DLBCL, Hypopharynx, Gallbladder, Nasopharynx, Spindle cell, Oropharynx, Cervix, Salivary gland, Chondrosarcoma, PNET of kidney, Synovial sarcoma, Prostate, Auditory canal, Penis, Periapillary, and Vulva. NHL – Non-Hodgkin's lymphoma; HL – Hodgkin's lymphoma; AML – Acute myeloid leukemia; DLBCL – Diffuse large B-cell lymphoma; PNET – Primitive neuroectodermal tumors; CKD – Chronic kidney disease; chronic lung diseases; CLD – Chronic lung diseases; IHD – Ischemic heart disease

males (45.42%). The present study is in concurrence with the reference study.<sup>[13]</sup>

In the present study, majority of the patients were in Stage III of cancer (51.3%) followed by Stage II (26.5%). Ramalakshmi *et al.*<sup>[3]</sup> reported that majority of the cancer patients were in Stage III of cancer (68%) followed by Stage II (22%). The present study findings are consistent with the previous study where most of the patients presented with Stage III of cancer.

In the present study, majority of the patients presented with breast cancer (21.7%) followed by esophagus (10%), lung (7.4%), ovary (6.5%), and other type of cancers. The study conducted by Pentareddy *et al.*<sup>[5]</sup> reported that carcinoma of breast (29.44%) was most commonly observed followed by carcinoma of head and neck (23.35%) and carcinoma of cervix (17.25%). This study resembles the previous study that breast cancer was most commonly observed but differs in other type of cancers.

In the present study, the most commonly prescribed chemotherapy regimen was double regimen, where pemetrexed and carboplatin were commonly prescribed in lung cancer (52.9%) followed by doxorubicin and cyclophosphamide in breast cancer (36%), paclitaxel and carboplatin in carcinoma of esophagus (34.7%), and lung cancer (17.6%). A study conducted by Pentareddy *et al.*<sup>[5]</sup> reported that among the commonly prescribed double therapy, doxorubicin and cyclophosphamide (51.72%) was mostly prescribed in breast cancer followed by paclitaxel and carboplatin prescribed in esophagus (50%) and lung cancer (33.3%) whereas pemetrexed and carboplatin (66.6%) was commonly used in lung cancer. This study was in correspondence with the previous study where double regimen is commonly prescribed.

Out of 230 patients, all patients received antiemetics include dexamethasone (100%) followed by palonosetron (81.3%),

ondansetron (66.5%), and aprepitant (41.3%) which was in concurrence with the study conducted by Ramalakshmi *et al.*,<sup>[3]</sup> where the majority of patients received dexamethasone and palonosetron (100%), respectively, followed by aprepitant (8%) and ondansetron (2%).

The most commonly prescribed antibiotics in this study were levofloxacin (9.56%), followed by trimethoprim and sulfamethoxazole (6.96%). A study carried out by Ramalakshmi *et al.*<sup>[3]</sup> reported that the majority of the patients received azithromycin (27.7%) followed by clindamycin (22.2%). The present study findings were contradictory to the reference study.<sup>[3]</sup>

Out of 230 patients, ranitidine (100%) was prescribed for all patients followed by rabeprazole and domperidone (91.30%) and pantoprazole (34.78%). A study conducted by Ramalakshmi *et al.* stated that all the patients received pantoprazole and sucralfate (100%) followed by laxatives (30%). The findings of the study were in contrary to the results of the previous study.<sup>[3]</sup> Tramadol and paracetamol (23.9%) were the most commonly prescribed analgesics during different chemotherapy cycles followed by morphine (10%). These findings are in contrary with the study carried out by Ramalakshmi *et al.*,<sup>[3]</sup> where paracetamol (62%) was mostly prescribed followed by aspirin (20%).

The average number of medications per prescription in the study was 9.63. A study conducted by Mugada *et al.*<sup>[4]</sup> reported that the average number of medications per prescription was 8.16 which is in contrast with the present study since it involves adjuvant therapies such as antiemetics, analgesics, and gastrointestinal agents for the prevention and management of expected adverse events.

In the present study, among all four cycles of chemotherapy, the percentage of antibiotics prescribed was 83.91%, and in the study conducted by Mugada *et al.*,<sup>[4]</sup> the percentage of antibiotics prescribed was 54.8% which is less compared to our study. It might be prescribed only for specific infections.

The percentage of cytotoxic injections and percentage of other injections prescribed were 100%. A study conducted by Mugada *et al.*<sup>[4]</sup> reported that the cytotoxic injections prescribed were 100% and the other injections were 75.5%, which is greater because the premedication given along with the cytotoxic drugs is prescribed in injectable form.

The percentage of drugs prescribed from the NLEM and the WHO model list was 80.84% and 78.92%, respectively, which resembles the study conducted by Mugada *et al.*,<sup>[4]</sup> where the percentage of drugs prescribed from the WHO model list was 80.70% while the NLEM was contrary to the study since EDL was calculated. The percentage of the drugs prescribed was finite since drugs were given to a particular patient based on their risk-benefit ratio and for specific infections; so, there will be difference in percentage of drugs prescribed from the WHO and the NLEM.

**Table 2: Most commonly prescribed chemotherapy regimens**

Cancer type	ICD code	Chemotherapy regimen	Number of patients (n=230) (%)
Breast	C50.9	Doxorubicin + cyclophosphamide	18 (36)
		Docetaxel + carboplatin	7 (14)
Ovarian	C57.9	Paclitaxel + carboplatin	8 (53.3)
Stomach	C16.9	Docetaxel + cisplatin + fluorouracil	3 (33.3)
Esophageal	C15.9	Paclitaxel + carboplatin	8 (34.7)
		Epirubicin + oxaliplatin + capecitabine	7 (30.4)
Tongue	C02.9	Paclitaxel + carboplatin	3 (100)
Buccal mucosa	C06.1	Cisplatin	4 (40)
		Paclitaxel + carboplatin	4 (40)
Rectum	C21.8	Oxaliplatin + capecitabine	7 (100)
Testis	C62.9	Etoposide + cisplatin	2 (100)
Lung	C34.1	Pemetrexed + carboplatin	9 (52.9)
Brain	C71.9	Pemetrexed + carboplatin	2 (50)
		Bevacizumab	2 (50)
Colon	C18.9	Oxaliplatin + capecitabine	7 (87.5)
Liver	C22.9	Gemcitabine + oxaliplatin	3 (60)
NHL	C85.80	Rituximab + doxorubicin + vincristine + cyclophosphamide	9 (69.2)

NHL – Non-Hodgkin's lymphoma; ICD – International Classification of Diseases

**Table 3: Most commonly prescribed supportive care medications**

Supportive care medications	ATC code	Number of patients, (n=230) (%)
Antiemetics		
Dexamethasone	A01AC02	230 (100)
Palonosetron	A04AA05	187 (81.30)
Ondansetron	A04AA01	153 (66.52)
Antibiotics		
Levofloxacin	J01MA12	22 (9.56)
Trimethoprim + sulfamethoxazole	J01EE01	16 (6.95)
Gastrointestinal drugs		
Ranitidine	A02BA02	230 (100)
Rabeprazole + domperidone	A02BC54	210 (91.30)
Pantoprazole	A02BC02	80 (34.78)
Analgesics		
Tramadol + Paracetamol	N02AJ13	55 (23.91)
Morphine	N02AA01	23 (10)
GCSFs		
Filgrastim	L03AA02	155 (67.39)
Miscellaneous		
Vitamins	A11	230 (100)
Chlorpheniramine maleate	R06AB04	191 (83.04)

GCSF – Granulocyte-colony stimulating factor; ATC – Anatomical Therapeutic Chemical Classification

The percentage of drugs prescribed in generic name was 7.98%, and in the study conducted by Mugada *et al.*,<sup>[4]</sup> the percentage of drugs prescribed by generic name was 93%, which is limited and it has to be encouraged since it helps to improve rational prescribing of drugs, to avoid dispensing errors, and to reduce cost of the therapy, thus reducing the overall medical expenditure.

## Conclusion

In the present study, majority of patients were in the age group of 45–60 years (47%). Females (51.7%) were predominant than males (48.3%). Most of the patients were in Stage III (51.3%) and had solid tumor (85.5%); among them, breast cancer (21.7%) was mostly observed. Doublet chemotherapy regimen (60.4%) was frequently prescribed, in which 36% of patients who received doxorubicin and cyclophosphamide had carcinoma of breast while paclitaxel and carboplatin (16.52%) were highly prescribed among the different cancer types. The most commonly prescribed supportive care medications – dexamethasone and ranitidine (100%), filgrastim (67.4%), tramadol and paracetamol (23.91%), and levofloxacin (9.56%) – were prescribed among all four cycles of chemotherapy. As per the WHO core drug prescribing indicators, the average number of drugs per prescription was 9.63. The percentage of antibiotics prescribed was 83.91%. The percentage of drugs prescribed from the NLEM and the WHO model list was 80.84% and 78.92%, respectively.

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## Conflicts of interest

There are no conflicts of interest.

**Table 4: The World Health Organization core drug prescribing indicators**

WHO core drug prescribing indicators	Cycle I	Cycle II	Cycle III	Cycle IV	All cycles
Average number of cytotoxic drugs per prescription	2.06	2.06	2.06	2.06	2.06
Average number of drugs per prescription	10.25	9.59	9.35	9.36	9.63
Percentage of encounters with an antibiotic prescribed	10.86	12.17	34.78	26.08	20.97
Percentage of encounters with an cytotoxic injectable prescribed	100	100	100	100	100
Percentage of encounters with an injectable prescribed	100	100	100	100	100
Percentage of drugs prescribed from NLEM	80.05	81.37	80.89	80.58	80.84
Percentage of drugs prescribed from WHO model list of essential medicines	80.58	80.92	82.33	80.95	78.92
Percentage of drugs prescribed by generic name	6.82	7.88	8.50	8.8	7.98

NLEM – National List of Essential Medicine; WHO – World Health Organization; NLEM – National List Essential Medicine

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