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# Clinical pattern and drug-related problems among colorectal cancer patients at oncology center in Ethiopia: A hospital-based study

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## Abstract

**Objective:** Despite the fact that cancer patients are highly susceptible to drug-related problems due to the effects of cytotoxic agents, data are limited due to a lack of studies on those patients. Hence, we aimed to investigate drug-related problems among patients diagnosed with colorectal cancer.

**Method:** A registry-based cross-sectional study was conducted on colorectal cancer patients at the Felege Hiwot Comprehensive Specialized Hospital. Socio-demographic and disease-related characteristics, treatment regimens, and drug-related problems were recorded by reviewing medical records. Standard guidelines, protocols, and databases were used to evaluate the occurrence of drug-related problems and the severity of adverse drug reactions. For the analysis, Stata version 16/MP for Windows was used. Logistic regression analysis was employed to investigate the potential-associated factors of drug-related problems. A $p$-value $\leq 0.05$ was used to declare the statistical significance of each independent variable.

**Results:** A total of 150 colorectal cancer patients were included, with a mean age of $51.4 \pm 13.8$ years. About 30% and 41.3% had stage II and stage III cancers, respectively. About three-quarters (73.8%) of the patients were given 5-fluorouracil-based combination regimens. The prevalence of drug-related problems was found to be 48.7%, with a mean of $2.12 \pm 0.93$ drug-related problems. In the Felege Hiwot Comprehensive Specialized Hospital, drug–drug interactions and adverse drug reactions were the most prevalent drug-related problems, which accounted for 50 (32.7%) and 49 (32%) cases, respectively. Being elderly (>50 years old) ($p = 0.013$), having co-morbidity ($p = 0.001$), and being on five or more medications ($p = 0.002$) were independent predictors of drug-related problems.

**Conclusion:** Fluorouracil-based chemotherapy was the most frequently used treatment regimen. Almost, half of the colorectal cancer patients had one or more drug-related problems. About one-third of patients had adverse drug reactions and drug–drug interactions. Furthermore, age, co-morbidity status, and the number of medications used were significantly associated with drug-related problems. Clinical pharmacy services should be implemented to optimize drug therapy because the majority of colorectal cancer patients have one or more drug-related problems.

## Keywords

Drug-related problems, colorectal cancer, Felege Hiwot Comprehensive Specialized Hospital, Ethiopia

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## Introduction

Cancer has become a major social burden in both economically developed and developing countries worldwide.[1] Although the burden of cancer is greater in developed countries, mortality is much higher in developing countries.[2] According to the International Agency for Research on Cancer estimates for 2018, colorectal cancer (CRC) accounted for approximately 1.8 million new cases and 0.9 million deaths worldwide,[1,3] making it the third most commonly diagnosed malignancy and the second leading cause of cancer-related deaths.[4,5] CRC is the first malignancy in Europe in terms of incidence and the second in terms of mortality in both sexes.[6] Similarly, the burden of non-communicable diseases, including cancer, is rising in Ethiopia. CRC was the third most common and fourth-leading cause of death in both sexes in 2020, with 3121 estimated new cases and a 5.9% mortality rate.[7] Sadly, a retrospective cohort study done among CRC patients treated at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia showed a mortality rate of 34.8% over 6 years.[8]

CRC patients have a high prevalence of co-occurring chronic diseases, and cancer treatment is complex and carries an inherent risk of drug-related problems (DRPs), which ultimately influences the treatment outcome.[9] In contrast to the intended effect of the drugs, DRP can result in increased morbidity and mortality. Extensive international research has revealed that DRPs harm a significant number of patients each year. A DRP is defined as an event involving drug therapy that has the potential to obstruct the achievement of therapy's desired goals.[10] Due to the complexity and narrow therapeutic index of most antineoplastic regimens[9,11] and the concomitant use of several drugs for the prevention of various complications associated with chemotherapy, DRPs have tremendous potential in cancer therapy.[12] DRPs caused by chemotherapy are more common in CRC patients, posing a significant challenge to healthcare providers.[13] Despite the fact that cancer patients are highly susceptible to DRPs due to the effect of cytotoxic agents on both normal and neoplastic cells, data are limited due to a lack of studies on DRPs in those patients.[14] In addition, in the absence of appropriate intervention, DRPs have a significant negative impact on patients' health in terms of prolonged hospitalization and increased healthcare costs.[15] Various studies have shown that DRPs cause 5%–13% of hospital admissions, with 50% of them being preventable,[16–18] and have a significant negative impact on the health of cancer patients.[15] The Netherlands[19] and India[20] studies reported the prevalence of DRPs caused by chemotherapy in cancer patients was 49.8% and 58.6%, respectively. Other studies showed that adverse drug reaction (ADR), the need for additional drug therapy, and drug–drug interaction (DDI) are the most prevalent DRPs.[21,22] DDIs are common since the agents used in the management of cancer and associated co-morbidities may have pharmacokinetic and pharmacodynamic effects on each other.[23,24] A previous study in Singapore demonstrated that potential DDIs (36.4%), ADRs (31.7%), and non-adherence (8.9%) were the most prevalent DRPs among cancer patients.[25] ADR (45.1%), non-compliance (25.4%), and need for additional therapy (23.9%) were the three most typical types of DRPs, according to a study among CRC patients in a Kenyan tertiary health facility.[21] Other studies in Ethiopia showed that ADRs and DRPs were observed in 52.86% and 74.7% of patients, respectively.[26,27] Various studies have shown that sex, age, length of hospital stay, histopathological grading and stages of cancer, number of medications, co-morbidity, and complications are determinants of DRP development.[22,24,28,29] A comprehensive study of DRPs would provide valuable insight for healthcare providers to reduce the incidence of DRPs and improve treatment outcomes in cancer patients.[30] DRPs can be prevented and managed with clinical pharmacists. Studies conducted in Turkey showed that clinical oncology pharmacists' recommendations significantly decreased the incidence of DRPs among CRC patients and improved the quality of life of those patients as it related to their symptoms.[31] A systematic review also shows that pharmacist interventions reduce nausea and vomiting while increasing adherence.[32]

However, DRPs of CRC patients have not been thoroughly studied and documented in Ethiopia, as previous research has primarily focused on communicable diseases, such as AIDS/HIV and tuberculosis.[33] Thus, we designed this retrospective cohort study to assess the prevalence of DRPs among CRC patients at the Amhara region oncology center in Ethiopia between 2016 and 2020.

## Methodology

### *Study setting and period*

The study was conducted at the oncology center of the Felege Hiwot Comprehensive Specialized Hospital (FHCSH). All medical records of CRC patients, who had been treated from January 1, 2016, to December 31, 2020, at the oncology center were retrospectively reviewed. The hospital is located in Bahir Dar and serves as an oncologic center for Amhara Regional State. In addition to its primary services, it also serves as a referral and training center. Since FHCSH is the largest tertiary hospital in the Amhara region, it has a diversified patient population drawn from across the region. The oncologic center has oncologists, trained nurses, and clinical pharmacists. It provides treatment for different kinds of cancers, such as cervical, breast, colorectal, head and neck, lung, and lymphomas and their complications. The data abstraction of medical cards was conducted from February 1 to May 31, 2021.

### *Study design*

A registry-based cross-sectional study of patients diagnosed with CRC and treated in this hospital was conducted.

### Study population

All adult patients with a histologically confirmed diagnosis of CRC, who were treated as inpatients or ambulatory at the oncology centers of FHCSH and who fulfilled the inclusion criteria were targeted.

*Inclusion criteria.* This study included all adult patients (⩾18 years old) with a histologically confirmed diagnosis of CRC who were receiving treatment at FHCSH's oncology center between January 1, 2016 and December 31, 2020.

*Exclusion criteria.* Patients with CRC whose medical records lacked sufficient information about their diagnosis, stage of cancer, and treatment modalities were not included in the study.

### Operational definition

*Drug-related problem.* In this study, DRP refers to the event of at least one of the following undesirable events: over-dosage, dosage too low, ADR, DDI, medication use without indication, and the need for additional drug therapy.[18]

### Sample size and sampling techniques

All medical records of patients who had been treated at FHCSH during 2016–2020 were eligible for this study. Based on these eligibility criteria, 150 medical records with confirmed CRC were included in this study. A total survey sampling technique will be employed to select the study population since the present study contains all patients with a confirmed diagnosis of CRC in the study setting. The relevant data were collected through chart reviews from February 1 to May 31, 2021.

### Data collection tool

The data abstraction format was used to collect socio-demographic characteristics, disease-related characteristics (histological types of cancer, stage of cancer, presence, and types of co-morbidities), treatment regimens and modalities, and DRPs. The occurrence of DRPs was assessed by comparing it to National Compressive Cancer Network (NCCN) and the European Society for Medical Oncology practice guidelines.[34,35] The incidence of DDIs was determined using standard drug interaction checkers, such as Lexicomp or Stockley's drug interactions. ADR severity was determined using the Modified Hartwig and Siegel ADR Severity Assessment Scale.[36] The data abstraction format was prepared in the English language.

### Data collectors' recruitment and training

The data collectors were three nurses and three clinical pharmacists. The data collectors got 1-day training, including the pretest with the focus data collection tool, research ethics, selection criteria, study objectives, and confidentiality.

### Data quality control

An expert oncology physician evaluated the data abstraction format for completeness and clarity. A pretest of eight patients was conducted prior to the start of the actual study to ensure the uniformity and clarity of the data collection instruments. Based on the pretest result, all necessary modifications were executed on the data collection instruments before the actual data collection. The investigators were closely supervising the data collection process throughout the data collection time. The collected data were checked for completeness and consistency on a daily basis. To ensure data quality, efforts were made during data collection, entry, analysis, interpretation, and representation.

### Statistical analysis

After checking for completeness and consistency of responses, the data were cleaned, verified, coded, and categorized. The data were then entered into the EpiData 4.6 software for Windows before being exported to Stata version 16/MP for Windows for further descriptive and analytical analysis. Analyses were stratified according to the stage of cancer, co-morbidity, complication status, and treatment modalities. A binary logistic regression model was used to assess the independent effects of each variable on the development of DRPs. All variables having a $p$-value of $\leqslant 0.25$ during binary logistic regression analysis were fitted into a multivariable binary logistic regression model to identify the independent contribution of each variable. For adjusted odds ratios (AORs), a 95% confidence interval (CI) was built to see the strength of associations. A $p$-value $\leqslant 0.05$ was used to declare the statistical significance of each independent variable.

## Results

### Socio-demographic and clinical characteristics of study participants

A total of 150 CRC patients were included in this study. Almost three-fourths of the study participants were females (107, 71.3%). The mean age of the study population was $51.4 \pm 13.8$ years, and the predominant portion of the study subjects (79, 52.7%) were aged greater than 50 years. More than half (56%) of the study participants were urban residents. As illustrated in Table 1, based on histological types, adenocarcinoma (53.3%) was the most common type, followed by squamous cell carcinoma (40.7%). The study showed that 30% and 41.3% of the study population had stage II and stage III cancers, respectively. Furthermore, 10.7% and 23.3% of the patients had recurrence and metastasis status, respectively. In this study, the liver, followed

**Table 1.** Socio-demographic and clinical characteristics of colorectal cancer patients at FHCSH between January 1, 2016 to December 31, 2020.

| Variables | Category | Frequency | Percent |
|---|---|---|---|
| Sex | Male | 43 | 28.7 |
| | Female | 107 | 71.3 |
| Age | 25–40 | 38 | 25.3 |
| | 41–50 | 33 | 22.0 |
| | ⩾51 | 79 | 52.7 |
| Residence | Rural | 66 | 44.0 |
| | Urban | 84 | 56.0 |
| Histological cell type | Squamous cell carcinoma | 61 | 40.7 |
| | Adenocarcinoma | 80 | 53.3 |
| | Not documented | 9 | 6.0 |
| TNM stage | Stage I | 11 | 7.4 |
| | Stage II | 45 | 30.0 |
| | Stage III | 62 | 41.3 |
| | Stage IV | 32 | 21.3 |
| Recurrence status | Yes | 16 | 10.7 |
| | No | 134 | 89.3 |
| Metastasis status | Yes | 35 | 23.3 |
| | No | 115 | 76.7 |
| Sites of metastasis | Liver | 15 | 42.8 |
| | Lung + liver | 7 | 20 |
| | Lung | 5 | 14.3 |
| | Lung + liver + lung | 3 | 8.6 |
| | LNs | 3 | 8.6 |
| | Ovary | 2 | 5.7 |
| Co-morbidity status | Yes | 42 | 28 |
| | No | 108 | 72 |
| List of co-morbidities | Hypertension | 6 | 14.3 |
| | Hypertension + diabetes mellitus | 5 | 11.9 |
| | Retroviral disease | 5 | 11.9 |
| | Deep vein thrombosis | 4 | 9.5 |
| | Small bowel obstruction | 4 | 9.5 |
| | Chronic kidney disease | 4 | 9.5 |
| | Benign prostatic hyperplasia | 3 | 7.1 |
| | Obstructive uropathy | 2 | 4.8 |
| | Cholestasis | 2 | 4.8 |
| | Hyperthyroidism | 2 | 4.8 |
| | Hepatic hemangioma | 2 | 4.8 |
| | Urinary tract infection | 2 | 4.8 |
| | Acute kidney injury | 1 | 2.4 |
| Complication status | Yes | 33 | 22.0 |
| | No | 117 | 78.0 |
| List of complications | Anemia | 10 | 30.3 |
| | Hypo-volume shock | 8 | 24.2 |
| | Hydronephrosis | 5 | 15.2 |
| | Hydronephrosis + anemia | 4 | 12.1 |
| | Acute kidney injury | 3 | 9.1 |
| | Ascites | 3 | 9.1 |

FHCSH: Felege Hiwot Comprehensive Specialized Hospital; TNM: tumor, node, metastases.

by the lung, was the major metastatic site. Regarding co-morbidity and complication status, 42 (28%) and 33 (22%) patients had co-existing co-morbidities and complications, respectively. Hypertension (HTN) and anemia were the most encountered co-morbid conditions and complications, respectively (Table 1).

Chemotherapy alone (76, 50.7%), followed by chemotherapy in combination with surgery (39, 26%), were the most

**Table 2.** Medication regimens of patients with colorectal cancer at FHCSH between January 1, 2016 to December 31, 2020.

| Variables | Category | Frequency | Percent |
|---|---|---|---|
| Number of medications | <5 | 58 | 38.7 |
| | ⩾5 | 92 | 61.3 |
| Prophylactic antiemetic regimens | Ondansetron and dexamethasone | 47 | 31.3 |
| | Metoclopramide and dexamethasone | 36 | 24 |
| | Ondansetron | 16 | 10.7 |
| | Metoclopramide | 9 | 6.0 |
| | No-antiemetics given | 42 | 28 |
| Analgesics regimens | Morphine | 42 | 28.0 |
| | Tramadol | 36 | 24.0 |
| | Paracetamol | 29 | 19.3 |
| | Diclofenac | 23 | 15.3 |
| | Ibuprofen | 17 | 11.3 |
| | Analgesic not given | 2 | 1.3 |
| Treatment modalities | Chemotherapy | 76 | 50.7 |
| | Chemotherapy + surgery | 39 | 26.0 |
| | Chemotherapy + radiotherapy | 17 | 11.3 |
| | Surgery | 14 | 9.3 |
| | Radiotherapy | 4 | 2.7 |

commonly used treatment modalities in the study settings. Ondansetron and dexamethasone 47 (31.3%), and metoclopramide and dexamethasone 58 (31.5%) combinations were the most commonly used prophylactic antiemetic regimens, followed by a combination of metoclopramide and dexamethasone 34 (24%). Conversely, 42 (28%) of the study participants did not receive any antiemetic medications. The findings of the study showed that morphine 42 (28%), tramadol 36 (24%), and paracetamol 29 (19.3%) were the most commonly used analgesics among the study participants (Table 2).

## *Types of regimens used in the management of CRC*

The combination of leucovorin, 5-fluorouracil (FU), and oxaliplatin (FOLFOX) (33.6%), followed by 5-FU and cisplatin (28.7%), was the most widely used treatment regimen in the management of CRC in FHCSH. Conversely, the combination of 5-FU and carboplatin was the least prescribed treatment regimen used in FHCSH (Figure 1).

## *Prevalence of DRPs*

A total of 153 DRPs were identified from 73 CRC patients, translating to a prevalence of 48.7% and a mean of $2.12 \pm 0.93$ DRPs per patient in FHCSH. In FHCSH, DDIs, ADRs, and the need for additional drug therapy were the most prevalent DRPs, which accounted for 50 (32.7%), 49 (32%), and 26 (17%) cases, respectively (Table 3).

DRPs were found in the majority of CRC patients treated with FOLFOX (leucovorin, 5-FU, and oxaliplatin) (38.4%), followed by cisplatin and paclitaxel (20.5%) (Table 4).

In terms of severity, 58% of the DDIs were significant, which required modification or close monitoring of the outcome of the DDIs. Tenofovir disoproxil fumarate with carboplatin, ciprofloxacin with oxaliplatin, metoprolol with hydrochlorothiazide, dexamethasone with tramadol, and metoprolol with ibuprofen were among the significant DDIs observed. However, 4% of DDIs were serious, which necessitates the use of alternative medications in the treatment regimen (Figure 2). In our study, we identified serious drug interactions between efavirenz and oxaliplatin, ciprofloxacin and ondansetron, and efavirenz and ondansetron.

Of the 50 ADRs identified in this study, the most common were nausea (54%), vomiting (46%), and dizziness (38%). On the other hand, constipation and thrombocytopenia were the least prevailing ADRs (Table 5).

## *Factors associated with DRPs*

In the uni- and multivariable binary logistic regression analyses, age, co-morbidity status, and the number of medications were significantly associated with DRPs. DRPs were four times more common in the elderly (>50 years old) than in younger (⩽40 years old) patients (AOR = 3.89, 95% CI = 1.34–11.34, $p = 0.013$). In addition, CRC patients with co-morbid conditions were five times (AOR = 5.47, 95% CI = 2.00–14.97, $p = 0.001$) more likely to have DRPs compared to their counterparts. Patients who had been treated with five or more drugs were also four times (AOR = 3.96, 95% CI = 1.63–9.62, $p = 0.002$) more likely to have DRPs as compared to patients treated with less than five medications (Table 6).

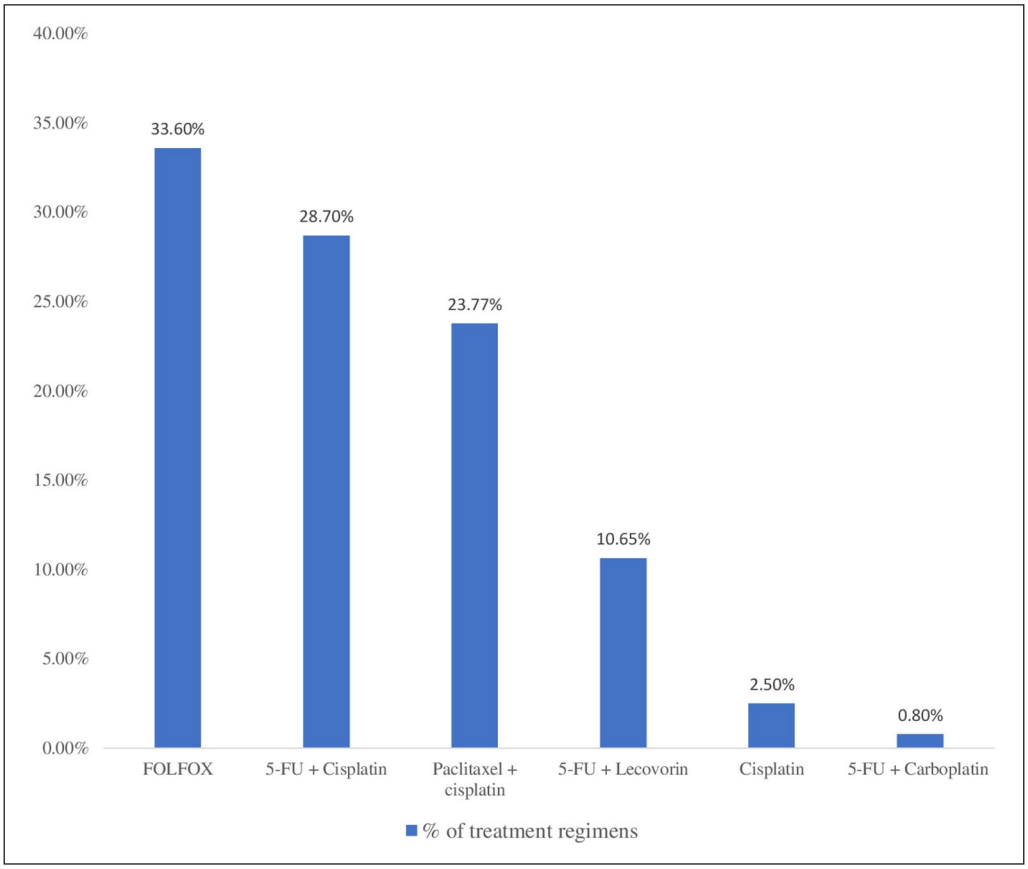


**Figure 1.** Types of regimens used in the management of colorectal cancer at FHCSH between January 1, 2016 to December 31, 2020.

**Table 3.** Categories of drug-related problems among patients with colorectal cancers at FHCSH between January 1, 2016 to December 31, 2020.

| Types of DRPs | Frequency | Percent |
|---|---|---|
| Drug interaction | 50 | 32.7 |
| Adverse drug reaction | 49 | 32 |
| Need for additional drug therapy | 26 | 17 |
| Sub-therapeutic dose | 17 | 11.1 |
| Medication use without indication | 6 | 3.9 |
| Over-dosage | 5 | 3.3 |

FHCSH: Felege Hiwot Comprehensive Specialized Hospital; DRP: drug-related problem.

## Discussion

Patients with CRC are at high risk for DRP due to the complexity of the management approach and the existence of different socio-demographic and clinical factors associated with the development of DRP.[37]

In the present study, the most prevalent histological pattern in CRC patients is adenocarcinoma (53.3%). Similarly, other studies have found that adenocarcinoma is the most common, though they have found a higher proportion of adenocarcinoma histology types (78–95%).[38–41] Adenocarcinoma is the most common histologic type seen in CRC patients because mutations caused by carcinogenic agents are mostly seen in mucus-producing (glandular) cells of the colorectal area. Based on the globally acceptable tumor, node, metastases (TNM) categorization of cancer cells,[42] the majority of our study subjects were in stage III (41.3%), followed by stage II (30%). This is consistent with previous studies conducted in Ethiopia (39.3%) and Armenia (38.0%), which found that stage III is more common in 39.3% and 38%, respectively.[40,43] Similarly, other studies have found that stage II CRC accounts for roughly one-third of all CRC diagnoses.[41,44] In Ethiopia, a previous study found that stage IV (47.8%) accounts for the majority of CRC diagnoses.[38] This variation in TNM staging could be attributed to differences in participant health-seeking behavior, societal awareness of CRC, and the implementation of screening programs. Screening of CRC is cost-effective in tackling CRC early in its stages and prevents disease progression.[45] The implementation of CRC screening programs using colonoscopy and fecal tests has resulted in a significant decrease in the disease's incidence, mortality, and progression in European countries.[46]

Forty-two (28%) of the participants had a co-existing co-morbid diagnosis, with HTN accounting for 30%. Similarly, co-morbidities were found in approximately 27.9% of CRC patients in an Ethiopian retrospective study.[38]

**Table 4.** Drug-related problems across different treatment regimens among colorectal cancer patients at FHCSH between January 1, 2016 to December 31, 2020.

| Treatment regimens | Number of patients with DRPs | Percent |
|---|---|---|
| Leucovorin + 5-FU + and oxaliplatin | 28 | 38.4 |
| Cisplatin + paclitaxel | 15 | 20.5 |
| Cisplatin + 5-FU | 13 | 17.8 |
| 5-FU + leucovorin | 9 | 12.3 |
| Surgery alone | 5 | 6.8 |
| Cisplatin | 2 | 2.7 |
| 5-FU + carboplatin | 1 | 1.4 |

FHCSH: Felege Hiwot Comprehensive Specialized Hospital; FU: fluorouracil.

**Table 5.** Types of adverse drug reactions in colorectal cancer patients at FHCSH between January 1, 2016 to December 31, 2020 ($n = 50$).

| Types of adverse drug reaction | Frequency | Percent |
|---|---|---|
| Nausea | 27 | 54 |
| Vomiting | 23 | 46 |
| Dizziness | 19 | 38 |
| Leucopenia | 17 | 34 |
| Neutropenia | 13 | 26 |
| Constipation | 7 | 14 |
| Thrombocytopenia | 4 | 8 |

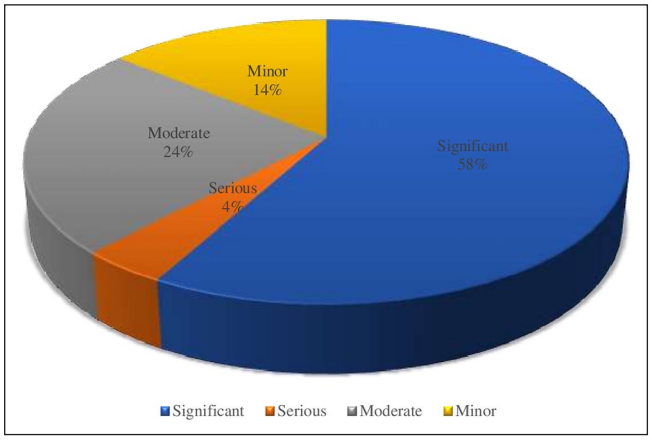


**Figure 2.** Severity of drug interactions among patients with CRC at FHCSH between January 1, 2016 to December 31, 2020 ($n = 50$).

In the same manner, a study conducted among CRC patients at a Kenyan tertiary care facility reported that cardiovascular disease (39.4%) is the leading co-morbid medical illness.[21] About 22% of patients had co-existing complications, with anemia (30.3%) being the most common. Likewise, anemia is seen in approximately 30%–75% of CRC patients,[47,48] and is a predictor of prognosis for CRC patients.[49] It is thought to be due to the presence of bleeding when the colon is involved.

Chemotherapy (50.7%) alone was the most commonly used treatment modality in the study setting, followed by chemotherapy in combination with surgery (26%). Other Ethiopian studies on CRC patients found that surgery with chemotherapy was the most commonly used treatment modality.[38,40] Treatment modalities may differ due to cancer staging, histological pattern, patient age and overall health, patient preference, and the availability of medications and interventions. The most commonly used treatment regimen in the management of CRC in FHCSH was a combination of 5-FU, oxaliplatin, and leucovorin (FOLFOX regimen) (33.6%), followed by 5-FU and cisplatin (28.7%). In agreement with our findings, a study at a Kenyan tertiary health facility found that FOLFOX/leucovorin, 5-FU, and oxaliplatin (54.9%) were the most commonly used regimens for CRC treatment, followed by XELOX/capecitabine and oxaliplatin and FOLFIRI/leucovorin, 5-FU, and irinotecan.[21] The FOLFOX regimen is widely used for CRC treatment. The FOLFOX regimen was recommended by the MOSAIC trial study for patients with stage III and above CRC because it slowed the growth and spread of cancer in stage III CRC patients and reduced symptoms and improved quality of life in stage IV CRC patients.[50]

Regarding antiemetic use, ondansetron PLUS dexamethasone (31.3%) and metoclopramide PLUS dexamethasone (31.5%) combinations were the most commonly used prophylactic antiemetic regimens followed by a combination of metoclopramide and dexamethasone (24%). This is understandable given the use of highly emetogenic agents in our study, such as FOLFOX and cisplatin-based regimens. Antiemetics are the most commonly used supportive medications in cancer patients undergoing chemotherapy.[51]

According to the study's findings, the most commonly used analgesics among study participants were morphine (28%), tramadol (24%), and paracetamol (19.3%). Cancer pain is common and, depending on the severity of the pain, requires the use of analgesics.[52]

A total of 153 DRPs were found in 73 CRC patients, resulting in a 48.7% prevalence. Studies conducted on DRPs in CRC are scarce, but when compared to studies done on solid tumors, the prevalence of DRPs is lower in the current study. For example, studies done in Ethiopia and Kenya on cervical cancer patients revealed that the prevalence of DRPs was 50.5% and 93.8%, respectively.[30,53] The prevalence is also lower than in a Chinese study of hospitalized cancer patients, where DRPs were found in 78.6% of patients.[54] It is also lower than the prevalence found in a study of cervical cancer patients, which was 89.2%.[55] The variation in DRPs might be due to the healthcare team compositions and the retrospective nature of the present study, which evaluates only treatment data on the chart, resulting in a lower prevalence of DRPs when compared to other prospective study designs.

**Table 6.** Uni- and multivariable binary logistic regression analyses of factors associated with drug-related problem among CRC patients at FHCSH between January 1, 2016 to December 31, 2020.

| | | Univariable analysis COR (95% CI) | *p* value | Multivariable analysis AOR (95% CI) | *p* value |
|---|---|---|---|---|---|
| Age (years) | 25–40 | 1 | | 1 | |
| | 41–50 | 0.94 (0.34–2.59) | 0.908 | 0.96 (0.27–3.36) | 0.948 |
| | ⩾51 | 3.95 (1.73–9.00) | 0.001 | 3.89 (1.34–11.34) | 0.013 |
| Co-morbidity | Yes | 5.23 (2.33–11.75) | <0.001 | 5.47 (2.00–14.97) | 0.001 |
| | No | 1 | | 1 | |
| Complications | Yes | 2.59 (1.15–5.82) | 0.022 | 2.68 (0.97–7.39) | 0.058 |
| | No | 1 | | 1 | |
| Stage of cancer | I | 1 | | 1 | |
| | II | 4.06 (0.47–35.03) | 0.202 | 2.36 (0.23–24.26) | 0.471 |
| | III | 15.83 (1.90–131.67) | 0.011 | 6.13 (0.62–60.85) | 0.122 |
| | IV | 19.09 (2.16–169.09) | 0.008 | 9.74 (0.91–104.63) | 0.060 |
| Number of medications | <5 | 1 | | 1 | |
| | ⩾5 | 4.89 (2.37–10.09) | <0.001 | 3.96 (1.63–9.62) | 0.002 |
| Recurrence status | Yes | 3.59 (1.10–11.70) | 0.034 | 4.06 (0.80–20.72) | 0.092 |
| | No | 1 | | 1 | |

COR: crude odds ratio; CI: confidence interval; AOR: adjusted odds ratio.

DDIs, ADRs, and the need for additional drug therapy were the most prevalent DRPs, which accounted for 32.7%, 32%, and 17%, respectively, in FHCSH. Similarly, a study in Kenya on CRC[21] and cervical cancer[30] patients reported that ADRs and DDIs were the most prevalent DRPs. In terms of severity, 58% of the DDIs were significant, necessitating modification or close monitoring of the drug interactions' outcomes. However, 4% of drug interactions were classified as serious DDIs. Serious DDIs are linked to higher healthcare costs, morbidity, and mortality.[56–58] When a serious drug interaction is discovered, the recommendation is to use an alternative medication if one is available, or to discontinue the least important agent. As a result, special emphasis should be placed not only on the presence of drug interactions but also on the severity of the interactions.

According to a review of DDIs in cancer patients, DDIs are common and occur in approximately one-third of patients receiving chemotherapeutic agents.[59] It has also been reported as a reason for hospitalization. Similarly, ADRs are common among cancer patients receiving chemotherapeutic agents, increasing their financial burden and compromising their quality of life.[60] It is frequent as these drug classes are non-selective and cause cellular toxicity to different organ systems.

The most common ADRs identified in this study were nausea (54%), vomiting (46%), and dizziness (38%). The study subjects received either FOLFOX or cisplatin-based regimens, which have been classified as highly emetogenic agents and are associated with severe nausea and vomiting unless the patient is taking prophylactic antiemetics.[61–63] Thus, the inclusion of clinical pharmacists is ideal for preventing and managing DRPs in cancer patients.

The study also identified that age, co-morbidity status, and the number of medications taken were all significantly associated with DRPs. Being elderly (>50 years old) was four times (AOR=3.89, 95% CI=1.34–11.34, $p=0.013$) more likely to have DRPs compared to younger patients (⩽40 years old). In accordance with our findings, a study conducted in the United States among patients with solid tumors revealed that there was a high burden of DRPs among older cancer patients.[24] Furthermore, patients with CRC who had co-morbid conditions were five times (AOR=5.47, 95% CI=2.00–14.97, $p=0.001$) more likely to have DRPs, and patients who had been treated with five or more drugs were four times (COR=3.96, 95% CI=1.63–9.62, $p=0.002$) more likely to have DRPs. Of patients with co-morbidities, patients with the retroviral disease, deep vein thrombosis (DVT) and HTN were more susceptible to DRPs. Similarly, a Zaria study found that being elderly, having co-morbidities, and being polypharmacy were all associated with the presence of DRPs.[55] The association might be due to the increased risk of co-morbidities in older patients, which warrants taking many drugs that ultimately interact with one another and lead to the risk of DRPs. Furthermore, the present study has some limitations. The data collected was based on what was written in medical records, which might be influenced by healthcare professionals' differences in the documentation of patients' related data and thus may not reflect the real practice on some occasions. Due to the lack of similar studies done in other African countries, we were also unable to compare our findings with these countries, which have related public health burdens and socio-economic status.

## Conclusion

The majority of the individuals had CRC in stages II and III. Nearly, one-fourth of the study participants had metastatic status and co-morbidity. FU-based chemotherapy was

the most frequently used treatment regimen. One or more DRPs were present in nearly half of CRC patients. About one-third of patients had ADR and DDI. Furthermore, age, co-morbidity status, and the number of medications used were significantly associated with DRPs. Given that the majority of CRC patients had one or more DRPs, clinical pharmacy services should be developed to optimize medication therapy.

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## Authors contribution

All authors made a significant contribution to the work reported in the conception, study design, execution, acquisition of data, analysis, and interpretation; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

## Availability of data and materials

The datasets used during the current study are available in the main document.

## Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

## Ethical approval

The study was approved by Debre Tabor University's Ethical Review Board (approval number: DTU/RE/1/3059/13), and subsequent permission was obtained from FHCSH's Medical Record and Oncology Department. Due to the nature of the study, the Ethics Committee and the hospital waived informed written consent from study participants. Patients' personal information and medication information were recorded while maintaining patient confidentiality and omitting their names and addresses. Our study was carried out in accordance with the Helsinki Declaration.

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## Informed consent

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## Supplemental material

Supplemental material for this article is available online.

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