

Evaluation of Medication-Related Problems and Drug–Drug Interactions in Cancer Patients with Co-morbidities

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Abstract

Cancer patients frequently present with multiple comorbid conditions that complicate therapeutic decision-making and increase the risk of medication-related problems (MRPs). This prospective interventional study, conducted over six months at a tertiary oncology center, evaluated the prevalence of comorbidities, identified and classified MRPs, assessed drug–drug interactions (DDIs), and documented pharmacist interventions in 251 cancer patients receiving active treatment. Cardiovascular (35.8%) and endocrine disorders (33.4%) were the most common comorbidities, with hypertension (33.4%) and diabetes mellitus (31.4%) being predominant. A total of 267 MRPs were identified, of which DDIs constituted the largest proportion (65.1%), followed by adverse drug reactions (12.7%) and failure to receive medications (11.9%). Among the 174 DDIs detected, 39% were major and 44% were moderate in severity, commonly involving combinations of anticancer agents or interactions between chemotherapy, premedications, and comorbidity drugs. Clinical pharmacists made 130 documented interventions, most of which were moderate in significance and focused on patient counseling, adherence improvement, therapy re-initiation, and monitoring recommendations. The findings highlight a substantial burden of polypharmacy, clinically significant DDIs, and adverse events among cancer patients with coexisting diseases. The study emphasizes the critical role of clinical pharmacists in minimizing MRPs, enhancing patient safety, and optimizing therapeutic outcomes in oncology care.

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Introduction

Cancer remains one of the leading causes of morbidity and mortality globally, and its management becomes increasingly challenging when patients present with coexisting chronic illnesses¹. Comorbidities such as hypertension, diabetes mellitus, cardiovascular disorders, renal impairment, pulmonary diseases, and immunological disorders are highly prevalent among cancer patients, particularly in older adults²⁻⁴. More than half of all cancer diagnoses occur in individuals aged over 65 years, a population in which multimorbidity is common and often requires long-term pharmacotherapy. These underlying chronic diseases complicate diagnostic evaluation, influence treatment decisions, necessitate dose adjustments, and increase susceptibility to treatment-related toxicities⁵⁻⁶.

Polypharmacy, which is almost unavoidable in cancer patients with comorbid conditions, further increases the risk of medication-related problems (MRPs). MRPs

include untreated indications, inappropriate drug selection, subtherapeutic dosing, adverse drug reactions (ADRs), therapy nonadherence, and drug–drug interactions (DDIs). The narrow therapeutic index of many chemotherapeutic agents, combined with metabolic and pharmacokinetic alterations in chronic illnesses, predisposes patients to clinically significant interactions and toxicity⁷. Systematic assessment of MRPs and DDIs is essential to strengthen patient safety and optimize therapeutic outcomes in oncology settings⁸.

Previous studies have shown that cancer patients with comorbidities experience reduced treatment compliance, increased complications, and poorer survival rates⁹⁻¹⁰. Findings from the current study similarly identify a high prevalence of comorbidities and pharmacotherapy issues in cancer patients receiving treatment¹¹. Common coexisting diseases such as hypertension and diabetes mellitus were seen in over half of the study population, and more than half of the patients experienced at least one potential drug interaction¹²⁻

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¹³. These observations highlight the critical role of clinical pharmacists in the early identification of MRPs, prevention of harmful interactions, and support in multidisciplinary oncology care.

This study, therefore, aims to evaluate comorbidities, identify and classify MRPs, assess drug–drug interactions, and examine the impact of pharmacist interventions in cancer patients attending a specialized oncology center. Such evidence is vital for developing strategies that improve therapeutic safety and enhance the quality of life in this high-risk patient group.

Materials and Methods

A prospective interventional study was conducted to identify and evaluate MRPs and DDIs in cancer patients with comorbid conditions. Regular patient follow-up, treatment chart review, and pharmacist-led interventions were carried out throughout the study duration. The study was carried out at Bharath Hospital and Institution of Oncology (BHIO), a tertiary cancer care center under Health Care Global (HCG) Enterprises Ltd. The hospital provides medical, surgical, and radiation oncology services and handles approximately 100 outpatient visits, 15 inpatient admissions, and 25 day-care chemotherapy sessions daily. The study was conducted for six months, from 23 October 2014 to 4 April 2015. Approval was obtained from the Institutional Human Ethics Committee of JSS College of Pharmacy, Mysore.

Inclusion criteria consisted of cancer patients with at least one comorbid condition. Patients admitted only for diagnostic evaluation and not yet started on cancer treatment were excluded. Patient information was collected from case records, medication charts, chemotherapy charts, laboratory reports, patient/caregiver interviews, and communication with clinical staff.

A structured data collection form was used to document demographics, diagnoses, co-morbidities, medications, MRPs, and DDIs. MRPs were classified using Hepler & Strand criteria. The clinical significance of MRPs was graded using Alderman's classification (Major, Moderate, Minor).

Drug–drug interactions were identified using Micromedex 2.0 and categorized into anticancer DDIs, anticancer + pre-medications, anticancer + co-morbidity drugs, co-morbidity + pre-medications, and pre-medication interactions.

Clinical pharmacists provided interventions including patient counseling, therapy modifications, re-initiation of medications, and laboratory monitoring advice. All data were computerized and analyzed using Microsoft Access and Excel.

RESULTS

A total of 251 cancer patients with one or more co-morbid conditions were included in the study. The demographic distribution indicated that the majority of patients were elderly, with the highest proportion belonging to the 60–69-year age group (29.8%), followed by 70–79 years (25.8%) and 50–59 years (21.1%), as shown in Table 1. The study population consisted of 52.1% males and 47.9% females, and most individuals (88%) had a single co-morbid condition, while 11.9% presented with two.

The assessment of co-morbidities revealed that cardiovascular disorders (35.8%) and endocrine disorders (33.4%) were the major physiological systems affected, followed by multiple organ system involvement (11.9%). The detailed breakdown of co-morbidities by organ system is presented in Table 2. Among the specific conditions observed, hypertension (33.4%) was the most prevalent, followed by **diabetes mellitus (31.4%), and co-existing hypertension and diabetes (10.3%), as illustrated in Table 3. Less common co-morbidities included asthma, HIV/AIDS, opportunistic infections, thyroid disorders, COPD, tuberculosis, acute kidney failure, peptic ulcer disease, depression, and jaundice.

A total of 267 medication-related problems (MRPs) were identified during the study period, with drug–drug interactions (DDIs) constituting the largest proportion (174 cases; 65.1%), as shown in Table 4. Other MRPs included adverse drug reactions (12.7%), failure to receive medications (11.9%), untreated indications (3.7%), subtherapeutic dosing (1.1%), and improper drug selection (0.3%).

Among the 34 recorded adverse drug reactions, the most frequently noted events were vomiting (23.5%), leukopenia (17.6%), and thrombocytopenia (14.7%). These ADRs were primarily associated with chemotherapeutic agents such as carboplatin, cisplatin, 5-fluorouracil, paclitaxel, docetaxel, and cyclophosphamide. The complete list of ADRs and implicated drugs is shown in Table 5.

Nonadherence to medication therapy for comorbid conditions was observed in 32 patients, with the highest rates seen in individuals with hypertension (43%) and diabetes mellitus (28.1%), as outlined in Table 6. Reasons for nonadherence included hospitalization, forgetfulness, poor documentation, and lack of patient awareness. Additionally, three cases of subtherapeutic dosing and one case of improper drug selection were identified, as shown in Table 7.

A total of 130 pharmacist interventions were documented during the study. These interventions were classified based on clinical significance into moderate (45.3%), minor (43.8%), and major (10.7%), as presented in Table 8. Interventions commonly involved patient counseling, addressing adherence, reinitiating necessary medications, recommending monitoring of vitals such as blood pressure and blood glucose, and providing symptomatic management.

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Regarding drug–drug interactions, 174 DDIs were identified, and 56.1% of patients experienced at least one interaction. The distribution of the number of DDIs per patient is summarized in Table 9, while the severity classification (major, moderate, minor) is provided in Table 10. Anti-cancer drug interactions were frequently seen with combinations such as cyclophosphamide + doxorubicin and paclitaxel + cisplatin, as detailed in Table 11

Interactions between anti-cancer drugs and pre-medications accounted for **34 cases**, with notable examples including paclitaxel + dexamethasone and docetaxel + fosaprepitant, shown in Table 12. A total of 23 interactions were identified between anti-cancer drugs and medications used for comorbidities, commonly involving combinations such as furosemide + cisplatin, as presented in Table 13.

In addition, 31 interactions occurred between comorbidity drugs and chemotherapy pre-medications, particularly involving combinations such as dexamethasone + amlodipine and metformin + dexamethasone, as outlined in Table 14. Furthermore, 26 interactions were observed solely among comorbidity medications, with several major interactions involving fluconazole and hypoglycemic agents (Table 15). Finally, 21 interactions were recorded among chemotherapy pre-medications, with dexamethasone + pantoprazole being the most frequent combination (Table 16).

Overall, the findings highlight a significant burden of comorbidities, extensive polypharmacy, and a high frequency of medication-related problems, including clinically important drug–drug interactions. These results underscore the crucial role of clinical pharmacists in identifying MRPs, preventing adverse interactions, and improving therapeutic outcomes for cancer patients with comorbid conditions.

Table 1. Patient Demographics

Parameter	Number	Percentage (%)
Age 30–39	20	7.9
Age 40–49	26	10.3
Age 50–59	53	21.1
Age 60–69	75	29.8
Age 70–79	65	25.8
Age 80–89	12	4.7
Male	131	52.1
Female	120	47.9
1 Co-morbidity	221	88.0
2 Co-morbidities	30	11.9

Table 2. Co-morbidities by Organ System

Organ System	N (%)
Cardiovascular	90 (35.8%)
Endocrine	84 (33.4%)
Multiple organ systems	30 (11.9%)
Pulmonary	16 (6.3%)
Immunological	10 (3.9%)
Genitourinary	7 (2.8%)
Gastrointestinal	3 (1.1%)
Hematologic	3 (1.1%)
Psychological	2 (0.7%)
Neurological	2 (0.7%)
Hepatic	2 (0.7%)

Table 3. Co-morbid Conditions

Condition	N (%)
Hypertension	84 (33.4%)
Diabetes mellitus	79 (31.4%)
Hypertension + Diabetes	26 (10.3%)
HIV–AIDS	10 (3.8%)
Asthma	8 (3.1%)
Acute kidney failure	5 (1.9%)
Thyroid disorders	5 (1.9%)
Opportunistic infections	5 (1.9%)
COPD	4 (1.5%)
HTN + Asthma	4 (1.5%)
Ischemic heart disease	4 (1.5%)
Tuberculosis	4 (1.5%)
Peptic ulcer disease	3 (1.1%)
Chronic kidney failure	2 (0.7%)
Stroke	2 (0.7%)
Depression	2 (0.7%)
Jaundice	2 (0.7%)

Table 4. Medication-Related Problems

MRP Category	N (%)
Drug interactions	174 (65.1%)
Adverse drug reactions	34 (12.7%)
Failure to receive drugs	32 (11.9%)
Untreated indication	10 (3.7%)
Sub-therapeutic dose	3 (1.1%)
Improper drug selection	1 (0.3%)
Others	13 (4.8%)

Table 5. Adverse Drug Reactions

Reaction	Suspected Drugs	N (%)
Vomiting	Carboplatin, Cisplatin, 5-FU	8 (23.5%)
Leucopenia	Cyclophosphamide, Carboplatin	6 (17.6%)
Thrombocytopenia	Paclitaxel, Docetaxel, Oxaliplatin	5 (14.7%)

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Neutropenia	Paclitaxel, Cyclophosphamide	4 (11.7%)	Major	69 (39%)
			Moderate	76 (44%)
Anaphylaxis	Paclitaxel, Rituximab	3 (8.8%)	Minor	29 (17%)

Table 11. Interactions Between Anti-cancer Drugs

Condition	Drug Pair	Description	Severity	N
Alopecia	Paclitaxel, Docetaxel			
IRIS	Tenofovir + Lamivudine + Efavirenz	Risk of cardiomyopathy	Major	14
Candidiasis	5-FU	Increased paclitaxel levels	Major	8
Arthralgia	Paclitaxel	Leucovorin + 5-FU	Moderate	7
Hypotension	Rituximab			
Diarrhea	Cyclophosphamide	Cisplatin + Docetaxel	Moderate	6
	Paclitaxel + Doxorubicin	↑ Doxorubicin exposure	Major	2
	Cisplatin + Rituximab	Renal failure risk	Major	2

Table 6. Failure to Receive Drugs

Condition	N (%)
Hypertension	14 (43%)
Diabetes mellitus	9 (28.1%)
Asthma	2 (6.2%)
HIV–AIDS	2 (6.2%)
Ischemic heart disease	2 (6.2%)
COPD	1 (3.1%)
CVA	1 (3.1%)
Depression	1 (3.1%)

Table 7. Improper Drug Selection & Sub-therapeutic Dose

Issue	Description	N
Improper drug selection	Fluconazole instead of antiviral	1
Sub-therapeutic dose	Inadequate antihypertensive dose	2
Sub-therapeutic dose	Inadequate insulin therapy	1

Table 8. Pharmacist Interventions

Intervention Type	N
Patient counseling	54
Medication adherence support	31
Therapy re-initiation	16
Monitoring advice	15
Symptomatic treatment	14

Table 9. Number of DDIs per Patient

DDIs per patient	Patients (n = 141)	%
1	121	85.8%
2	15	10.6%
3	3	2.1%
4	2	1.4%

Table 10. Severity of Drug–Drug Interactions

Severity	N (%)
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Table 12. Anti-cancer Drugs + Pre-medications

Drug Pair	Description	Severity	N
Paclitaxel + Dexamethasone	Metabolism interaction	Moderate	9
Docetaxel + Fosaprepitant	↑ Docetaxel exposure	Major	4
Dexamethasone + Prednisolone	Altered metabolism	Major	4
Doxorubicin + Dexamethasone	↓ Doxorubicin exposure	Major	4
Vincristine + Dexamethasone	↓ Vincristine levels	Major	2

Table 13. Anti-cancer Drugs + Co-morbidity Drugs

Drug Pair	Effect	Severity	N
Furosemide + Cisplatin	↑ Nephro-/Ototoxicity	Major	5
Cisplatin + Phenytoin	↓ Phenytoin levels	Major	1
Methotrexate + Ibuprofen	↑ MTX toxicity	Major	1
Paclitaxel + Fluconazole	↑ Paclitaxel levels	Major	1

Table 14. Co-morbidity Drugs + Pre-medications

Drug Pair	Effect	Severity	N
Dexamethasone + Amlodipine	↓ Amlodipine effect	Moderate	8
Metformin + Dexamethasone	Hyperglycemia risk	Moderate	7
Aprepitant + Fluconazole	↑ Aprepitant levels	Moderate	4

Table 15. Co-morbidity Drug Interactions

Drug Pair	Effect	Severity	N
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Fluconazole + Glimepiride/Metformin	↑ Hypoglycemia	Major	4	reported and are known to increase the risk of cardiotoxicity, nephrotoxicity, or reduced therapeutic effectiveness. The high number of moderate and major interactions underscores the clinical significance of careful therapeutic monitoring.
Levofloxacin + Fluconazole	QT prolongation	Major	2	
Warfarin + Diclofenac	↑ Bleeding	Major	1	

Table 16. Pre-medication Interactions

Drug Pair	Effect	Severity	N
Dexamethasone + Pantoprazole	↓ Pantoprazole effect	Minor	14
Fosaprepitant + Dexamethasone	↑ Dexamethasone exposure	Moderate	7

Discussion

The present study assessed co-morbidities, medication-related problems (MRPs), and drug–drug interactions (DDIs) among cancer patients receiving treatment in a tertiary care oncology setting. The findings demonstrate a high prevalence of chronic co-existing diseases, extensive polypharmacy, and clinically significant therapeutic complications. These results emphasize the importance of structured pharmaceutical care and multidisciplinary collaboration in optimizing oncology treatment.

The age distribution showed that most patients were older adults, particularly between 60 and 79 years. This aligns with international cancer epidemiology, which reports that the incidence of cancer increases with age and that older adults commonly present with multiple chronic illnesses. In this study, cardiovascular and endocrine disorders were the most frequent co-morbidities. Conditions such as hypertension and diabetes mellitus were highly prevalent and correspond with previously published literature indicating that metabolic and cardiovascular diseases commonly coexist with cancer and may adversely affect treatment tolerance and clinical outcomes.

A total of 267 medication-related problems were recorded, and drug–drug interactions constituted the largest proportion. The identification of 174 DDIs reflects the complexity of managing multiple medications in cancer patients, who often receive anticancer agents, supportive therapies, and drugs for co-morbid conditions simultaneously. Many of the interactions observed in this study, including combinations such as cyclophosphamide with doxorubicin, paclitaxel with cisplatin, and dexamethasone with amlodipine, have been widely

Adverse drug reactions were also common, with vomiting, leukopenia, and thrombocytopenia being the most frequently reported. These effects are consistent with the toxicity profiles of commonly used chemotherapeutic agents. The occurrence of these reactions can lead to dose delays, treatment interruptions, and reduced patient adherence if not managed appropriately.

Non-adherence to medications for chronic diseases such as hypertension and diabetes was noted in a substantial number of patients. Poor adherence may worsen underlying disease conditions and potentially compound the adverse effects of cancer treatments. This finding highlights the need for continuous patient education and improved follow-up, particularly in patients managing multiple long-term medications.

Instances of improper drug selection and subtherapeutic dosing were identified, suggesting gaps in medication review and therapeutic planning. These errors may lead to uncontrolled comorbid conditions, resulting in avoidable complications during cancer therapy. Regular medication reconciliation and close monitoring are essential to prevent such issues. Pharmacist interventions played a significant role in improving therapeutic outcomes. A total of 130 interventions were documented, ranging from patient counseling to medication adjustments and monitoring recommendations. The interventions addressed critical issues such as adherence, drug interactions, and symptom management. The inclusion of clinical pharmacists in oncology teams has been shown in various studies to reduce medication errors, improve patient safety, and enhance the effectiveness of therapy. The positive impact of interventions observed in this study reinforces their importance in cancer care.

Overall, the findings demonstrate that cancer patients with comorbidities are at increased risk of medication-related complications due to polypharmacy and the complexity of treatment regimens. Systematic pharmaceutical care, routine assessment of drug interactions, regular patient counseling, and strong interdisciplinary communication are essential to improve treatment safety and patients' quality of life.

CONCLUSION

This study demonstrates that cancer patients with comorbidities are at a significantly increased risk of medication-related problems, particularly drug–drug interactions, due to the complexity of polypharmacy involved in oncology care. Cardiovascular and endocrine disorders

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were the most common coexisting conditions, and drug interactions formed the largest category of identified problems. Adverse drug reactions, treatment nonadherence, and instances of subtherapeutic dosing further contributed to therapeutic challenges. The findings emphasize the essential role of clinical pharmacists in identifying and resolving medication-related problems through systematic medication review, patient counseling, monitoring, and timely interventions. Pharmacist involvement contributes to improving adherence, minimizing risks associated with interactions, and supporting safer and more effective cancer therapy. Strengthening pharmaceutical care services and incorporating routine medication assessment into oncology practice can greatly enhance treatment safety and overall patient outcomes.

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