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ASSESSMENT OF CLINICAL PHARMACY SERVICES IN THE DEPARTMENT OF MEDICAL ONCOLOGY, KIMS HOSPITAL AND RESEARCH CENTRE, BANGALORE

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Abstract

Cancers are important non-communicable diseases with great morbidity and mortality worldwide. The clinical pharmacist makes sure the patient is receiving an optimized medication treatment. The primary objective of the study was to perform comprehensive medication chart review on hospitalized oncology patients and to report and document potential side effects and drug-drug interactions prescribed for oncology patients. A prospective interventional study was conducted for 6 months from Jan 2022 to July 2022 in the Department of Medical Oncology of KIMSH & RC. The detailed information of the patients like age, gender, occupation, residence, cancer type, anti-cancer medications given, side effects reported, potential drug-drug interactions found was collected and documented into well-structured self-designed study specific data collection form. A total of 42 prescriptions of chemotherapy patients were analyzed. Medication chart review showed that eight (19.04%) patients had a requirement of additional drug other than the treatment regimen. About 35.71% patients had developed side effects for anticancer drugs, including hair loss, generalized weakness, neuropathic pain, elevated blood pressure, loose stools, and insomnia. Out of 42 prescriptions, 36 potential drug-drug interactions were found, XI among which maximum drug interactions were minor. Comprehensive medication chart review lead to identification of drug-related problems such as requirement of additional drug apart from the chemotherapy regimen. The results of this study demonstrate that a clinical pharmacist led comprehensive medication chart review program was feasible and effective at identifying drug related problems and improving safe medication use among adult cancer patients.

Keywords: *Cancer, Drug Related Problems, Side Effects, Drug- drug Interactions, Medication Chart Review.*

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1. Introduction

Cancer is a non-communicable disease, referred to as the development of malignant, fast-growing abnormal cells in various tissues of the body, including lungs, breasts, liver, stomach, intestine and cervix. These conditions not only substantially threaten the human health, but also they inflict additional financial costs (1). In total, different cancers have caused a morbidity and mortality rate of about 19.3 and 9.9 million cases worldwide in 2020, among which lung cancer was the most prominent with 1.8 million deaths within 2.3 million affected individuals (2). In the Indian subcontinent, it is the fourth most common cancer following breast, cervical and oral cavity cancers, with particular involvement in men (3). Tobacco smoking, domestic fuel smoke, radon exposure, *Mycobacterium tuberculosis* infection, asthma and several other conditions may predispose one to lung cancer (4). During last decades, the incidence of colorectal cancer (CRC) has substantially influenced by changes in dietary patterns, lifestyle and physical activities, along with increased smoking and alcohol consumption, leading to an estimated incidence and mortality of 1.93 million cases and 935,173 individuals, respectively (2). Reportedly, the incidence of CRC in India has been elevated by about 20%, from 5.8 per 100,000 people during 2004-2005 to 6.9% during 2012-2014 (5). Nevertheless, cost-effective treatment strategies such as laparoscopic surgery, palliative chemotherapy as well as radiotherapy would alter the outcome of CRC and increase the survival rate (6).

Based on cancer diagnosis, the cervical cancer (CC) is the second most common type, and it is placed third regarding cancer death among women of developing countries (7). The global burden estimations have shown a mortality rate of 341,831 among 604,127 affected individuals for CC in 2020 (2). In this context, India contributed 28% of mortality rates due to CC, with 87,090 cases (8). About one-fifth of CC cases occur in African women, majorly caused by human papilloma virus (HPV) infection as two most common types: squamous cell carcinoma (SCC) and adenocarcinoma (25%) (7). Another particularly important cancer in women is breast cancer, with almost metastatic nature which frequently disseminates to other organs, including liver, lung, bone and brain. Accordingly, early diagnosis using mammography along with a more sensitive screening method, magnetic resonance imaging (MRI), is a very crucial step for good prognosis. The breast cancer ranks first among Indian female population, with age-adjusted mortality and morbidity of 25.8 and 12.7 per 100,000 individuals, and females with a younger age are probably more prone to the breast cancer (9).

In recent decades, the incidence of gastric cancer has declined in shade of early surgical resection using standardized lymphadenectomy as a gold standard therapy, improved hygiene and nutrition as well as *Helicobacter pylori* eradication. Human population residing in Central and South America, Eastern Asia and Eastern Europe are at higher risk of gastric cancer (10), while it is less common in India, with the exception of some certain areas within country, including southern and northeastern states (11). Hepatocellular carcinoma (HCC) is the most common form of liver cancer causing destructive liver disease and cirrhosis, with about two-fold incidence in males (2). The 5-year survival of HCC is not satisfactory, even in early-diagnosed, small tumors (<3cm). Most patients are diagnosed during advanced stages, hence are not qualified for curative therapies. This type of cancer is highly prevalent in the southeast Asia and western Africa, with hepatitis B virus (HBV) and hepatitis C virus (HCV), along with non-alcoholic fatty liver disease and alcohol-associated cirrhosis as the most important risk factors (12).

The society of health-system pharmacists (ASHP) clearly delineated a pharmacist's function not only in medicine safety, preparation and dispensing, but also as a health provider with direct responsibility outlined for medication-associated care to enhance the quality of life of the patient (13). In hospitals, clinical pharmacists assist in detection and correction of drug anomalies during transition care through reconciliation process (14). Modern anticancer treatment implicates the utilization of multiple techniques, including endocrine therapies and conventional cytotoxic medicines, analog drug development and novel formulations, as well as targeted therapy. The latter constitute an important

aspect in anticancer therapy, which may be enzyme inhibitors impairing signal pathways of tumors with long-term oral administration, or specific monoclonal antibodies having particular interaction with surface receptors or circulating ligands, with intermittent intravenous (i.v.) or subcutaneous (s.c.) administration (15). In this sense, clinical oncology pharmacists (OPs) would play a major role in face of targeted agents, which may present new action mechanisms and unforeseen side-effects and/or require specific supportive care measures. Moreover, OPs can guide oncologists in suitable drug selection and even customize specific treatment-care programs relied on patient's health. Other prominent roles of OPs include timely and accurate dosage instructions to improve treatment adherence, locating new treatment options, scheduling medication therapies and counseling patients and/or their caregivers, which in turn decrease anticancer drug failures and life-threatening drug interactions (16).

As mentioned earlier with the pattern of incidence and mortality of various cancers, a great number of Board-Certified Oncology Pharmacists (BCOPs) are demanded in India, which will perform 2.9-4.1 million patient visits at 50% workforce capacity through 2025 (17). The clinical activities of BCOPs are shared with nurse practitioners and physician assistants, which will together involve in patient education and treatment management (18). The present elaborative study was performed to review medication charts and avoid drug-related problems (DRPs), including side-effects and drug-drug interactions, in cancer patients in the Department of Medical Oncology at Institute of Medical Sciences Hospital and Research Centre, (KIMSH & RC), Bangalore, India.

2. Materials and Methods

Study Area

The study was conducted at the Department of Oncology Medicine at KIMSH & RC, Bangalore, as the capital and largest city of Karnataka state in southern India. It is a tertiary care 940-bed super special teaching hospital, providing specialized health care services. Various departments are present in KIMSH & RC, comprising General Medicine, General Surgery, Dermatology, Orthopedics, Gynecology, Neurosurgery and others, which cater patients in and around Bangalore.

Study Design, Study Period and Source of Data

This study was designed as interventional prospective on cancer patients undergoing chemotherapy at the Department of Oncology Medicine at KIMSH & RC, during a six-month period (Jan – July 2022). All information required for this study was collected from the patient's personal note, patient's record, laboratory reports, treatment charts and drug information literature.

Inclusion and Exclusion Criteria

The inclusion criteria for the current study were: i) patients of both genders undergoing anticancer chemotherapy, ii) aged between 20-70 years, and iii) those consenting to participate in this study. It is, also, noteworthy that patients with immunocompromised conditions, having multi-organ failure and those on an outpatient department were totally excluded from this study.

Data Collection Procedure

A well-structured data collection form was designed in order to obtain patient's data, including demographic information (age, gender, occupation, social history and habits), treatment details (drug interactions, side effects or adverse drug reactions), disease-related factors (current complaints, past medical and medication history, cancer type) examinations (such as blood pressure, pulse rate, respiratory system (RS) and central nervous system (CNS)) and laboratory findings. Also, data was collected from patient's personal notes (health condition, cancer type, treatment plan, oral pre-treatment, used drugs, due for chemotherapy cycle, laboratory tests and supportive care) which was maintained by the Medical Oncologist. The details of prescribed medications such as name, dose, frequency and order of the pre medications given before chemotherapy, chemotherapeutic drugs, and post medications given after chemotherapy were also taken from Patient's Treatment Chart, along with the laboratory data including Complete Blood Count (CBC) before each cycle of chemotherapy. If necessary, renal function test (RFT), liver function test (LFT) and calcium levels were evaluated; however, they are performed after 2 cycles of

chemotherapy in most cases. Of note, following few cycles of chemotherapy, positron emission tomography (PET) Scan was advised to check patient's response for the treatment given.

In the following, medication chart of patients was reviewed to highlight potential DRPs (inappropriate, unnecessary and/or additional drugs, either administered by the healthcare professional or the patient as well as under- or over-dosing). The LEXICOMP online server was used for gathering information about general monitoring of the chemotherapy drugs. Specific patient monitoring was done based on chemotherapy drugs given and patient's health condition. Standard online drug interaction servers such as LEXICOMP and MEDSCAPE were used for regular checking of drug-drug interactions between pre-medications and chemotherapeutic agents. Potential Side Effects due to the anticancer treatments were reported to the medical oncologist through the regular interaction. Besides, information about general side effects of the anticancer drugs were obtained from LEXICOMP server. In the meanwhile, adverse drug reactions were monitored during the study period and documented using adverse drug reporting form of the Central Drugs Standard Control Organization (CDSCO).

Statistical Analysis

The whole data was sorted and analyzed for simple statistics in a Microsoft Excel© Spreadsheet.

Ethical Consideration

The present study was carried out according to the permission granted by Institutional Ethical Committee of KIMSH & RC, Bangalore, India.

3. Results

In the current study, 42 patients undergoing chemotherapy in the Department of Oncology Medicine at KIMSH & RC in Bangalore were included, most of which were women (n = 28; 66.7%), and the remaining were men (n = 14; 33.3%). Based on age, the included patients were sorted into three age groups, enclosing 11-30 (n = 2, 4.76%), 31-50 (n = 17; 40.47%) and 51-70 (n = 23; 54.76%). Most of the patients (n = 27; 64.28%) were homemaker, followed by farmer (n = 7; 16.66%), self-employed (n = 5; 11.9%) and student (n = 1; 2.38%). Also, two male patients had other occupations like cashier and retired lecturer. About two-third of the patients (n = 32; 76.19%) were residents of urban areas (**Table 1**).

Table 1: Distribution of Cancer Patients Examined in the Present Study, based on Different Parameters

Parameter		No. (%)
Gender	Male	14 (33.3)
	Female	28 (66.7)
Age	11-30	2 (4.76)
	31-50	17 (40.47)
	51-70	23 (54.76)
Occupation	Homemaker	27 (64.28)
	Farmer	7 (16.66)
	Self-employed	5 (11.9)
	Student	1 (2.38)
	Others	2 (4.76)
Residence	Urban	32 (76.19)
	Rural	10 (23.8)
Type of cancer	Carcinoma	33 (78.57)
	Lymphoma	1 (2.3)
	Myeloma	2 (4.76)
	Leukemia	2 (4.76)
	Tumor	2 (4.76)
	Others	2 (4.76)

According to the cancer type, a great deal of individuals was affected by carcinoma (n = 33; 78.57%), while lymphoma was the lowest in number (n = 1; 2.3%). In the former group, five patients (11.90%) had left side breast carcinoma, five patients (11.90%) had ovary carcinoma, five patients (11.90%) with metastatic breast cancer, two patients (4.76%) with pancreas carcinoma, one female patient (2.38%) with periampullary carcinoma locally advanced, one male patient (2.38%) with recto sigmoid carcinoma recurrence, one male patient (2.38%) with pyriform fossa carcinoma advanced, one male patient (2.38%) with hypopharynx carcinoma, one female patient (2.38%) with duodenum adenocarcinoma, one female patient (2.38%) had bladder carcinoma + renal cell cancer, one male patient (2.38%) was a case of colon mixed adenocarcinoma + advanced neuroendocrine cancer, one male patient (2.38%) had colon carcinoma, one male patient (2.38%) had lung carcinoma, one male patient (2.38%) had metastatic squamous cell carcinoma, one male patient (2.38%) had buccal mucosa carcinoma, one male patient (2.38%) was a case of stomach carcinoma and one female patient (2.38%) had cervix carcinoma recurrence. Two multiple myeloma patients (4.76%) were both male, whereas two leukemia patients were both female,

contracted with lymphoblastic leukemia and promyelocytic leukemia. Tumor affected patients were a male with glioblastoma recurrence and a female with malignant phyllodes tumors. Non-Hodgkin lymphoma was found in a female patient, and two other female patients were affected by renal amyloidosis and haemophagocytic lymphohistocytosis.

Out of 42 patients, 15 cases (35.71%) developed side effects for chemotherapy drugs (Fig 1).

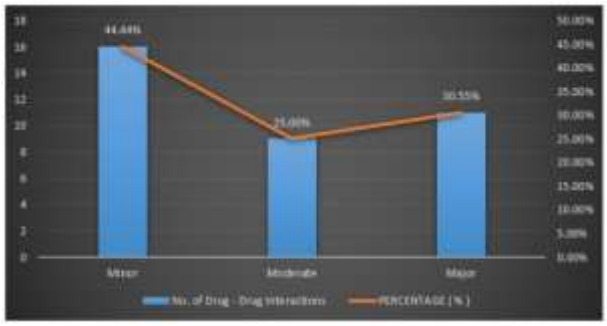

Figure 1: Distribution of Possible Drug – drug Interaction According to their Severity

Notably, almost all side effects had occurred in female patients, manifested as hair loss in 4 cases (due to carboplatin, nab-paclitaxel and vincristine), generalized weakness in 4 cases (paclitaxel, nab-paclitaxel and cyclophosphamide), neuropathic pain in 2 cases (cyclophosphamide), as well as single cases of neuropathic pain plus mouth ulcers (arsenic trioxide), loose stool (cyclophosphamide) and insomnia (gemcitabine) (Fig 2).

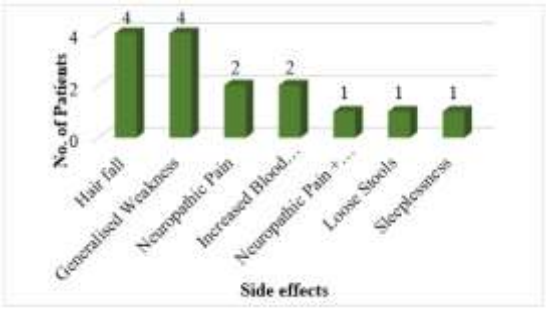

Figure 2: Distribution of Side Effects Reported by Cancer Patients on Chemotherapy

The reported side effects in two male patients were increased blood pressure due to the bevacizumab. After reviewing the prescriptions of 42 cancer patients, 36 drug-drug interactions were found, most of which (n = 16; 44.4%) had minor severity, whereas 11 interactions (30.55%) were of major significance (**Table 2**).

Table 2: Possible drug – drug Interactions

Drug - Drug Interactions	No. Of Interactions	Severity	Consequences	Steps to manage
PACLITAXEL < > DEXAMETHASONE	**10**	Minor	Dexamethasone will decrease the level or effect of paclitaxel by affecting hepatic/intestinal enzyme CYP3A4 metabolism	Monitor for evidence of reduced therapeutic response to paclitaxel during co-administration. Maintain Spacing
DEXAMETHASONE < > VINCRISTINE	1	Minor	Dexamethasone will decrease the level or effect of vincristine by affecting hepatic/intestinal enzyme CYP3A4 metabolism.	Maintain Spacing between administrations of both the drugs.
DEXAMETHASONE < > BORTEZOMIB	**2**	Minor	Dexamethasone may decrease the serum concentrations of Bortezomib.	No action required
GRANISETRON < > OXALIPLATIN	**3**	Minor	oxaliplatin will increase the level or effect of granisetron by Other	Caution and Clinical Monitoring are recommended if multiple agents associated with QT interval prolongation are prescribed together.
CARBOPLATIN < > DENOSUMAB	**1**	Moderate	Denosumab may enhance the adverse/toxic effect of Immunosuppressants. Specifically, the risk for serious infections may be increased.	Monitor patients for signs/symptoms of serious infections when using denosumab together with an immunosuppressant
DEXAMETHASONE < > DENOSUMAB	**1**	Moderate	Denosumab may enhance the adverse/toxic effect of Immunosuppressants. Specifically, the risk for serious infections may be increased.	Monitor patients for signs/symptoms of serious infections when using denosumab together with an immunosuppressant.
PEMETREXED < > DENOSUMAB	**1**	Moderate	Denosumab may enhance the adverse/toxic effect of Immunosuppressants. Specifically, the risk for	Monitor patients for signs/symptoms of serious infections when using denosumab together with an

			serious infections may be increased.	immunosuppressant
DEXAMETHASONE < > ETOPOSIDE	**1**	Moderate	Dexamethasone will decrease the level or effect of etoposide by affecting hepatic/intestinal enzyme CYP3A4 metabolism	Monitor Closely, Maintain Spacing between administrations of these drugs.
BEVACIZUMAB < > PACLITAXEL	**2**	Moderate	Bevacizumab will decrease the level or effect of paclitaxel. Possible decreased paclitaxel exposure after 4 treatment cycles of bevacizumab in combination with paclitaxel and carboplatin.	Maintain Spacing between administrations of these drugs
DEXAMETHASONE < > ADRIAMYCIN	**3**	Moderate	Coadministration with inducers of CYP450 3A4 may decrease the plasma concentrations of doxorubicin, which is primarily metabolized by the isoenzyme.	Close monitoring for potentially reduced efficacy of doxorubicin is recommended if co-administration is required.
ADRIAMYCIN < > CYCLOPHOSPHAMIDE	**3**	Major	Cyclophosphamide may enhance the cardiotoxic effect of Anthracyclines	Monitor Cardiac function particularly closely when anthracyclines and cyclophosphamides are used in combination.
PACLITAXEL < > CARBOPLATIN	**7**	Major	Platinum derivatives can enhance myelosuppressive effects of taxane derivatives	Administer paclitaxel before carboplatin, when given as sequential infusions, to limit toxicity
ONDANESTRON < > ARSENOX	**1**	Major	QT-prolonging Agents (Highest Risk) may enhance the QTc-prolonging effect of Ondansetron	Consider alternatives to this combination. If use is necessary, monitor for QTc interval prolongation and arrhythmias (including torsades de pointes)

Monitoring vital parameters such as CBC, LFT and RFT were performed for all 42 patients by the medical oncologist. In case of zoledronic acid administration, calcium levels were monitored. Also, instructions were given to the patients receiving bevacizumab to regularly check their blood pressure levels even at home. Also, granisetron was given as prophylactic drug for all chemotherapy patients to avoid anticancer induced nausea and vomiting. Infusion site monitoring was only checked for those patients prone to the extravasation. No unnecessary and inappropriate drugs were prescribed for the patients, and no under-dosing or over-dosing was observed. This was the same regarding inappropriate drug use administered by healthcare professional and/or patient himself/herself. Additional therapy was required only for 19.04% of patients due to the developed symptoms during anticancer treatment. With respect to those patients suffering from neuropathic pain as a potential side effect, pregabalin and methylcobalamine capsules were prescribed, while patients with increased blood pressure were given antihypertension drugs such as injectable labetalol (in-patients) or amlodipine (at discharge). Also, other useful drugs were prescribed to alleviate the raised side effects by anticancer treatment regimens, including loperamide hydrochloride (loose feces), tricyclic antidepressants such as amitriptyline hydrochloride (insomnia) as well as B-complex forte with vitamin C and choline salicylate ointment (generalized weakness).

4. Discussion

The present study provided a clinical pharmacy services assessment on 42 patients undergoing chemotherapy in the Department of Medical Oncology, KIMSH & RC, Bangalore, India. The female (N = 28) to male (N = 14) ratio in our study was estimated to be 2, similar to another study in a south Indian tertiary teaching hospital, reporting 43 and 32 female and male patients, respectively (19). Also, a Moroccan study examined 526 adult patients, with a male to female ratio of 0.6 (20). Based on our results, the highest number of cancer cases (N = 23; 54.76%) in both genders belonged to 51 to 70-year-old age group, whereas the prevalence was lowest among 11-30 years age group (2 cases; 4.76%). This finding is in line with 2021 cancer

statistics report, which demonstrates a higher chance of cancer by increasing age in males and females (21). Moreover, a study done in Georgia remarked that the cumulative risk of cancer diagnosis during a person's life increases up to age 70, then declines slightly (22). The most prevalent cancer type reported in the present study was carcinoma (N = 33; 78.57%), among which ten patients were affected by breast cancer, revealing its predominance in the examined cancerous population in our study. Notably, other prevalent cancers in the present investigation were ovary cancer, pancreas cancer and multiple myeloma. In a similar study in a medical oncology ward in Istanbul, Turkey, lung cancer was the most prevalent, followed by CRC, gastric cancer and breast cancer (23). In a Malaysian general hospital, reproductive cancers, including ovarian (36.7%), uterine (23.3%) and cervical (20%) cancers along with breast cancer (6.7%) were highly prevalent among examined patients (24).

In the current study, four different drug classes, including antiemetics, analgesics, antibiotics and corticosteroids were used along with medications for comorbidities (antihypertension and antidiabetic agents). All patients were on a clear prophylactic plan (*e.g.*, proton pump inhibitor or histamine-2 receptor antagonist) in order to prevent chemotherapy-induced nausea and vomiting. The chemotherapy regimens included in the present study were as follows: carboplatin (n = 10, 16.39%), paclitaxel (n = 9, 14.75%), bevacizumab (n= 5, 8.19%), nab-paclitaxel (n= 5, 8.19%), cisplatin (n = 4, 6.55%), doxorubicin (n = 4, 6.55%), cyclophosphamide (n = 3, 4.91%), gemcitabine (n = 3, 4.91%), oxaliplatin (n = 3, 4.91%), bortezomib (n = 2, 3.27%), trastuzumab (n = 2, 3.27%), methotrexate (n = 2, 3.27%), etoposide (n = 1, 1.63%), pemetrexed (n = 1, 1.63%), rituximab (n = 1, 1.63%) and vincristine (n = 1, 1.63%), dacarbazine (n =1, 1.63%), denosumab (n = 1, 1.63%), arsenox (n =1, 1.63%), carfilzomib (n = 1, 1.63%) and fulvustrant (n = 1, 1.63%). With reference to a standard drug information database LEXICOMP, no patient was given either too high dose or too low dose than the required. The only identified DRP was need for an additional drug in about 19.04% of patients for the symptoms developed during anticancer treatment.

Two different studies reported various frequencies of DRPs in oncology patients, including inappropriate medication selection (20.6%) (25) and inappropriate dose (25%) (26). In a study by Delpeuch *et al.* (2015), about 14.8% untreated indications were reported in patients (25). Nightingale *et al.* (2017) performed a comprehensive medication management study in elderly oncology patients and initially demonstrated 123 DRPs, while after pharmacist involvement, they were reduced to 78 at 30-day and 67 at 60-day follow-up intervals. They concluded that despite a few problems in communicating their recommendations, pharmacist intervention was feasible and effective in reducing medication-related problems (27). Among different types of medical errors, inadvertent drug discrepancies are the most common, occurring at transitions between healthcare sites (28, 29). Nevertheless, in a Sri Lankan resource-limited hospital, 130 among 400 evaluated prescriptions had at least one prescription error (32.5%), and actually 115 suffered from at least one medication error (30). Analgesics were reported in association with DRPs in a study in a hematology/oncology ward in Morocco, while very few concerned anticancer drugs (20). This was not uncommon because hospitalized patients require supportive care in relation with advanced disease (cancer symptoms), complications of cancer treatment, and intensive chemotherapies for hematological cancers. In 33 hospitalized patients suffering from solid tumors in Sweden, untreated indications were recognized as the major DRPs (31). Another study in the Netherlands examined 4618 prescriptions in a population of 546 patients undergoing anticancer therapy in an outpatient settings and reported a higher rate of DRPs (20%), including contradictions (46.9%) and drug-drug interactions (44.4%) (32). A study by Delpeuch *et al.* (2015) reported medication-related problems that included inappropriate medications (20.6%), untreated indications (14.8%), drug-drug interactions (14.3%), inappropriate administrations (14.1%), under-dosing (11.7%), lack of monitoring (9.6%), overdosing (8.9%), administration omissions (3.5%) and side effects (2.5%) (25).

The most prevalent side effects in the present study were hair loss (N = 4), generalized weakness (N = 4), neuropathic pain (N = 2) in women, along

with blood pressure (N = 2) in men. Mouth ulcers, loose stool and insomnia were the other, less common, anticancer therapy-induced side effects in our study. Reportedly, 88% of 814 respondents in a large US survey of cancer patients undergoing chemotherapy or radiotherapy reported at least one side effect during treatment course (33). Another study by Griffin *et al.* (1993) showed hair loss and loss of appetite as common side effects due to chemotherapy in cancer patients (34), similar to our study. In a Malaysian study, 83.3% of the patients undergoing chemotherapy manifested nausea, vomiting, followed by dry mouth or thirst, hair loss, weakness, loss of appetite, coldness, numbness in fingers or toes, confusion, depression, and reduced sense of touch. It is also noteworthy that peripheral neuropathies were experienced by three patients in our study, a side effect that is poorly studied and it is usually underreported (35).

Based on the drug-drug interaction severity, most were of minor importance in the present study (N = 16; 44.4%), as screened by LEXICOMP and MEDSCAPE servers. Of note, most interactions (N = 21; 58.33%) were of pharmacodynamics form, particularly between paclitaxel and carboplatin, where platinum derivatives can promote myelosuppressive effects of taxane derivatives. Other major pharmacodynamics interactions were between adriamycin and cyclophosphamide, and between ondansetron and arsenox; cyclophosphamide may enhance the cardiotoxic effect of anthracyclines, and QT-prolonging agents (highest risk) may enhance the QTc-prolonging effect of ondansetron. Moderate pharmacodynamics interactions were reported between carboplatin and denosumab, dexamethasone and denosumab, pemetrexed and denosumab (denosumab enhances toxic effects of immunosppressants), as well as between bevacizumab and paclitaxel (bevacizumab decreases the effect of paclitaxel. The highly frequent, minor pharmacodynamics interactions were reported between dexamethasone and bortezomib (the former decreases the level of the latter), as well as between granisetron and oxaliplatin (oxaliplatin decreases the effect of granisetron).

Pharmacokinetic interactions were, also, reported (N = 15; 41.66%) in the present study, without major interactions. Moderate interactions in the present study were between dexamethasone and etoposide (dexamethasone decrease the effective level of etoposide by affecting cytochrome P3A4), and between dexamethasone and adriamycin (co-administration with cytochrome P450 3A4 inducers will decrease the plasma level of doxorubicin). Minor pharmacokinetic interaction was between paclitaxel and dexamethasone as well as between dexamethasone and vincristine, which the metabolism of both other drugs are affected by dexamethasone through its effect on cytochrome P3A4. In contrast to our results, Kannan *et al.* (2011) (19) performed a study in a south Indian tertiary care hospital and reported 213 interactions (121 moderate, 71 minor and 21 major), in which 87.79% and 5.16% were of pharmacokinetic and pharmacodynamics in nature, respectively. Another study done in Princess Margaret hospital in Toronto, Canada, documented that over a quarter of cancer patients are at a risk of potentially life-threatening drug interactions, and drugs used for co-morbidities and cancer supportive care were more likely to be involved (36). As mentioned in previous studies (37, 38), the number of prescribed drugs in the present study was significantly correlated with the incidence of drug-drug interactions, so that increased number of drugs would substantially elevate the risk of drug interactions in our population. A study done by Delpeuch *et al.* (2015) (25) 79 drug interactions were reported among 552 DRPs, and only major interactions were intervened. Remarkably higher rates of drug-drug interactions (27-58%) have been documented in more specific studies, such as ambulatory patients undergoing intravenous anticancer treatment. Since cancer patients concurrently receive different drugs, they are highly prone to drug-drug interactions. Detection of such interactions is a fundamental step in pharmacotherapy management in these patients, and implementation of a systematic review of all patient's medications seem to be a necessity (39). Finally, we did not report any adverse drug reactions during the study period. A study conducted in Turkey reported 376 adverse drug reactions in 137 patients (23). In a similar manner, a study done in National cancer center of Singapore reported 114 adverse drug reactions in 118 patients (40).

The present study met some limitations, as follow: 1) inappropriate sample size owing to COVID-19 pandemic lockdown, 2) it was done as a single-center study, without external validity, 3) due to the sensitivity of online drug screening servers, some interactions with low level of clinical evidence and/or with low to moderate clinical consequences were shown. It is highly recommended to perform the present study in other oncology hospitals, assess the quality-of-life study in the Department of Oncology, evaluate the chemotherapy drug utilization and expenditure in all cancer patients of the KIMS hospital, and comprehensively review the medication chart in other Departments of KIMS hospital such as gynecology, cardiology, nephrology and pediatrics.

5. Conclusion

Our study reported that among the study population, 15 patients developed some of the chemotherapy related side effects (hair loss, generalized weakness, neuropathic pain and blood pressure) that are commonly experienced by local cancer patients. From our study, it was observed that potential drug-drug interactions were frequent; even though maximum interactions were minor in severity, development of alert guidelines and computer-based screening would help physicians to recognize and prevent potentially dangerous drug interactions. During our study period, we recorded no adverse drug reactions. Also, comprehensive medication chart review done in this study revealed that out of 42 patients, eight patients were in the need for additional drug other than the treatment regimen. The results of this study demonstrate that a clinical pharmacist led comprehensive medication chart review program was feasible and effective at identifying drug related problems and improving safe medication use among adult cancer patients. Integration of clinical pharmacy services in oncology will help reduce drug related problems.

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