IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS)
e-ISSN:2278-3008, p-ISSN:2319-7676. Volume 12, Issue 4 Ver. V (Jul – Aug 2017), PP 87-95
www.iosrjournals.org

Pattern of Adverse Drug Reactions in Cancer Patients at a Tertiary Care Hospital In Telangana Region of South India

K.Prathyusha[1], A.Y.Rao[2], G.Praneeth[1], P.Kishore[1]
[1]*Department of Pharmacy Practice, Care College of Pharmacy, Warangal, Telangana, India*
[2]*Head, Department of Oncology, MGM Hospital, Warangal*
Corresponding author:Dr. P. Kishore,
Head, Department of Pharmacy Practice, Care College of Pharmacy, Oglapur (V), Damera (M), Warangal Urban, Telangana. India.

Abstract:*Pattern of adverse drug reaction studies in cancer patients is rare in India. Adverse drug reactions associated with the use of anticancer drugs are a worldwide problem which cannot be ignored. Adverse drug reactions can range from mild reaction like nausea, vomiting or any other to severe myelosuppression. This study was planned to observe adverse drug reactions in cancer patients receiving radiation therapy or chemotherapy aged above 18 years and visiting MGM Hospital for treatment and regular check-ups. During the study period, 201 cancer patients who came to the hospital were screened for occurrence of adverse drug reactions during their treatment with chemotherapy and radiotherapy. Almost each and every patient was suffering with at least 2-3 ADRs. Female sufferers are more than male patients. Breast cancer prevalence is more when compared to any other types of cancer. A total of 3370 ADRs were observed in our study population. In the study population mostly affected organ systems were gastrointestinal system -31%, CNS & PNS systems-30% followed by musculoskeletal system-16%, respiratory system-8%, sensory system-7% and skin and appendages-7% respectively.*

Keywords:*Adverse drug reactions [ADRs], chemotherapy. Radiation therapy, anti-cancer drugs.*

Date of Submission: 20-07-2017 Date of acceptance: 05-08-2017

I. Introduction

Adverse drug reactions (ADRs) are any noxious, unintended and undesired effects of a drug which occur at doses normally used in man for prophylaxis, diagnosis or treatment of disease, or for the modification of physiological function [1]. The safe use of medicine is an important issue and an on-going ADR monitoring and reporting program can provide benefits to the organization, pharmacists, and other health care professionals and more importantly to patients. Following the thalidomide disaster in 1960 which reported increased frequency of birth defects (seal limbs) that left 10,000 babies disabled for life, monitoring centres were started all over the world. ADRs have been implicated as a leading cause of considerable morbidity and mortality. The incidence of ADR varies with studies which show incidences ranging from as low as 0.15% to as high as 30.3%. ADRs account for approximately 2.1% of hospital admissions, with 39.3% of them being life threatening. Elderly and hospitalized patients are reported to be more susceptible to ADRs than the adult population[2]. Around 5% of all hospital admissions are due to ADRs and 10%-20% of inpatients will have at-least one ADR during hospital stay [3] while the studies based on medical records review in the UK and other countries have reported that the prevalence of hospital admissions caused by ADRs ranges from 2.3-21.2% [4]. With the dramatic advances in the medical science, treatment of many cancers (like testicular cancer, lymphoma, and leukaemia) is not palliative, but rather curative in today's world. Chemotherapy is employed as part of a multimodal approach to the treatment of many tumours [5].

A study which was done recently stated antineoplastic agents as the common class of drugs causing the ADRs accounting for a total of 21.8% of the reported ADRs. Compromising dose intensity of drug or by delaying the doses, ADRs can be minimized but it can greatly affect their efficacy[5]. In India, certain factors such as large number of patients, poor doctor-patient ratio, self-medication, and usageof alternative systems of medicine, usage of counterfeit drugs and presence of highest number of drug combination products lead to a higher incidence of ADRs. Thus it becomes mandatory to identify, understand, predict and ultimately reduce the burden of ADRs. Rising costs of patient care, increasing awareness of patients towards the untoward effects of the drugs and the rise in the frequency of litigation cases against cliniciansand hospitals have made health care providers aware of the necessity to closely monitor adverse drug reactions [6]. ADRs should be quickly identified and managed to limit their detrimental effects on the patient [3].

Pharmacovigilance studies are essential in oncology. Antineoplastic agents are well studied and are extremely beneficial in cancer treatment, but they are used with caution due to their high toxicity and narrow therapeutic

window [7]. ADRs are so common and predictable in oncology that they came around to being accepted as an inevitable component of the treatment [8].Thus, onco-pharmacovigilance was developed, which is a subsystem of monitoring drugs derived from pharmacovigilance to monitor ADRs to cytotoxic antineoplastic drugs [9,10].
Main types of cancer treatment include surgery, radiation therapy, chemotherapy, immunotherapy, targeted therapy, hormone therapy, stem cell transplant and precision medicine [11]. Anticancer therapy may be either curative [adjuvant treatment and neoadjuvant treatment] or palliative, and this distinction influences the approach to management of individual patients [12].

II. Methods And Materials

The study is being carried out at Mahatma Gandhi Memorial Hospital,Warangal, Telangana, India. Patients from various places visit this tertiary care hospital on a regular basis for treatment of various disease conditions. This is a prospective-observational study and it was carried out for a period of six months from January to June 2016. Patients diagnosed with cancer and receiving treatment in outpatient oncology department of age >20years were considered for inclusion. Patients who are able to respond to the questionnaire, received at least two cycles of chemotherapy or at least five days of radiation therapy and patients receiving supportive therapy were included in the study. Prescriptions were reviewed to obtain demographic details. Medical/medication history interview was conducted on identified patients and information such as duration of existing condition, presence of other co morbidities, their duration, complaints of any drug or disease related problems and any other pertinent information concerned to treatment, lifestyle, type of diet, working status, residence and quality of life was collected. Patients who are non-co-operative and unable to respond to the questionnaire or not receiving treatment regularly, pregnant women, patients with HIV/AIDS or TB were excluded.

III. Results

Of the 201patients, 136 patients were female and 65 were male. Female patients [67.6%] suffering from cancer were twice as male patients [32.3%]. At the age of 40-49 years most of the patients [both male and female] are suffering from cancer followed by the age group 60-69 years [23.38%] and 50-59 years [21.39%]. The patients who are at the age group of 20-29 years were accounting the least. We found that patients with habit of drinking alcohol/toddy/gudumba [a local brew illicitly made] accounts for 57.6% [n=140] whereas smoking and tobacco chewing accounts for 23% [n=56] and 19.3% respectively [n=47]. Some of the patients had both chewing and smoking habits along with drinking habits. Among the study population most of them were non-vegetarian/mixed diet [91.5%] and only few of them were vegetarian [8.5%]. We found that most of the patients are agricultural workers [61.2%] followed by house wives and aged people [13.93%]. The people who are doing ancestral works like pottery, carpentry, toddy topper, black smith etc. stood third in the study population. Half of the study population was illiterate and of the remaining 38% were school dropouts and only 12% graduated from high school.

Amongst different types of cancers observed in the study population, most of the patients were suffering with breast cancer, of 53.23% breast cancer patients females were 97 and males were 10. Oral cancers [which include cancer of buccal mucosa, cancer of hypo pharynx, cancer of hard and soft palate, cancer of vocal cord] are the second most prevalent [17.4%] cancers. It was found that 46% of the males and 4% of female were suffering with these oral cancers. Cancers affecting reproductive system were observed only in female patients which include cervical cancer, endometrial cancer and ovarian cancer i.e. 7.96%. Cancers affecting gastro-intestinal system or digestive system include colon cancer, rectum cancer, stomach cancer, esophageal cancer were found to be of 11.5%. Head and neck cancers [tonsils, thyroid, and throat cancers] were found to be 7%. In both GI and head & neck cancers males were predominantly seen than females.

Table-1: Distribution of patients according to the type of cancer.

System/Part affected by cancer	% Female	% Male	Total %
Breast	71.32	15.38	53.23
Reproductive system	11.76	0	7.96
Respiratory system/Lung	0	1.54	0.50
Gastro intestinal system	8.09	18.46	11.44
Oral/mouth	3.68	46.15	17.41
Dermatology/skin	2.94	3.08	2.99
Head & neck	2.21	15.38	6.47

In the study population most of the patients were treated with FAC [5-fluorouracil, adriamycin, cyclophosphamide], CMF [cyclophosphamide, methotrexate, fluorouracil] and VAC [vincristine, Adriamycin, cyclophosphamide] regimens for breast cancer, Cisplatin and Carboplatin regimen for ovary, head & neck

cancers, Carboplatin, Oxaliplatin regimens for lung cancer, Cisplatin and Calcium leucovorin or Cisplatin/Oxaliplatin alone for esophageal, colon and rectal cancers. The dosage regimen is discussed in Table-2

Table-2: Anti-neoplastic agents used for cancer treatment [standard regimens][13]
Carboplatin:200–400 mg/m^2 intravenously every 4 weeks used for cancers of the ovary, head and neck, and lung
Cisplatin: 50–100 mg/m^2 intravenously every 3–4 weeks; 20 mg/m^2/d intravenously for 5 days every 3 weeks, used for cancers of the bladder, ovary, and testicles
Cyclophosphamide[C]:500–1000 mg/m^2 intravenously every 3 weeks; 100 mg/m^2/d orally for 14 days every 4 weeks used for lymphoma, breast cancer, and ovarian carcinoma
Doxorubicin/Adriamycin[A]: 15–20 mg/m^2 intravenously weekly; 45–60 mg/m^2 intravenously every 3 weeks used for breast cancer, lymphoma, and multiple myeloma
Etoposide: 50–100 mg/m^2 intravenously for 3–5 days every 3 weeks, oral dose is twice the intravenous dose used for cancers of the lung, testicles, leukaemia, and lymphoma
Fluorouracil (5-FU)[F]: 500–600 mg/m^2 iv bolus weekly for 6 weeks, repeat every 8 weeks; in combination with Oxaliplatin: 400 mg/m^2 intravenous bolus followed immediately by 600 mg/m^2 iv over 22 hours on days 1 and 2 or 400 mg/m^2 iv bolus followed immediately by 2400 mg/m^2 iv over 46 hours; 1000 mg/m^2 iv via continuous infusion for 4–5 days every 3–4 weeks used for cancers of the colon, breast, stomach, and head and neck.
Vincristine (Oncovin)[V]: 0.5–1.4 mg/m^2 intravenously every 3 weeks; 0.4 mg/m^2 intravenously via continuous infusion for 4 days; maximum single dose usually limited to 2 mg
Leucovorin: 10 mg/m^2 intravenously or orally every 6 hours until serum methotrexate level is below 0.01 micro molar; 20 mg/m^2 or 200–500 mg/m^2 intravenously before fluorouracil Used to rescue after high-dose methotrexate; in combination with fluorouracil for colon cancer

***Note*:** Dose and dosage regimen varies from patient to patient and depends primarily on the type, stage of the cancer.

Chemotherapy is given in cycles. A cycle is a period of chemotherapy treatment followed by a period of rest. For instance, chemotherapy may be given every day for 1 week followed by 3 weeks with no chemotherapy. These 4 weeks make up one cycle. The rest period gives body a chance to recover and build new healthy cells [13]. In the study population most of the patients were treated with FAC regimen [65%], around 17% of the patients were treated with cisplatin based regimen or cisplatin alone followed by CMF, AC, VAC, 5-fluorouracil based regimens as discussed in Table-3.

Table-3: Distribution of patients according to treatment regimen

Regimen	**No. of patients**	**%**
FAC	93	65.49
CMF	7	4.93
CISPLATIN based	24	16.90
AC	1	0.70
CARBOPLATIN based	1	0.70
OXALIPLATIN based	2	1.41
VAC	1	0.70
5FU based	11	7.75
5FU+CISPLATIN	2	1.41
TOTAL	**142**	**100**

In the study population mostly affected organ systems due to ADRs were gastrointestinal system - 31%, CNS & PNS systems-30% followed by musculoskeletal system-16%, respiratory system-8%, sensory system-7% followed by skin and appendages-7%. ADRs observed in the patients who are treated with chemotherapy [CT], radiation therapy [RT] and who received follow up care treatment were listed in the Table-4. Total 3370 ADRs were observed in 201 patients ranging from common adverse effect like nausea, vomiting to rare adverse effect like seizures.

Table-4: Description of adverse drug reaction in various study groups

Adverse Effect	**Fu**	**%**	**Rt**	**%**	**Ct**	**%**	**Total**	**%**
Fatigue	60	89.55	67	100	66	98.51	193	96.02
Body Pains	62	92.54	67	100	62	92.54	191	95.02
Lethargy	59	88.06	65	97.01	66	98.51	190	94.53
Headache/Backache	56	83.58	62	92.54	64	95.52	182	90.55
Arthritis/Joint Pains	52	77.61	59	88.06	61	91.04	172	85.57
Insomnia	50	74.63	54	80.60	59	88.06	163	81.09

Anorexia	48	71.64	58	86.57	56	83.58	162	80.60
Changes In Weight	45	67.16	51	76.12	62	92.54	158	78.61
Tremors/Tingling Sensation	49	73.13	42	62.69	56	83.58	147	73.13
Unable To Concentrate	44	65.67	41	61.19	52	77.61	137	68.16
Memory Loss	43	64.18	34	50.75	52	77.61	129	64.18
Blurred Vision	47	70.15	34	50.75	47	70.15	128	63.68
Episodes Of Fever	32	47.76	52	77.61	42	62.69	126	62.69
Nervousness	30	44.78	49	73.13	45	67.16	124	61.69
Short Of Breath	32	47.76	49	73.13	33	49.25	114	56.72
Nausea	21	31.34	36	53.73	54	80.60	111	55.22
Nervousness	30	44.78	49	73.13	45	67.16	124	61.69
Heart Burn	25	37.31	38	56.72	44	65.67	107	53.23
Cough	27	40.30	49	73.13	28	41.79	104	51.74
Ringing Of Ears/Hearing Problems	34	50.75	21	31.34	44	65.67	99	49.25
Vomiting	14	20.90	41	61.19	42	62.69	97	48.26
Constipation	30	44.78	29	43.28	35	52.24	94	46.77
Leukoplakia/Erythroplakia	8	11.94	32	47.76	35	52.24	75	37.31
Darkening Of Nails/Hands	2	2.99	12	17.91	53	79.10	67	33.33
Loss Of Hair	6	8.96	12	17.91	48	71.64	66	32.84
Hoarseness Of Voice	17	25.37	29	43.28	19	28.36	65	32.34
Diarrhea	9	13.43	31	46.27	17	25.37	57	28.36
Seizures	1	1.49	7	10.45	6	8.96	14	6.97
Fu=Follow Up Care Patients; Rt=Patients Receiving Radiation Therapy; Ct=Patients Receiving Chemotherapy								

IV. Disscussion

In our study, we found that majority of the patients were female i.e., 67.7% which is similar to many studies [14, 15], while it is in contrast Ali Dehkordi et al., where majority of the patients were males i.e., 55% [16]. Though the exact reason for this is unknown, increased exposure to hormones [estrogens which increases risk of uterine and breast cancers], lack of physical activity and dietary habits could be the main risk factors. Among 201 patients, 30.35% patients were of age 40-49 years. In 40-49 years age group both male [28%] and female [32%] patients were suffering from cancer, with the mean age of 46.5 years similar to that of the study by Smita Khandelwal et al.,**[6]** cancer is more common as we age because, of gene mutations and slow progression of cancer usually it can occur at any age but the risk increases as we get older. The risk factors found in our study were alcohol/ toddy/gudumba (illicit liquor), tobacco chewing and smoking. Around 58% of the patients had the habit of drinking, 23% have smoking habit and 20% have the habit of tobacco chewing. Among the study population, we found that not only men but women also have the habit of either chewing tobacco/betel nuts or drinking toddy/gudumba (illicit liquor).

Among the study population most of them were non-vegetarian/mixed diet [91.5%] and only few of them were vegetarian [8.5%]. A vegetarian diet is considered to be beneficial in reducing cancer incidence. Epidemiological studies have suggested that diet rich in vegetables and fruits reduces the risk of certain cancers [17]. For example, diet rich in fiber, vitamins A, C, and E, beta-carotene, retinols, alpha-tocopherol, polyphenols, & flavonoids, minerals like selenium and zinc have cancer preventive effect. Fruits and vegetables are rich sources of cancer preventive chemicals. These acts as inhibitors of carcinogen formation, blocking agents (block conversion of pro-carcinogens to carcinogens), stimulators of detoxifying system, trapping agents (trap and eliminate potential carcinogens) and suppressing agents (suppress the different steps of metabolic pathways leading to cancer)[17].

Majority of the patients [62%] are working in the agricultural sector. Having exposed to sunlight/ radiation, fertilizers/pesticides might have caused mutations in the DNA. Occupational, social and dietary factors may be one of the reason for the disease in these patients. Half of the study population was illiterate and of remaining 38% were school drop outs and only 12% were graduated from high school. Most of the patients were unaware of the disease and treatment pattern. Risk of cancer was more in married people [85%] similar to the study conducted by Sneegdha Poddar et al[18].By this study we found that illiterate persons have higher risk for developing ADRs than the educated due to lack of awareness of disease, adverse effects, and how to cope with adverse effects.

In our study population most of our male and female patients were suffering from Breast cancer [53%], followed by oral/mouth [buccal mucosal, hypo pharynx, tongue and laryngeal cancers], gastrointestinal cancers [like colon, rectal and gastric cancers], head & neck cancers[thyroid, throat, tonsils and vocal cord], skin cancers and lung cancers but Smita Khandelwal et al**[6]** found gastrointestinal cancers were more prevalent followed by

genitourinary, breast, lung, head & neck, thyroid, lymphoma and leukemia, myeloma, bone, brain cancers. In females, breast cancer stands first and cervical, endometrial cancers stands second while in males oral/mouth cancers are more prevalent and colorectal cancers stand second in our study population. In our study we found that there is a correlation between risk factors and the disease. Drinking habit lead to GI cancers and tobacco chewing and smoking lead to oral cancers in male patients. People who are exposed to pesticides for a long period and working in the sun light for long hours together were suffering with skin cancer.

Chemotherapeutic drugs have a narrow therapeutic index [15, 18] and the dosage needed to achieve a therapeutic response usually proves toxic to the body's rapidly proliferating cells. The normal tissues adversely affected by these drugs are rapidly dividing such as the bone marrow, gastrointestinal tract and hair follicles. Some agents have other organ specific toxicities[13]. Additionally, some drugs are associated with immediate adverse reactions which are a result of their biochemical nature rather than their action against tumours. Use of cancer chemotherapeutic drugs is associated with several adverse effects (AE) ranging from mild nausea to fatal myelosuppression. During the last decade, it has been demonstrated by a number of studies that drug induced morbidity and mortality is one of the major public health problems [19].

5-fluorouracil, cisplatin, carboplatin, paclitaxel, doxorubicin, and cyclophosphamide were more commonly associated with adverse drug reactions because it acts primarily in rapidly dividing tissues such as bone marrow, gastrointestinal tract, mucosal cells and reproductive system. The most common side effect of chemotherapy administration is nausea with or without vomiting, diarrhea, alopecia, darkening of skin and nails, darkening of the injection site, myelosuppression, mucositis, gonadal dysfunction, hyper-uremia, neuropathy, cardiomyopathy, hemorrhagic cystitis, impaired renal function, electrolyte imbalance, etc. [13].

The drug regimens which were used in the study population were mainly based on 5-fluorouracil, Cisplatin, Cyclophosphamide and Adriamycin. Commonly prescribed chemotherapeutic agents in our study site were similar to the prescriptions in Mangalore[20]. So most of the adverse reactions found in the patients were related to these drugs. In the present study, ADRs are commonly seen more in females than males due of alterations in the pharmacokinetics of drugs due to hormonal changes in the body[21] because and ADRs are mostly observed at the age group of 40-50 years, may be because of impaired renal function or hepatic function resulting in accumulation of drugs. We observed that majority of the ADRs were effecting gastrointestinal system-31% [nausea-55%, vomiting-48%, anorexia-80%, constipation-47%, diarrhea-28%, fatigue-96%, heartburn-53%, mouth sore and mucositis-37%], musculoskeletal system-16% [joint pains-86%, body pains-95%], CNS and PNS system-30% [Fever and chills-63%, Headache-90%, Tingling and numbness-73%, nervousness-61%], sensory system-7% [hearing problems/ ringing of ears-49%], skin & appendages-7% [itching, loss of hair-33%, discoloration of skin and nails-33%], respiratory system-8% [cough-52%, short of breath-57%, hoarseness of voice-32%] , and cognitive problems such as unable to concentrate-78%, unable to remember things-68% which is similar to other studies [6,19].

In our study patients were mostly affected by fatigue, anorexia, insomnia, lethargy and joint pains and our findings was consistent with the study conducted by Khandelwal et al. [6] and Krithi et al [20] but it was in contrast to the study conducted by Poddar et al [19]. We observed that patients receiving follow up/supportive care therapy were suffering from long term effects such as insomnia [74%], body pains [92%], fatigue[90%], lethargy [88%], anorexia [72%], and headache, back ache, tremors, tingling sensation, blurred vision, changes in body weight, & arthritis [all consisting more than 60%]. While patients receiving radiation therapy [$\geq$600gy] were suffering from body pains, fatigue & lethargy [100%], anorexia, cough, joint pains, nausea and nervousness [consisting more than 60%]. Patients receiving chemotherapy had similar type of adverse effects as of radiation therapy patients along with cognitive impairment like unable to concentrate, unable to remember. Adverse drug reactions such as nausea and vomiting were less reported in the present study since it was well managed with adequate pre-medication. Adverse drug reactions were managed by different approaches to reduce the severity level without making any changes in the drug regimen.

Chemotherapy-induced nausea and vomiting is one of the most unpleasant side effects of treatment, and is consistently reported by patients as one of their greatest fears while taking treatment course. It is not a pathological but it is a physiological process of the body to get rid of toxic substances. This reaction is controlled by many reflexes coordinating vomiting centre and chemo trigger zone. Prevention of chemotherapy-induced nausea and vomiting is the ultimate goal, and using appropriate antiemetics depending on the emetogenicity of the chemotherapeutic regimen is key. Modern antiemetics are very effective in the majority of cases, but this is by no means 100%. 5HT-3 antagonists (e.g., ondansetron) have no doubt changed the impact of chemotherapy-induced nausea and vomiting, and most recently, introduction of NK1 antagonists, e.g.: aprepitant, is making a similar impact, although these are often restricted due to cost. Nausea remains substantial for some patients, and is one side effect that greatly affects their quality of life.

Diarrhoea is common in patients receiving chemotherapy and radiation therapy. Pathophysiology of it is extensive and complex likely to be the result of mechanisms such as secretory, osmotic, malabsorption, exudative and dysmotility [22]. Understanding the probable cause is the key component. Direct damage to the mucosa lining of the gastrointestinal tract is often thought to be the cause, but overuse of antibiotics, underuse of

antidiarrheal agents, malabsorption syndromes, and infection are also implicated [23]. Untreated diarrhoea could be fatal and it can be managed by using agent such as loperamide and also by ensuring hydration. Octreotide can be tried for persistent diarrhoea [20]. It is important for the patient to understand their own baseline bowel habits before treatment and feel comfortable in discussing their bowel habits. On-going diarrhoea can have a profound effect on performance status and may interrupt treatment schedules. Patients are reluctant to attend hospital when suffering from diarrhoea because it is difficult to travel and embarrassing. In addition, patients are often reluctant to contact health care professionals repeatedly if their symptoms were not resolved during a previous cycle.

Constipation is mainly caused by neurotoxic chemotherapy drugs[21]. There is subsequent increase in intestinal absorption of fluid and electrolytes. It can be minimised by taking a high fibre diet, rich in fruits, vegetables and adequate fluids. A bowel regimen consists of mild stool softeners, bulk laxatives and bowel stimulants.

Chemotherapy affects the growth of both cancerous and noncancerous cells [25].The root of a hair has a high blood flow, allowing for uptake of chemotherapy. Hair can be lost from all over the body and not just the head, a fact that is often overlooked [26].The loss of facial hair for a man can leave them feeling much younger and possibly less virile [27]. Alopecia, although not life-threatening, is the most visible side effect of chemotherapy, having the ability to threaten body image and self-confidence [28, 29]. In 2008, Hilton et al concluded that, contrary to common belief, men also have negative feelings about hair loss. It can also leave the patient feeling that they have lost control of any choice about telling others about their condition and treatment [27] . It offers an opportunity for the nurse/pharmacist to discuss the psychological impact of alopecia by advising tips and strategies for managing hair loss as well as sensitively reinforcing messages about regrowth [28].

Stomatitis/mouth sores is a common side effect of chemotherapy, and is characterized by pain and inflammation of the surface of the mucous membrane in the oral cavity. It is developed as a direct result of chemotherapy destroying healthy cells in the mouth. Overall, 40% of people who have chemotherapy as part of their cancer treatment will develop some degree of stomatitis[30]. Its severity depends on the type of chemotherapeutic agent and the dose used. Stomatitis can vary from gum sensitivity to widespread painful ulcers. The duration is short, but can be debilitating and painful for the patient. A patient with stomatitis can suffer from isolation, nutrition problems, and infection [31, 32]. Severely compromised oral mucosa will result in reduction in the chemotherapy dose, with possible consequences in terms of optimal treatment outcome, although mouth repairs quickly in most patients, with a return to normal health within a few days.

Smell and taste changes occur during chemotherapy have a significant impact on patients ability to eat, which may ultimately lead to anorexia, weight loss and malnutrition [33, 34]. This side effect could also result in prolongation of other possible side effects, decrease in the patient's quality of life, poor compliance with treatment, and a possible decrease in response to treatment [35]. However, this side effect is not life-threatening and it is often overlooked by professionals. This can be managed by taking small amount of meals throughout the day.

One of the most frequent and distressing side effects of cancer and chemotherapy is fatigue [36]. The actual prevalence of fatigue in patients undergoing chemotherapy is unknown, but it is very likely all patients have some degree of fatigue, that persists beyond treatment in some cases [36, 38]. Fatigue is a common subjective complaint associated with chemotherapy, and symptoms such as total body tiredness, forgetfulness (often patients describe a "chemo head") and wanting to rest increases over time during chemotherapy. Management strategies include planning activities and ensuring plenty of rest. There is increasing evidence of the benefit of exercise during treatment to maintain muscle bulk. Ensuring adequate calorie intake and correcting anaemia are other measures to consider; along with determining if depression is present [41].

Peripheral neuropathy is becoming a challenging clinical problem for cancer patients receiving chemotherapy. Several of the commonly used drugs cause peripheral nerve damage (i.e., the taxanes and oxaliplatin) and if not treated by vitamin supplements like pyridoxine, methyl cobalamin, cyanocobalamin could lead to further damage irreversibly. Management strategies include preventing further damage, symptomatic relief, and psychological support [38]. Correcting dietary deficiencies is also thought to be beneficial.

People receiving chemotherapy and radiation therapy are more likely to have infections because they have lower numbers of the white blood. So frequent episodes of fever is observed in these patients which can be managed by having enough rest, plenty of fluids and acetaminophen. In cancer patients short of breath and cough can be seen because of compression of the large airways, pulmonary metastases, pleural effusion, and cachexia with weakness of the respiratory muscles, infection and pulmonary embolism [42]. But in the present study, cause of short of breath is decreased blood supply because of less oxygen carrying capacity of blood cells and damage to the rapidly growing cells in the respiratory tract, dryness of the tract which might also cause cough and hoarseness of voice/changes in voice.

Hyperpigmentation of skin and nails is due to stimulation of melanocyte receptor which is reversible. Melatonin hormone is responsible for sleep &stimulation of this hormone by cancer treatment results in insomnia. Other causes associated with sleep disturbances are anxiety, depression, fatigue &pain. Mainly

platinum based chemotherapy drugs particularly cisplatin and radiation therapy are responsible for ototoxicity, which produces free radicals that can damage cell walls, cellular structures, and genetic material in the ears. This can be reversible or irreversible based on the type of treatment used. The damage can be prevented by early detection. Ocular toxicity is caused by many drugs like antimetabolites, alkylating agents, platinum compounds, antimetabolites etc. by different mechanisms which is permanent where oncologist and ophthalmologist should work together to prevent irreversible ocular damage. Itching might be due to dry skin, dehydration and can be managed by using moisturizers, emollients and taking adequate fluids. Generalized body pains in cancer patients might be due to stimulation of nociceptors and neuropathic pathways which can be managed by using narcotic analgesics and anti-inflammatory drugs.

The drugs used in our study for the prevention and management of ADRs were antiemetics [ondansetron-4-8mg], antidiarrheal drugs [loperamide-4mg up to 16mg/day], analgesics [diclofenac-75-150mg/day, acetaminophen-500-4000mg/day, aceclofenac-100-150mg, anti-histamines [cetirizine-5mg, chlorpheneramine maleate-4-16mg/day], antacids [sucralfate-1g/day], pantoprazole-40mg, ranitidine-150mg, IFA-elemental iron-100mg/folic acid-5mg, calcium-500mg, zinc supplements along with nutrition supplements [protein powder, multivitamin tablets and syrup].

Quality of life in patients undergoing chemotherapy depends on the number of the cycles of chemotherapy received. During the first cycle patients are newly exposed to the chemo-drugs, so the side-effects of the drugs are not well tolerated and it is indirectly related to the intake of nutrition by the patient. The severity of the side effects will be less during third and fourth cycle body develops tolerance. Adverse effects are usually observed after 7-14 days of chemotherapy and lasts for 10-12 days, in meanwhile patients are scheduled for the next/phase-II chemotherapy cycle, resulting in continuous adverse events. In patients receiving radiation therapy, adverse effects regarding musculoskeletal system [body pains, joint pains, lethargy, fatigue, and headache], dehydration [dryness of eyes, mouth, mucositis, mouth sores, and cough] were commonly seen. These side effects indirectly affect the patient's quality of life.

The type A reactions [such as constipation, diarrhoea, alopecia] are predictable, reversible and are treated with dose adjustments and they can be avoided where the role of the clinical pharmacist gains importance. The notifications that include type A reaction demonstrate a clear need for a clinical pharmacist to monitor the patients. With respect to the type B reactions [such as blood dyscarias, pulmonary embolism, cardiac toxicity], though they are unpredictable and of unknown mechanism of reaction, the pharmacist must be aware, for example, patients with previous exposure to platinum compounds, must be ensured that corticosteroids and antihistamines are administered prior to the infusion of the drug to prevent hypersensitivity reactions (Cortijo-Cascajares et al., 2012) [44]. In addition, the pharmacist should warn the patients about the hyperpigmentation reaction, and advice to avoid exposure to the sun.

The presence of clinical pharmacists in wards helps in regular reporting of adverse drug effects, continuous monitoring, suggesting alternate drugs to prevent ADRs and managing ADRs by doing dosing adjustments thus improving the patients' health related quality of life. Even though ward based pharmacists were present in some of the hospitals, they were not involved full time in monitoring & detection of adverse effects, interacting with patients and doctors, or other ward-based error prevention activities.

Pharmacists specialized in oncology are responsible for a wide variety of functions, including monitoring, notification, prevention, and relief of reactions associated with chemotherapy [45]. In a Japanese study, pharmacists were responsible for the prevention and treatment of emesis, peripheral neuropathy, hand-foot syndrome, mucositis, localized pain, constipation, vascular pain, allergy, hyperglycaemia, diarrhoea and other conditions [44]. Lau et al., (2004) studied the preventability of reactions in oncology patients and found that 53% of the reactions such as alopecia cannot be prevented, whereas 45% and 2% of the reactions are probably and definitely preventable, respectively [8]. ADRs indirectly affect the patients' health related quality of life, so it is necessary for the identification and management of ADRs to improve patients QoL [6].

A clinical pharmacist participating in physician rounds in a cancer department can decrease the preventable ADRs. In addition, ward-based interventions may reduce costs of care. However, in India the impact of ward-based clinical pharmacists has not been assessed in the department of Oncology. ADRs associated with chemotherapeutic drugs decrease the quality of life, and increases the mortality as well as the healthcare budget [43]. It has been found that ADR profile of cancer chemotherapeutics is very less reported [43] and the situation is even worse in India. The reason might be that the data collected by regulatory authorities and pharmaceutical industries is inaccessible. The total contribution of India in adverse drug reaction information is only 1% of global data, which shows the under-reporting [44] and/ or under-detection as physicians are not so aware about pharmacovigilance or do not have adequate knowledge about ADR monitoring and reporting, due to which the exact incidence of ADR is still unknown [14].

During a 3-month study, a clinical pharmacist made 345 interventions in an adult ICU, leading to a $24000 cost reduction [42]. But in India no such study is reported. In our study period of six months, we observed 3370 ADRs and did 114 interventions, there is a need of a in house clinical pharmacist to identify, report,

monitor and manage ADRs, prevent medication errors, reduce cost of treatment, improve medication adherence and improve QoL of patients

V. Conclusion

Our study has shown that science of ADRs i.e., pharmacovigilance is gaining more importance in the hospital setting, especially in the oncology field. However, educating health care professionals about the need to identify and reporting adverse reactions is more important than studying ADRs. It was observed that oncology patients present several ADRs, including mild to severe reactions, which should be reported in the pharmacovigilance system. However, these reactions pass by unreported, which contributes to the under-reporting in oncology. The training of health care professionals working in hospitals on how, when and what to notify is essential to reduce under-reporting. In addition, it is proposed that a clinical pharmacist should be recruited in every speciality care division, as they are the ideal professionals to efficiently perform the pharmacovigilance role. The present study hints that pharmacists' involvement may not only greatly increase the reporting rate but also quality of reporting.

References

[1]. Poddar S, Sultana R, Sultana R, Akbar MM, Azad MA, Hasnat A; Pattern of adverse drug reactions due to cancer chemotherapy in tertiary care teaching hospital in Bangladesh. Dhaka Univ J Pharm Sci 2009; 8:11‐ 6.

[2]. World Health Organization. International Drug Monitoring: The Role of the Hospital. Geneva: World Health Organization; 1996. (Technical Report Series: No. 425.)

[3]. Stephanie N. Schatz and Robert J. Weber; Adverse drug reactions, CNS/Pharmacy practice, PSAP 2015; https://www.accp.com/docs/bookstore/psap/2015B2.SampleChapter.pdf.

[4]. Sze Ling Chan, XiaohuiAng, Levana L. Sani, Hong Yen Ng, Michael D. Winther, Jian Jun Liu, Liam R. Brunham and Alexandre Chan; Prevalence and characteristics of adverse drug reactions at admission to hospital: a prospective observational study.Br J ClinPharmacol. 2016 Dec; 82(6): 1636–1646.

[5]. Anju Prasad, Pratyay Pratim Datta,Jibak Bhattacharya, Chaitali Pattanayak, Ashok Singh Chauhanand Parbaty Panda; Pattern of Adverse Drug Reactions Due to Cancer Chemotherapy in a Tertiary Care Teaching Hospital in Eastern India J Pharmacovigilance 2013, 1:2

[6]. Smita Khandelwal1, KL Bairy, MS Vidyasagar, Bhartichogtu and Krishna Sharan; Adverse drug reaction profile of cancer patients on Chemotherapy in a tertiary care hospital Int J Pharm Bio Sci 2015 April; 6(2): (P) 233 - 244

[7]. Gandhi T.K; Bartel. S.B; Shulman, L.N; Verrier. D; Burdick E; Cleary A; Rothschidl J.M; Leape L.L; Bates D.W; Medication safety in ambulatory chemotherapy setting. Cancer, 2005, v.104, n.11, 2477-2483.

[8]. Lau, P.M; Stewart, K; Dooley, M. The ten most common adverse drug reactions (ADRs) in oncology patients: do they matter to you? Support. Care Cancer, 2004, v.12, n.9, p.626-633.

[9]. Cobert, B.L; Biron, P. Pharmacovigilance from A to Z: adverse drug event surveillence. Massachussets: Blackwell Science, 2002. 235 p.

[10]. Albini, .A. Donatelli. F; Noonan. D; Delios. M.M; Prisco. D. Bringing new players into the field: Onco-pharmacovigilance in the era of cardio-oncology. Intern. Emerg. Med., 2012, v.7, n.2, p.99-101.

[11]. US. Department of Health and Human Services, national institute of health/ national cancer institute/ USA.gov: http://www.cancer.gov/about - cancer/treatment/types.

[12]. Cancer Institute A National Cancer Institute, Designated Comprehensive Cancer Center. Available from http://cancer.stanford.edu/information/cancertreatment.

[13]. H.P.Rang, M.M.Dale, Rand and Dales Pharmacology, Topic-55 Anticancer drugs, 7th edition, 673-676.

[14]. David Soboba, Health related quality of life and cancer clinical trials. Therapeutic Advances in Medical Oncology Rev 2011:3[2] 57-71.

[15]. Andrew Bottomley, The cancer patient and quality of life. J of The oncologist; 2002, 7:120-125.

[16]. Ali Dehkordi, M. SaeedHeydarnejad,Daryoush, Quality of Life in Cancer Patients undergoing Chemotherapy, Oman Medical Journal 2009, Volume 24, Issue 3.

[17]. Stavric B. Role of chemo preventers in human diet. Clin. Biochem, 1994, 27, 319-332.

[18]. Sneegdha Poddar1, Razia Sultana1, Rebeka Sultana, Maruf Mohammad Akbor, Mohammad Abul Kalam Azad and Abul Hasnat, Pattern of Adverse Drug Reactions Due to Cancer Chemotherapy in Tertiary Care Teaching Hospital in Bangladesh; Dhaka Univ. J. Pharm. Sci. 8(1):2009 (June), 11-16.

[19]. V.K.Saini, R.Sewal, Yusra Ahmad, B.Medhi, Prospective observational study of adverse drug reactions of anticancer drugs used in cancer treatment in a tertiary care hospital, Indian J Pharm.Sci, V77(6),2015, 687-693.

[20]. Anekha Antony, Juno J Joel, Jayaram Shetty, Neethu Fathima Umar; Identification and analysis of adverse drug reactions associated with cancer chemotherapy in hospitalized patients; International Journal of Pharmacy and Pharmaceutical Sciences, 2016, Vol 8, Issue 7.

[21]. Sewunet Admasu Belachew, Daniel Asfaw Erku, Abebe Basazn Mekuria, and Begashaw Melaku Gebresillassie, Pattern of chemotherapy-related adverse effects among adult cancer patients treated at Gondar University Referral Hospital, Ethiopia: A cross-sectional study, Drug Healthc Patient Saf. 2016; 8: 83–90.

[22]. Kirthi C, Afzal A, Reddy M, Ali SA, Yerramilli A, Sharma S, A study on the adverse effects of adverse drug reactions in oncology patients: A prospective observational survey on the adverse drug effects of anticancer drugs in an oncology center of a tertiary care hospital. Int J Pharm Pharm Sci. 2014; 6:580–3.

[23]. Stergios Boussios, George Pentheroudakis, Konstantinos Katsanos and Nicholas Pavlidisa, Systemic treatment-induced gastrointestinal toxicity: incidence, clinical presentation and management, Ann Gastroenterol. 2012; 25(2): 106–118.

[24]. Massey C. A multicentre study to determine the efficacy and patient acceptability of the Paxman scalp cooler to prevent hair loss in patients receiving chemotherapy. Eur J OncolNurs. 2004; 8:121–130.

[25]. Engelking C, Rutledge DN, Ippoliti C, Neumann J, Hogan CM. Cancer related diarrhea: a neglected cause of cancer-related symptom distress. OncolNurs Forum. 1998; 25: 859–860.

[26]. Roe H. Chemotherapy-induced alopecia: advice and support for hair loss. Br J Nurs. 2011a; 20:S4–S11.

[27]. Hilton S, Hunt K, Emslie C, Salinas M, Ziebland S. Have men been overlooked? A comparison of young men and women's experiences of chemotherapy-induced alopecia. Psycho-Oncology. 2008; 7:577–583.
[28]. Yeager CE, Olsen EA. Treatment of chemotherapy-induced alopecia. DermatolTher. 2011; 24:432–442.
[29]. Hunt NC. The Viviscal Report; the hidden impact of hair loss. 2009. Available from: http://www.managinghairloss.com/_pdf/Hair-loss-report-summary.pdf. Accessed January 5, 2016.
[30]. Mynewhair. Advice and support if you lose your hair. 2011. Available from: http://www.mynewhair.org. Accessed March 15, 2016.
[31]. Treister N, Sook-Bin W. Chemotherapy-induced oral mucositis. 2008. Available from: http://emedicine.medscape.com/article/1079570-overview. Accessed February 16, 2016.
[32]. Borbasi Cameron K, Quested B, Olver I, To B, Evans D. More than a sore mouth: patients' experience of oral mucositis. OncolNurs Forum. 2002; 29:1051–1057.
[33]. Mais K. Mucositis from radiotherapy to the head and neck: an overview. Oncology News. 2006; 1. Accessed February 16, 2016.
[34]. Available from: http://www.oncologynews.biz/pdf/jun_jul/ON_junjul06_18.pdf.
[35]. UK Oral Mucositis in Cancer Group. OM guidelines. Available from http://www.ukomic.co.uk/new-om-guidelines.html. Accessed Aug 2016.
[36]. Rehwaldt M, Wickham R. Purl S, et al. Self-care strategies to cope with taste changes after chemotherapy. Oncology Nursing Forum. 2009; 36(2):E47–E56.
[37]. Sánchez-Lara K, Sosa-Sánchez R, Green-Renner D, et al. Influence of taste disorders on dietary behaviours in cancer patients under chemotherapy. Nutr J. 2010; 9:15.
[38]. Steinback S, Hummel T, Böhner C, et al. Qualitative and quantitative assessment of taste and smell changes in patients undergoing chemotherapy for breast and gynecologic malignancies. J ClinOncol. 2009; 27:1899–1905.
[39]. Bernhardson BM, Tishelman C, Rutqvist LE. Self-reported taste and smell changes during cancer chemotherapy. Support Care Cancer. 2008; 16:275–283.
[40]. Schlairet M, Heddon M, Griffis M. Piloting a needs assessment to guide development of a survivorship program for a community cancer center. OncolNurs Forum. 2010; 37:501–508.
[41]. Bower JE, Ganz PA, Desmond KA, Rowland JH, Meyerowitz BE, Belin TR. Fatigue in breast cancer survivors: occurrence, correlates, and impact on quality of life. J ClinOncol. 2000; 18:743–753.
[42]. Broeckel JA, Jacobsen PB, Horton J, Balducci L, Lyman GH. Characteristics and correlates of fatigue after adjuvant chemotherapy for breast cancer. J Clin Oncol. 1998; 16:1689–1696.
[43]. Nyholm CB. Side effects of cancer treatment: "chemo head" chemotherapy causes chemo brain. Available from: http://voices.yahoo.com/side-effects-cancer-treatment-chemo-head-389300.html?cat=68 Accessed February 68.British Pharmacological Society. 2013. Available from: http://www.bps.ac.uk/view/index.html. Accessed February 14, 2014.
[44]. Niraula S, Seruga B, Ocana A, Shao T, Goldstein R, Tannock IF, et al. The price we pay for progress: A meta-analysis of harms of newly approved anticancer drugs. J ClinOncol. 2012; 30:3012–9. [PubMed]
[45]. Claudia Bausewein, Shortness of breath and cough in patients in palliative care, DeutschesArzteblatt International, available from www.ncbi.nlm.nih.gov
[46]. Cortijo-Cascajares, S; Jiménez-Cerezo, M.J; Herreros De Tejada, A. Review of hypersensitivity reactions to antineoplastic agents. Farm. Hosp., 2012, v.36, n.3, p.148-158.
[47]. Liekweg, A.; Westfeld, M.; Jaehde, U. From oncology pharmacy to pharmaceutical care: new contributions to multidisciplinary cancer care. Support. Care Cancer, 2004, v.12, n.2, p.73-79.
[48]. Iihara, H; Ishihara, M; Matsuura, K; Kurahashi, S; TakahashI, T; Kawaguchi, Y; Yoshida, K; Itoh, Y. Pharmacists contribute to the improved efficiency of medical practices in the outpatient cancer chemotherapy clinic. J. Eval. Clin. Pract.2011, v.18, n.4, p.1-8.

IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS) is UGC approved Journal with Sl. No. 5012, Journal no. 49063.

Dr.P.Kishore. "Pattern of Adverse Drug Reactions in Cancer Patients at A Tertiary Care Hospital In Telangana Region of South India." IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS) 12.4 (2017): 87-95.