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Original Article

Prevalence of Drug-Related Problems in Elderly Cancer Patients: A Prospective Observational Study in a Cancer Specialty Hospital

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ABSTRACT

Background: The geriatric population comprises the majority of patients with oncological disorders. They are highly vulnerable to drug-related problems (DRPs) due to multiple comorbidities, polypharmacy, altered pharmacokinetics and pharmacodynamics. This study aimed to determine the rate and pattern of drug-related problems in elderly cancer patients. **Materials and Methods:** A observational study was conducted prospectively for a period of 4 months, where cancer patients of any gender above 60 years were enrolled and followed daily. All necessary data like patient demographics, past and current medication history were obtained from various data sources including medical records, treatment charts, patient interviews etc. DRPs were identified and assessed. **Results:** A total of 50 patients were enrolled into the study. From which, 96 DRPs were identified among 74% of the patients. Commonly observed DRPs were Adverse Drug Reactions (40%) and Drug-Drug Interactions (20.8%). More than half of the patients who developed DRPs (67.6%) had comorbidities, 86% were currently on chemotherapy alone or in combination and majorly (81%) were in the advanced cancer stage (Stage III and stage IV). Hyper polypharmacy was observed in 67.6% of the patients with DRPs. **Conclusion:** Our study revealed that DRPs are highly prevalent amongst elderly cancer patients and geriatric cancer patients need careful follow-up to identify DRPs and reduce adverse outcomes.

Keywords: Drug-related problems, Geriatric oncology, Cancer, Polypharmacy.

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INTRODUCTION

Oncological disorders are a considerable cause of morbidity as well as mortality globally majorly in the geriatric subpopulation.[1,2] Based on the worldwide statistics by the international agency for research on cancer, the risk of cancer development in this population increases 12-36 fold.[3] Elderly patients are also routinely associated with DRPs due to multiple factors including pharmacokinetic and pharmacodynamic alterations, comorbidities and polypharmacy.[4-6] DRP is defined as "an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes" according to the Pharmaceutical Care Network of Europe (PCNE).[7] Thus, DRPs are considered a major safety concern worldwide. Geriatric patients with cancer are at a higher risk for these problems because of the intricacy of the disease and its treatment which can consequently lead to substantial health and economic burden.[8,9] Since, the elderly are a rapidly growing population, proper and safe use of medications is of paramount importance for which identification and categorization of DRPs is the primary step.[4,10,11] In our study we explore this initial step of appropriate use of medications in aged cancer patients by determining the rate and pattern of DRPs.

MATERIALS AND METHODS

This was a prospective observational study conducted at Bharat Hospital and Institute of Oncology, Mysuru, Karnataka for a period of four months. Inpatients who were treated for any type of cancer, patients of any gender aged 60 years and receiving either standardized treatments or supportive care were included in the study. Outpatients except day-care patients were excluded. The approval from the institutional ethics committee of HCG-Bharat Hospital and Institute of Oncology was obtained prior to the commencement of the study (Clearance number ECM/31/22).

All admitted and day-care patients were followed on a daily basis. Eligible patients meeting the study criteria were enrolled into the study. All requisite data including demographics of the patient, clinical characteristics, type of cancer, comorbidities, past

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medications and current medications were sourced from various data sources including inpatient case notes, current treatment chart, laboratory tests and direct patient/caretaker (s) interviews. This information was then recorded in a well-designed data collection form and later transcribed into an Excel sheet. The clinical pharmacist obtained a clear past medical and medication history of the patient's adherence pattern and reassessed the treatment chart for DRP identification, if any and categorized them according to Hepler and Strand Classification.[12]

RESULTS

Overall, 50 geriatric oncology patients were enrolled into the study. The patient's clinical and demographic details are as mentioned in Table 1. 56% of the study patients were males and 44 % were female. Patients belonging to the age group of 60-70 years were in majority (66%). 70% of the subjects were presently married, 26% were widowed and 4% were single. A larger part of the patients were illiterate (46%) or completed primary education (40%). The majority (64%) of the patients followed a non-vegetarian diet. 20 patients (40%) who were enrolled into the study were smokers, 30% were alcoholics and 16% were tobacco chewers. The performance status (PS) of the individual subjects was assessed using the Eastern Cooperative Oncology Group (ECOG) performance scale according to which, 44% had a PS-0, 34% had a PS-1, 18% had PS-2 and 4% had PS-3. Half of the study, patient's treatment expenses were covered by the government-organized Suvarna Arogya Suraksha Trust (SAST) scheme, whereas 26% of the patients had to pay the treatment expenses personally. Other schemes through which patient expenses were covered in this study were private insurance companies (8%), Ex-servicemen Contributory Health Scheme (ECHS) (6%), Employees State Insurance Corporation (ESIC) (4%) and Arogya Bhagya Yojana Scheme (ABY) (4%).

About 61% of the elderly cancer patients had comorbid conditions as mentioned in Table 2. Of which hypertension (40%) was the most common followed by type 2 diabetes (30%) and ischaemic heart diseases (10%). Other comorbities included asthma (6%), stroke (2%), anaemia (2%), tuberculosis (2%), gastritis (2%), chronic liver disease (2%), arrhythmias (2%), benign prostate hypertrophy (2%), osteoarthritis (2%), hypotension (2%) and aortic valve disease (2%) Almost all the study patients (96%) had polypharmacy which is defined as the use of 5 medications at the same time. Amongst which, more than half of the geriatric subjects (56%) had hyper polypharmacy which is the administration of 10 medications per day.

The diagnosis, stage of cancer and current type of treatment given to the study participants are as illustrated in Table 3. The most common types of cancer seen among enrolled geriatric patients were gastrointestinal cancers (34%) followed by head and neck cancers (14%), liquid tumours (10%) and lung cancers (10%). Other types of carcinoma like cancer of the breast (6%), cervix (6%), ovary (4%), urothelial (4%), endometrium (4%), smooth muscle (4%), prostate (2%), penis (2%) and skin (2%) were observed.

A greater number of aged patients (38%) were diagnosed at the end stage (Stage IV) of cancer followed by locally advanced (30%) stage (Stage III). Only 30% of the patients were diagnosed at an early stage of cancer (Stage I and II).

About 78% (n=39) of the study patients were currently on chemotherapy, 8% (n=4) were on combination treatment with radiotherapy and chemotherapy, 4% (n=2) of the patients were on post-operative treatment or immunotherapy and 2% (n=1) were on radiotherapy alone, supportive care or on hormonal therapy.

Table 1: Demographic and Clinical status of the study subjects.

Total Number of Patients = 50		
Demographics		**N (%)**
Gender	Male	28 (56)
	Female	22 (44)
Age (years)	60-70	33 (66)
	71-80	13 (26)
	80	4 (8)
Marital Status	Married	35 (70)
	Widowed	13 (26)
	Single	2 (4)
Education	Illiterate	23 (46)
	Middle/High school/ Pre-university	20 (40)
	Degree	7 (14)
Diet	Vegetarian	18 (36)
	Non-vegetarian	32 (64)
Social Habits	Smoking	20 (40)
	Alcoholic	15 (30)
	Tobacco chewing	8 (16)
ECOG Performance Scale (PS)	PS 0	22 (44)
	PS 1	17 (34)
	PS 2	9 (18)
	PS 3	2 (4)
	PS 4	0 (0)
Payment Scheme	SAST	25 (50)
	Cash	13 (26)
	Private Insurance	4 (8)
	ECHS	3 (6)
	ESIC	2 (4)
	ABY	2 (4)

Note: ECOG: Eastern Cooperative Oncology Group, SAST: Suvarna Arogya Suraksha Trust, ECHS: Ex-servicemen Contributory Health Scheme, ESIC: Employees State Insurance Corporation, ABY: Arogya Bhagya Yojana

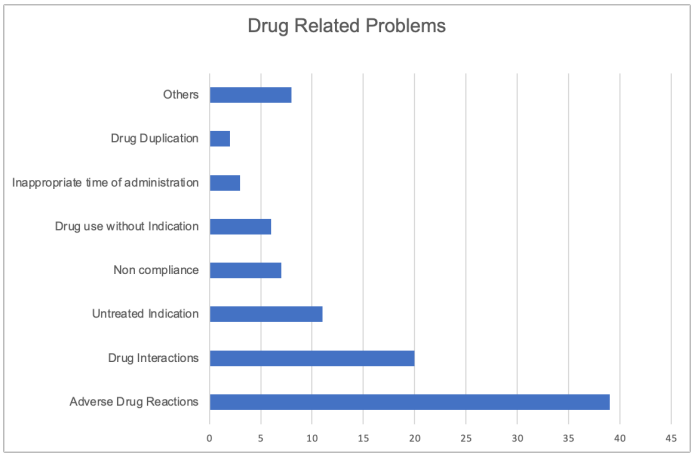

Figure 1: Types of Drug-related problems identified in the study.

Table 2: **Comorbidities and Polypharmacy.**

Comorbidities and Polypharmacy		N(%)
Number of comorbidities	Nil	19 (38)
	1	12 (24)
	2	14 (28)
	3	4 (8)
	4	1(2)
Type of comorbidity	Hypertension	22 (44)
	Type 2 Diabetes Mellitus	15 (30)
	Ischaemic Heart Disease	5 (10)
	Others	14 (28)
Total number of medications	Polypharmacy (5 medications)	48 (96)
	Hyper polypharmacy (10 medications)	28 (56)

Out of 50 patients, 37 (74%) were identified to have DRPs. A total of 96 DRPs were recognized. Common DRPs identified were ADRs (40%), drug interactions (20.8%), untreated indication (11%), medication non-adherence (7%), drug use without indication (6%), inappropriate time of administration (3.1%) and drug duplication (2%) as illustrated in Figure 1. Other medication-related problems included the wrong drug dispensed (2%), wrong dose dispensed (2%), wrong drug mentioned in the discharge summary (2%) and wrong dose mentioned in the discharge summary (2%).

All patients with DRPs had a history of social vices like smoking, alcoholism and/or tobacco chewing. 86% of the patients were currently undergoing chemotherapy and 81% were in the advanced stage of the disease. Amongst the 37 patients who developed DRPs, 26 patients were of the age group between 60 to 70 years. Hyper polypharmacy was observed in 67.6% of the patients and an equal number of patients had comorbidities as shown in Table 4.

Table 3: **Types of Cancer diagnosed along with Stages.**

Type of Cancer	N (%)	Stage of Cancer: N (%)
Gastrointestinal cancer	17 (34)	Early Cancer: 3 (6)
		Locally Advanced: 7 (14)
		Metastatic:7 (14)
Head and Neck cancer	7 (14)	Early Cancer: 3 (6)
		Locally Advanced: 4 (8)
Liquid tumours	5 (10)	Early Cancer: 2 (4)
		Locally Advanced: 1 (2)
		Metastatic: 1 (2)
Lung cancer	5 (10)	Locally Advanced: 2 (4)
		Metastatic: 3 (6)
Breast cancer	3 (6)	Early Cancer: 2 (4)
		Metastatic: 1 (2)
Cervical cancer	3 (6)	Locally Advanced: 2 (4)
		Metastatic: 1 (2)
Ovarian cancer	2 (4)	Early Cancer: 1 (2)
		Locally Advanced: 1 (2)
Urothelial cancer	2 (4)	Early Cancer: 1 (2)
		Metastatic: 1 (2)
Endometrial cancer	2 (4)	Early Cancer: 1 (2)
		Metastatic: 1 (2)
Sarcoma	2 (4)	Early Cancer: 1 (2)
		Metastatic: 1 (2)
Prostate cancer	1 (2)	Metastatic: 1 (2)
Penis carcinoma	1 (2)	Metastatic: 1 (2)
Melanoma	1 (2)	Metastatic: 1 (2)

DISCUSSION

Cancer is a common disease of geriatrics, where drug-related problems (DRPs) are a crucial issue in safety.[2,8] Our study on the prevalence of DRPs in geriatric oncology, even though limited is to the best of our knowledge, the earliest study done in India. According to our study, 74% of aged cancer patients developed DRPs. Various studies done in geriatric settings demonstrated the prevalence of developing DRPs was between the range of 15-81%, our study prevalence rate fits well into that range.[5,13,14-16] An average of 1.9 DRPs were observed per patient which is consistent with a study conducted by Halu *et al.* on drug-related problems in a geriatric setting.[5] However, in a study done on elderly cancer patients by Yeoh *et al.* the average DRPs per patient was 3.[13] This is higher when compared to our study because both inpatients and outpatients were included in the former whereas the latter only enrolled inpatients. Ageing develops a powerful cocktail

Table 4: Patterns of DRPs observed.

Total number of patients with Drug-related problems *n*=37 (%)	
History of social vices (Smoking, alcoholism, tobacco chewing)	37 (100)
Current treatment: Chemotherapy	32 (86.4)
Advanced stage of cancer (Stage III and IV)	30 (81)
Age (60-70 years)	26 (70.2)
Hyper polypharmacy (10 medications/day)	25 (67.6)
Patients with comorbidities	25 (67.6)

of comorbidity, polypharmacy or functional loss for developing DRPs.

The most common DRPs identified were ADRs which accounted for 40% of the total DRPs. Elderly patients have a negative association with ADRs due to age-related changes in their bodies. This risk further increases with cancer due to the perplexity of the disease and treatment. All the patients who developed ADRs were currently on chemotherapy. This can be explained by the fact that the toxicity of chemotherapeutic agents is amplified in older adults due to a decline in the functional and protective capacity of multiple organ systems. Our study results are similar with a study done by Yeol and colleagues, where the ADRs were observed in about 81.5% of geriatric patients who were currently on chemotherapeutic agents.[13]

Polypharmacy is universally defined as the use of 5 medications.[17,1] In addition, the use of more than 10 medications is usually termed as hyper polypharmacy. Various studies have analysed the prevalence of polypharmacy in elderly cancer patients to be between 20% to 96%.[18-20] In a study done by Nightingale *et al*, the prevalence of polypharmacy and hyper polypharmacy was found to be 84% and 43% respectively.[20] Similar results were obtained from our study where polypharmacy was observed in 96% and hyper polypharmacy was observed in 56% of our patients. One of the main reasons for increased rates of polypharmacy can be multiple comorbid conditions in the concerned population. According to our data, more than half of the study subjects had one or more comorbid conditions and the most common among them were hypertension and type 2 diabetes mellitus. 67% of the patients who developed DRPs had comorbidities. Another probable cause can be that most of the cancer patients in our study were in the advanced stage of disease (Stages III and IV) and mostly on chemotherapy. Treatment and supportive management for advanced cancers are highly complex, difficult and often accompanied by the use of an increased number of medications. It is important to note that 89% of the patients with hyper polypharmacy developed DRPs. Polypharmacy also increased the chances of drug interactions which was the common secondary DRP (20.8%) observed in our study. This is similar to an interventional study in Singapore where drug-drug interactions were observed in 30% of the patients.[12] Most of the drug interactions identified were significant in nature. While many of the drugs given to elderly cancer patients are inappropriate, numerous patient-related issues remain untreated as reflected in our study where about 11% of the indications were untreated.

This study had various limitations. Firstly, it was conducted in a solitary institution with limited sample size. Secondly, outpatients were excluded from the study, which resulted in the loss of critical outpatient-based data. Thirdly, the study did not collect information on Complementary Alternative Medicine (CAM) which can be potentially crucial in the assessment of DRPs in vulnerable cancer populations. Another important disadvantage of this study was the lack of interventions for the identified DRPs. When identified Medication-related problems are appropriately intervened and resolved, it can prevent potential harm from occurring and improve health and economic outcomes in the concerned subject.

A clinical pharmacist can play a key role in this setting by identifying a DRP, assessing the significance, appropriately intervening, resolving the problem if possible and providing alternative solutions.

The field of geriatric oncology and the impact of clinical pharmacists in improving care and preventing DRPs are yet to be rigorously explored and remain a grey area. More studies with a large sample size are warranted and needed for the fastest-growing demographic fighting a nasty disease.

CONCLUSION

In conclusion, DRPs are substantially prevalent among geriatric patients with cancer. Multiple comorbidities, age, polypharmacy, and cancer stage increase the susceptibility to developing DRPs. Adverse drug reactions and drug interactions are commonly identified. Elderly cancer patients need careful follow-up and clinical pharmacists have a window of opportunities in this area to improve and optimise patient care outcomes.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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