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Emergency department visits among patients receiving systemic cancer treatment in the ambulatory setting

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Abstract

Background Most patients receive systemic cancer treatment in the ambulatory setting. However, during their treatment journey, patients experience complications that necessitate emergency department (ED) visits. Few studies evaluated the burden of such visits and their characteristics. This study aimed to evaluate the incidence and characteristics of ED visits among adult cancer patients receiving systemic cancer treatment in the ambulatory setting.

Methods A retrospective observational study was conducted at a comprehensive cancer center in Jordan. Utilizing the medical records database, we identified all patients treated in the chemotherapy infusion units, between January and December 2021. Patients who received only supportive therapy were excluded. The proportion of patients who required ED visits, their characteristics, types of cancer treatments received, and reasons for ED visits were recorded.

Results Over the study period, 4985 patients received 38,803 treatment cycles in the infusion units. Among those, 2773 (55.6%) patients had 10,061 ED visits. Patients who presented to the ED had a mean age of 53.7 ± 13.8 (SD) years and 1763 (63.6%) were females. The most common types of malignancies were breast (39.5%) and gastrointestinal (20%). The most common cancer treatments associated with ED visits were platinum-based (24.8%), immune-mediated/targeted therapy (15.3%), and hormonal (12.3%). The most common admission diagnoses were neuromuscular/skeletal symptoms (34.8%) and gastrointestinal symptoms (20.2%).

Conclusions In a large cohort of cancer patients receiving cancer treatment in the ambulatory setting, over half of them required at least one ED visit. Most visits were for neuromuscular/skeletal and gastrointestinal symptoms. Future studies should identify measures to reduce ED visits to enhance the patients' quality of life and outcomes and optimize resources.

Keywords Emergency service, Drug-related side effects and adverse reactions, Neoplasms, Antineoplastic agents, Ambulatory care

Background

Cancer is a major public health problem that continues to rise globally. According to the most recent report from the Global Cancer Observatory, an estimated 19.3 million new cancer cases and around 10 million cancer deaths occurred in 2020 [1]. The burden of cancer is expected to increase worldwide, with 28 million new cases expected in 2040, reflecting approximately 50% increase from 2020 [1].

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Patients with cancer receive various systemic cancer treatments, such as chemotherapy, immune-mediated therapies, targeted therapies, and hormonal agents [2]. Historically, patients received their cancer treatment in the inpatient setting [3]. However, with the advancement in oncology clinical practice, the administration of cancer-related treatments gradually shifted to the ambulatory setting to optimize hospital capacity and resource utilization, as well as improve patient quality of life and satisfaction [3].

Nevertheless, during their treatment journey, patients may experience various complications associated with the administered treatment or related to the underlying malignancy or other co-morbidities. Such complications may require visits to the emergency department, which place a substantial burden on hospital resources, expose patients to potential infections during their visit, impact the quality of life, and may necessitate changes to the treatment plan, which could negatively alter patient outcomes.

Several studies evaluated ED visits among cancer patients [4–19]. However, those that specifically assessed patients on active cancer treatment were limited to a specific type of malignancy, had relatively small sample sizes, and/or were conducted more than 10 years ago and thus do not reflect the regimens and treatment modalities currently used in clinical practice [10–19]. Furthermore, there have not been such studies from Jordan or other low-middle-income countries in which the healthcare systems and infrastructure are different from high-income countries. To understand the burden and significance of ED visits in patients receiving cancer treatment and to be able to identify potential measures to reduce such visits, a comprehensive assessment of the incidence and characteristics of ED visits is necessary. This study aimed to evaluate the incidence and characteristics of visits to the ED among cancer patients receiving systemic cancer treatment in the ambulatory setting at a comprehensive cancer center in Jordan.

Methods

This was a retrospective study conducted at King Hussein Cancer Center (KHCC), a comprehensive cancer teaching hospital in Amman, Jordan. KHCC is a 350-bed hospital that treats adult and pediatric patients with all types of malignancies. The hospital has two adult ambulatory infusion units in which systemic cancer treatments are administered to over 200 patients with various types of malignancies, on a daily basis, 6 days a week. In addition, there are two adult ED units, with a total of 36 beds, operating 24 h a day, 7 days a week. Patients treated at KHCC receive all their cancer and non-cancer medical

care at KHCC, including any type of illness or complication that requires ED visits.

A senior medical records specialist identified all patients who were treated in our adult ambulatory infusion units between January and December 2021. The treatments received during each visit were also identified. Eligible patients were adults (≥ 18 years) who received at least one cycle of systemic cancer treatment at the infusion unit. Patients who received only supportive treatment, such as bisphosphonates and electrolytes, were excluded. The characteristics of patients treated in the infusion units were electronically extracted, which included age, gender, type of malignancy, number of cancer treatment cycles received during the study period, and smoking history. The data was entered into a secured data collection sheet.

Among the patients included, the medical records specialist identified those who had ED visits following the administration of the cancer treatment, during the 1-year study period. For each ED visit, the following information was also electronically extracted: ED admission diagnosis, date and type of cancer treatment received prior to the ED visit, and whether the ED visit resulted in hospital admission.

The ED admission diagnoses were classified into the following, based on the main organ system involved: cardiovascular, dermatologic, endocrine and metabolic, gastrointestinal, hematological, hepatic, respiratory, neurological, neuromuscular and skeletal, genitourinary, ophthalmic, otic, and renal. In addition, we added infection as a separate category since this is a common ED admission diagnosis in cancer patients. The types of systemic cancer treatments were classified based on whether they were single agents or a combination. For those that consisted of multiple cancer treatments, the entire regimen was recorded and then categorized based on the main agent in the regimen. The investigators met to discuss the classification based on the available literature, and once agreed, utilized that approach in the electronic classification of the chemotherapy regimens.

Descriptive statistics were used to report the findings. Continuous data was reported as mean \pm standard deviation (SD) and/or median with interquartile range (IQR), while categorical data was reported as count numbers and percentages. Prior to data analysis, data cleaning was performed and any extreme outliers were assessed by the primary investigator. We calculated the proportion of patients who developed ED visits out of the entire study cohort. In addition, we reported the characteristics of patients who required and those who did not require ED visits. Since some patients may have had more than one visit to the ED, we recorded the characteristics associated with each ED visit.

Results

During the 1-year study period, 4985 patients received 38,803 cancer treatment cycles at our ambulatory infusion units. Patients had a mean age of 54 ± 14 (SD) years, about two thirds were females, the most common type of malignancy was breast cancer, and patients had received a median of 6 (range 3–11) cycles during the study period. Table 1 outlines the characteristics of the patients.

Among the study cohort, 2773 (55.6%) required a total of 10,061 ED visits during the study period. Patients with breast cancer had the highest number of ED visits during the study period, but gastrointestinal cancers had the highest frequency; 65.9% of patients with gastrointestinal cancers had at least one ED visit. For patients who visited the ED, the median number of visits was 2 (IQR 1–3), the highest median number of visits was reported with gastrointestinal cancer (median 3, IQR 1–5). Hospital admission was reported in 1414 (14%) of the ED visits, with breast cancer as the most type to require hospital admission (34.3%) followed by gastrointestinal cancer (20.9%). Of those who required hospital admission, 45 (3.2%) required admission to the intensive care unit. The characteristics of the patients who required ED visits during the study period and those who did not are outlined in Table 1. In addition, a description of the ED visits is reported in Table 2.

The median number of days between the administered systemic cancer treatment and the ED visits was 6 days

(IQR 3–13). The most common reason for ED visits was neuromuscular and skeletal symptoms (34.8%), which consisted of pain, generalized weakness, muscle spasm, and myalgias. Gastrointestinal symptoms (20.2%) were the second most common reason for ED visits, which included nausea, vomiting, and diarrhea. Cancer treatment regimens that patients had received prior to their ED visits consisted mostly of platinum-based regimens (24.8%), followed by immune-mediated/targeted therapies (15.3%) and hormonal therapies (12.3%).

Discussion

This study evaluated the incidence and characteristics of ED visits among a large cohort of patients with solid and hematological malignancies. The study reflects a real-world journey of patients who received systemic cancer treatment in the ambulatory setting. In a cohort of close to 5000 patients who received a median of 6 cycles of cancer treatment over 1 year, more than half of the patients had a median of 2 ED visits during the study period. This represents a large burden on healthcare systems, patients, and caregivers in terms of resources, quality of life, and outcomes.

Prince et al. [20] conducted a systematic review and meta-analysis to evaluate unplanned ED visits and hospitalizations in adults receiving adjuvant or palliative systemic therapy. Though the authors conducted a comprehensive search of MEDLINE and EMBASE from inception to 2016, only 20 articles reported ED

Table 1 Patient characteristics

Characteristics	All patients <i>N</i> = 4985	No ED visits <i>N</i> = 2212	At least one ED visit <i>N</i> = 2773	
Age (years), mean \pm SD	54 \pm 14	55 \pm 14.1	53.7 \pm 13.8	
Gender, <i>N</i> (%), female	3081 (61.8%)	1318 (59.6%)	1763 (63.6%)	
Smoking, <i>N</i> (%)	1228 (24.6%)	503 (22.7%)	725 (26.1%)	
Type of malignancy, <i>N</i> (%)			Proportion from entire population visited ED, <i>n</i> (%)	Proportion from each cancer type, <i>n</i> (%)
Solid	4421 (88.7%)	1989 (89.9%)	2432 (87.7%)	2432 (55%)
Breast cancer	2046 (41%)	951 (43%)	1095 (39.5%)	1095 (53.5%)
Gastrointestinal cancer	843 (17%)	287 (13%)	556 (20%)	556 (65.9%)
Prostate cancer	324 (6.5%)	224 (10.1%)	100 (3.6%)	100 (30.4%)
Genitourinary cancer	233 (4.7%)	146 (6.6%)	87 (3.1%)	87 (37.33%)
Lung cancer	287 (5.7%)	89 (4%)	198 (7.1%)	198 (68.9%)
Others	688 (13.8%)	292 (13.2%)	396 (14.2%)	396 (57.5%)
Hematology/<i>N</i> (%)	564 (11.3%)	223 (10.1%)	341 (12.3%)	341 (60.4%)
Leukemia	70 (1.4%)	17 (0.8%)	53 (1.9%)	53 (75.7%)
Lymphoma	387 (7.8%)	166 (7.5%)	221 (7.9%)	221 (57.1%)
Multiple myeloma	107 (2.1%)	40 (1.8%)	67 (2.4%)	67 (62.6%)
Chemotherapy cycles received, median (IQR)	6 (3–11)	5 (2–10)	2 (1–3)	

Table 2 Characteristics associated with visits to the emergency department (ED) ($n = 10,061$)

Characteristic	Value
Emergency visits per patient	
Median (IQR)	2 (1–4)
Mean \pm SD	3.6 \pm 4.7
Emergency visits per patient according to cancer type	Median (IQR)
Solid	
Breast cancer	2 (1–4)
Gastrointestinal cancer	3 (1–5)
Prostate cancer	2 (1–4)
Genitourinary cancer	2 (1–4)
Lung cancer	2 (1–5)
Others	3 (1–4)
Hematology	
Leukemia	2 (1–5)
Lymphoma	2 (1–4)
Multiple myeloma	2 (1–4)
Resulted in hospitalization, n (%)	1414 (14%)
Solid	1215 (86%)
Breast cancer	483 (34.2%)
Gastrointestinal cancer	295 (20.9%)
Prostate cancer	63 (4.4%)
Genitourinary cancer	45 (3.2%)
Lung cancer	119 (8.4%)
Others	210 (14.9%)
Hematology	199 (14%)
Leukemia	55 (3.9%)
Lymphoma	108 (7.6%)
Multiple myeloma	36 (2.5%)
Primary reason for ED visit, n (%)	
Neuromuscular and skeletal	3498 (34.8%)
Gastrointestinal	2034 (20.2%)
Infection	1261 (12.5%)
Respiratory	1244 (12.4%)
Neurological	595 (6%)
Endocrine/metabolic	358 (3.5%)
Renal	298 (2.9%)
Hematologic	242 (2.4%)
Others	531 (5.3%)
Cancer treatment received prior to ED visit, n (%)	
Monotherapy	5602 (55.7%)
Combination therapy	4459 (44.3%)
Type of systemic cancer treatment received prior to ED visit, n (%)	
Platinum-based chemotherapy	2490 (24.8%)
Immune-mediated/targeted therapy	1541 (15.3%)
Hormonal therapies	1241 (12.3%)
Anthracycline-containing regimens	1206 (12%)
Taxanes	1157 (11.5%)
Others	2426 (24.1%)

frequency. The studies included between 14 and 104,473 patients who had various types of malignancies and treatment intents. The proportion of patients who had ED visits ranged from 6 to 83%. However, given the time-frame of the literature search, most of the included studies evaluated cytotoxic chemotherapy (>80%). In our study, we included patients who received various types of treatments reflective of more recent practice guidelines, which included chemotherapy as well as immune therapies, targeted therapies, and hormonal treatment.

Dufton et al. [10] conducted a study similar to our study in which they evaluated ED visits among patients treated in the Day Oncology Unit of a large public tertiary hospital in Australia between 2014 and 2017. Most of the patients had hematological malignancies, followed by breast and lung cancer, but they did not report the type of treatments patients had received. Unplanned ED visits were reported in about half of the patients (45%) within 28 days of receiving systemic cancer treatment and 10% of the patients attended the ED four or more times within a 12-month period.

Sanoff et al. [19] reported ED visits in about 20–40% of patients with stage III colon cancer receiving 5-fluorouracil with and without oxaliplatin. However, among the Medicaid cohort, ED visits were reported in 83% of the patients. The authors attributed this high rate of ED use to factors related to the health system and access to oncologists, such as race, poverty, and communication. This highlights the importance of more social support for disenfranchised groups in the society, as well as the importance of a comprehensive health system to support cancer patients during their treatment journey and effectively manage complications that patients frequently encounter.

Among the reported ED visits in our study, 14% required hospitalization. This is different from the experience of other institutions. Mayer et al. [21] evaluated the characteristics of ED visits and unplanned hospitalizations among patients with cancer in North Carolina. The study included 27,644 cancer patients who required 37,760 ED visits. The study reported hospital admission in 63.2% of the ED visits, with lung cancer being the most common type of cancer that required admission. The differences may reflect differences in healthcare systems; our institution is a comprehensive cancer center in which patients receive all their cancer and non-cancer-related care and are advised to go to the ED for any complications they develop during their treatment journey.

McKenzie et al. [12] evaluated the characteristics of ED visits in a group of 581 patients with solid malignancies treated with chemotherapy in the ambulatory setting. The majority of patients presented to the ED within 2–7 days of chemotherapy. In our study, the median time

from receiving treatment to presentation to the ED was 6 days. The most common reasons for ED visits reported in the study by McKenzie et al. were nausea and/or vomiting (45.2%), followed by pain (27%). Though the most common reasons reported in our study were similar, pain and weakness were more common than gastrointestinal symptoms. This could be attributed to the use of more non-chemotherapy treatment regimens in our study as well as our practice of prescribing prophylactic supportive medications to all patients at high risk for nausea, vomiting, and/or diarrhea. Nevertheless, given that gastrointestinal symptoms and pain were still common reasons for our ED visits, additional measures should be examined to reduce or prevent such complications.

Barbera et al. [22] examined the relationship between patients' first assessment with the Edmonton Symptom Assessment System and the likelihood of an ED visit within 7 days. In their study of over 45,000 patients with cancer, they demonstrated that worsening symptoms contributed to ED visits. In addition, specific symptoms identified in the assessment such as pain, nausea, and shortness of breath were associated with ED visits. Such findings demonstrate the importance of ongoing patient follow-up and assessment in the outpatient setting to avoid ED visits.

In our study, the most common type of systemic cancer treatment patients received prior to their ED visit were platinum-based regimens, followed by immune-mediated/targeted therapies. Though immune-mediated/targeted therapy agents are considered to be relatively safer and with fewer side effects, compared to conventional chemotherapy, the results demonstrated that patients receiving such agents may still require ED visits during their treatment.

This study is unique in that it describes the real-world treatment journey of a large cohort of patients receiving systemic cancer treatment in the ambulatory setting. However, there are several limitations that we will highlight. The major limitation is related to the retrospective nature of the study, which limited our ability to evaluate some important patient-related and cancer-related characteristics and outcomes that could provide a deeper assessment of ED visits. For example, patients who required ED visits received less chemotherapy cycles, compared to patients who did not require ED visits; however, since we did not report the mortality, stage of malignancy, and other patient characteristics, it was difficult to determine if ED visits were associated with less treatment cycles received or if there were other contributing factors. In addition, given the diversity of patients and the limited characteristics available, we were unable to perform a comparison between the two groups, those who required and those who did not require ED visits.

Furthermore, given that ED visits were evaluated during the 1-year study period, this could lead to under-reporting of ED visits for the included patients due to censoring at the end of the study period, compared to an approach that followed each patient for 1 year from initiation of antineoplastic therapy.

Conclusions

Among a large cohort of patients with solid and hematological malignancies who received systemic cancer treatment in the ambulatory settings, over half of them required at least one ED visit. Neuromuscular/skeletal and gastrointestinal symptoms were the most common reason for these visits. Future studies should investigate predictors and identify measures to reduce such visits and improve the outcomes and quality of life of patients.

Abbreviations

ED	Emergency department
KHCC	King Hussein Cancer Center
SD	Standard deviation
IQR	Interquartile range

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Not applicable.

Authors' contributions

All authors contributed to the study conception and design. Material preparation, data collection, and data analysis were performed by NS. All authors reviewed and approved the final version of the manuscript.

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Availability of data and materials

The datasets analyzed during the current study are available from the corresponding author upon request.

Declarations

Ethics approval and consent to participate

The study protocol was approved by the institutional review board of King Hussein Cancer Center (KHCC), with a waiver of consent due to the retrospective nature of the study (IRB number 20KHCC134 /Aug 19, 2020).

Consent for publication

Not applicable.

Competing interests

The authors have no relevant financial or non-financial interests to disclose.

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