Original Research

Inappropriate Medications Use among Elderly Cancer Patients According to Beer's Criteria

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Abstract

Background: The global population of elderly has substantially increased in recent years due to heightened life expectancy and improved survival rates for numerous diseases, including cancer. Cancer treatment often entails complex regimens involving multiple medications. Additionally, advancing age is associated with a higher prevalence of co-morbidities, rendering older individuals more susceptible to inappropriate medications use and adverse drug events. **Objective:** We aimed in our study to examine the extent of Potentially Inappropriate Medications (PIMs) prescribing and factors associated with more PIMs instances in elderly cancer patients. **Methods:** The data of this study was evaluated utilizing medical records of included study subjects and was conducted over more than 3 years period (January 1, 2019 to January 31, 2022) at King Abdullah University Hospital, Al Ramtha, Jordan. Beer's criteria 2019 was used to evaluate and identify the potentially inappropriate drugs prescribed and used among elderly cancer patients. **Results:** A total number of 250 geriatric cancer patients were included in this study. The mean age of the patients was 73.4 years. Males represented 50.4% of the total patients (n=126). The average number of medications reported was 10.7 medications. Eighty three percent (n=203) of patients had polypharmacy (prescribed at least five medications or more), A total of 179 medications were considered inappropriate according to the 2019 updated BEERS criteria and 71.6% of patients (n=179) received at least one PIM. The most common classes of PIMs were gastrointestinal medications (e.g., metoclopramide). **Conclusion:** According to this study, the incidence of PIMs in geriatric oncology practice is concerning, and extra consideration should be given to reduce any risks associated with this kind of prescribing in elderly cancer patients. Polypharmacy was found to be a major predictor of PIM prescription in this research.

Keywords: cancer patients, Jordan, Potentially Inappropriate Medications (PIMs), Beer's criteria, elderly

INTRODUCTION

Patients with concomitant disease conditions frequently receive a cancer diagnosis. Therefore, the treatment of cancer patients involves complex regimens that include antiemetics, analgesics, chemotherapeutic agents, supplements, and medications to manage chronic illness and adverse drug reactions. In these situations, the cancer patients take multiple medications concurrently, a condition known as polypharmacy.[1]

According to the literature, there are 24 definitions of

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polypharmacy, ranging from inappropriate medications to excessive medications use. The basic definitions of polypharmacy, however, depend on how many medications a patient is taking. On the other hand, a focus on the absolute quantity of pharmaceutical doses neglects to consider the positive effects and sensible use of polypharmacy in certain instances.[2] Even if polypharmacy does not mean inappropriate medication, as the number of medications rises, so does the likelihood of inappropriate medication.[3] Therefore, several researchers consider that inappropriate medications prescribing and polypharmacy are interchangeable.[4]

The incidence of cancer has increased during the previous ten years, particularly among older people. Increased life expectancy has resulted in an increase in cancer prevalence among these patient groups.[5] By 2030, older individuals will account for almost 70% of all cancer diagnoses in the United States.[6] Jordan's population aged 65 and up accounted for 4% of the population in 2021. Jordan's population of people aged 65 or above increased from 3.2 percent in 1972 to 4 percent in 2021, expanding at a 0.51 percent annual pace. This is projected to continue to increase by 2030 to become around "8.6%" (World Population Ageing 2015, 2015).

With aging, physiological changes occur (decreased renal and hepatic clearance, altered metabolism, and altered motility patterns occur in the gastrointestinal system) that affect the efficacy and toxicity of drugs. In addition, cancer can affect a patient's physiological functions, exposing them to risk for drug-related problems.[7]

The prevalence of polypharmacy has been shown to be high among elderly Jordanian patients with chronic disease, and it has been linked to incorrect prescribing, adverse drug reactions, and excessive use of health resources.[8] Several studies have examined the frequency of polypharmacy among elderly cancer patients, with reported rates ranging from 11% to 96%, depending on how polypharmacy is defined. Two studies from Canada and the United States found that 92% and 93% of geriatric oncology patients take more than five medications, while other research has reported that elderly cancer patients consume a median of 5 to 9.1 drugs.[4,9,10]

Polypharmacy has been associated with more comorbidities, more inappropriate pharmaceutical usage, poor function status, frailty syndrome, inferior physical function, and mortality in cancer settings.[11] To address these concerns, several measures have been developed, including the identification of potentially inappropriate medications (PIMs).[12] Current National Comprehensive Cancer Network (NCCN) guidelines recommend the use of Beers Criteria and STOPP to identify PIMs and/or polypharmacy at every visit.[13]

Studies using either the Beers or STOPP criteria have found that 12% to 63% of the general elderly population is exposed to PIMs, with the majority of studies examining PIMs in cancer patients employing the Beers criteria.[14,15] Nearly one-third of geriatric oncology patients are at risk of serious, potentially inappropriate medications (PIMs) .[15] However, PIMs and polypharmacy in elderly cancer patients are understudied, particularly in the Middle East, where only a limited number of studies have been conducted in Saudi Arabia, Lebanon, Kuwait, and Qatar.[12,16-20]

To the best of our knowledge, no research has been conducted in Jordan on the issues of polypharmacy and inappropriate medication among cancer patients. Therefore, this study aims to determine the prevalence of PIMs and polypharmacy among geriatric oncology patients in a primary hospital using Beer's criteria to close this knowledge gap.

METHODS

Study design and Population

This was a retrospective cross-sectional study exploring PIMs among geriatric patients in an oncology unit over three years period between (January 1, 2019, and January 31, 2022) at King Abdulla University Hospital (KAUH) in Al-Ramtha, Jordan. Data of the study subjects were assessed using medical records and collected by a research associate who is a licensed clinical pharmacist practicing in Jordan.

The study population were patients aged 65 years and more, diagnosed with any type of cancer. and received at least one inpatient prescription that includes at least one prescribed drug.

Data from demographic and clinical variables, including age, weight, height, gender, comorbidities related to the Beers Criteria, prescribed drugs, and the most recent measured blood creatinine level, were retrieved after reviewing electronic inpatient medical records. The Cockcroft-Gault formula was used to calculate the creatinine clearance for each patient based on their most recent serum creatinine level.

Sample Size Calculations

A total number of 246 subjects were required in this study to obtain 95% confidence level, 5% margin of error, and population proportion was set at 20%.

Primary outcomes

Polypharmacy among participants was identified and further classified into regular and extreme polypharmacy with patients taking Five or more medications were classified as regular polypharmacy, whereas patients having ten or more were considered extreme polypharmacy.[21,22]

The potentially inappropriate medications (PIMs) for participants were recorded and then listed into one of the following groups based on the 2019 American Geriatrics Society (AGS) Beers Criteria[23]:

1) Medicines should be avoided by many or even most elderly people. PIMs were any of the prescribed drugs that were administered to a study group participant.

2) Drug-disease or drug-syndrome interactions that may make the disease or syndrome worse in older adults.

3) Drugs that elderly persons should use cautiously. PIMs were any of the prescribed drugs that were administered to a study group participant.

4) Combinations known to cause harmful drug-drug interactions.

5) Based on the patient's renal function, medications should be avoided, or their dosage should be changed. A PIM was defined as the use of one or more of the listed medicines in conjunction with a patient's creatinine clearance is less than the suggested limits.

Ethical Approval

This study was approved by the Institutional Review Board (IRB) of King Abdullah University Hospital (KAUH). The ethical approval number is KAUH-2022/147/61.

Statistical analysis

Both descriptive and analytical statistics were conducted. Descriptive statistics were used to describe patient characteristics and calculate the prevalence of PIM and polypharmacy use among geriatric cancer patients. In addition, a multivariable logistic regression model was utilized to evaluate potential risk factors related to PIM use. Statistical significance was defined as a P value less than 0.05. SPSS (version 22) was used to conduct statistical analyses.

RESULTS

In total, 250 geriatric cancer patients' records were identified as potential participants for the study. The average age was

73.4 (SD= 7.3) years and 50.4% were males. The most common cancer type was breast cancer (14.4%) followed by colon cancer (10%).

Prevalence of Polypharmacy and PIM

The average number of medications reported was 10.7 medications per patient. An 83% of patients had polypharmacy, while 54.2% of patients had excessive polypharmacy (more than 10 drugs).

A total of 179 medications were considered inappropriate according to the 2019 Beers Criteria. The mean number of PIMs per patient was 1.32 (range: 0-7), and 71.6% of patients received at least one PIM. The most common classes of PIMs were first-generation antihistamines.

Out of the 250 patients were evaluated, 71.6% of participants received at least one PIM prescription according to the 2019 Beers Criteria. More than half of these participants (57.6%) received one (38.8%) or two (18.8%) PIMs; On the other hand, 6.8% of patients received three PIMs, 3.6% of the patients received four PIMs, and only 2% of the patients had received Five PIMs. Of the identified PIMs, 77% were drugs to avoid in geriatrics, while 74.8% were drugs to use with caution in geriatrics. Additionally, 14.8% of medications should be avoided or have their dosage changed in accordance with kidney function, 15.6% were potentially clinically important drug-drug interactions, and 3.6% were drugs to avoid for geriatrics with specific diseases or syndromes. Among the majority of older patients, the most frequently prescribed drug types that were deemed PIMs to avoid were gastrointestinal medications (37.6%), followed by central nervous system medications (13.2%) and anticholinergics (1st generation antihistamines) (12%). (Table 1)

A small percent (3.6%) of all identified PIMs had potential drug-disease or syndrome interactions. Patients diagnosed with lower urinary tract symptoms, BPH (3.2%), and heart failure (0.4%) were the most often prescribed PIMs in this category. (Table 2)

The majority (74.8%) of all PIMs prescribed were from drug groups that should be used with caution in elderly patients. The most common PIMs in this class were diuretics (38%), tramadol (18.8%), and aspirin for the primary prevention of cardiac events in older persons aged >=70 years (11,6%). (Table 3)

Drug-drug interactions were the cause of (15.6%) of all prescribed PIMs. At least two separate CNS-active drugs were prescribed at the same time, which led to most of the identified interactions. (Table 4)

Medication that should be avoided or whose dosage should be adjusted due to older persons' renal function varies, has contributed to nearly (14.8%) of total PIMs encountered. The most of PIMs in this category were caused by prescribing enoxaparin when CrCl was below 30 ml/min. (Table 5)

There was a significant correlation between polypharmacy and having at least one diagnosed PIM. (p-value less than 0.001).

Other examined factors such as gender and age were not associated with increased to odd of developing PIMs. (Table 6)

Table 1. Potentially inappropriate medications to avoid in many or most older adults

Class\medication	%of total	QOE	SOR
Gastrointestinal medications	37.6		
Metoclopramide		moderate	Strong
Central Nervous System (CNS) medications	13.2		
Benzodiazepines		moderate	strong
Antidepressants		high	strong
Anticholinergics (1st generation antihistamines)	12.0%	moderate	strong
Chlorpheniramine			
Endocrine medications	7.6%		
Glyburide (Glibenclamide)		high	strong
Glimepiride		high	strong
Cardiovascular medications	3.6%		
Digoxin		moderate	strong
Nifedipine, IR		high	strong
Pain medications	2.8%		
NSAIDs		moderate	strong
Orphenadrine		moderate	strong
Antispasmodics	2.0%		
Atropine		moderate	strong
Clidinium-chlordiazepoxide		moderate	strong

NSAIDs: selective non-steroidal anti-inflammatory drugs; IR: Immediate Release; QOE: Quality of Evidence; SOR: Strength of Recommendation.

Table 2. Medications to avoid in older adults with specific diseases or syndromes

Object System/ Disease	Interacting class/ Medication	% of total	QOE	SOE
Kidney and Urinary tract		3.2%		
Lower Urinary Tract Symptoms, BPH	Anticholinergics (Strong)		Moderate	Strong
Cardiovascular		0.4%		
Heart failure	Non-dihydropyridine CCBs		moderate	strong

CCBs: Calcium channel blockers; BPH: Benign Prostatic Hyperplasia; QOE: Quality of Evidence; SOR: Strength of Recommendation.

Table 3. Medications to be used with caution in older adults			
Class/Medication	% of total	QOE	SOE
Diuretics	38.0%	moderate	Strong
Aspirin for primary prevention of cardiac events	11.6%	moderate	Strong
Antidepressants	5.2%		
Mirtazapine		moderate	Strong
SSRI		moderate	strong
TCAs		Moderate	Strong
Carbamazepine	1.2%	Moderate	Strong
Tramadol	18.8%	Moderate	strong

TCAs: Tri-Cyclic Antidepressants; SSRIs: Selective Serotonin Reuptake Inhibitors; QOE: Quality of Evidence; SOR: Strength of Recommendation.

Table 5. Drugs to be avoided or have their dosage adjusted with varying levels of kidney function in older adults					
Medication	CrCl (ML\MIN)	Action required	% of total	QOE	SOE
Gabapentin	<60	Reduce dose	2.0%	Moderate	strong
Enoxaparin	<30	Reduce dose	4.8%	Moderate	Strong
Levetiracetam	<=80	Reduce dose	1.2%	Moderate	Strong
Ranitidine	<50	Reduce dose	2.0%	Moderate	Strong
Tramadol	<30	Avoid	1.6%	low	weak
Ciprofloxacin	<30	Reduce dose	2.8%	Moderate	Strong
Spironolactone	<30	Avoid	1.2%	moderate	Strong

CrCl: Creatinine Clearance; QOE: Quality of Evidence; SOR: Strength of Recommendation.

DISCUSSION

To the best of our knowledge, this is the first study evaluating PIMs prevalence among oncology patients over the age of 65 years in Jordan using the 2019 AGS Beers Criteria as a screening method. In accordance with the most recent AGS Beers Criteria, the study's findings revealed a significant prevalence of PIM prescribing among geriatric cancer Jordanian inpatients (71.6%).[1] The prevalence of PIMs in our study is relatively comparable with various published studies. Finding from a cohort study demonstrated a high prevalence of PIM (21%–66%) among older adults with cancer.[13, 24] In the United States, a study was conducted using both the Beers and STOPP criteria in senior adult oncology patients. PIMs were found in 51% of the population, 38% depending on STOPP criteria, and 40% depending on the 2012 Beers criteria.[4] In a secondary study using the 2019 Beers criterion and Screening Tool of Older Persons' Prescriptions, 62.3% of patients received at least one PIM.[22] Another study in the Middle East from Saudi Arabia demonstrated that 52.5% of the 798 elderly were on >=1 PIMs, as per Beers' criteria.[16]

Our study revealed that the most common inappropriate medications which can be avoided with alternative medications

Table 4. Potential clinically important drug-drug interactions in older adults (15.6%)				
Object Drug/Class	Interacting Drug/Class	% of total	QOE	SOE
Anticholinergic	Anticholinergic	2.8%	moderate	strong
CNS-active drug*	≥ 2 other CNS-active drugs	8.4%	Moderate	Strong
Peripheral α-1 blockers	Loop diuretics	3.6%	Moderate	strong
Theophylline	Ciprofloxacin	0.4%	Moderate	strong
Warfarin	Ciprofloxacin	0.4%	moderate	Strong

CNS: Central Nervous System; QOE: Quality of Evidence; SOR: Strength of Recommendation.

Table 6. Predictors of potentially inappropriate medications prescribed among elderly patients		
Variable	aOR (95% confidence Interval)	P Value
Gender (Female vs Male)	1.31 (0.78-2.20)	0.469
Polypharmacy **	1.32 (1.23-1.41)	<0.001
Age	0.99 (0.95-1.03)	0.614

*P value is significant at <0.05

**: Polypharmacy was defined as ≥ 5 prescribed medications

CI, confidence interval; OR, odds ratio; PIM, potentially inappropriate medication.

are metoclopramide as an antiemetic, chlorpheniramine as an antiallergy, and tramadol. Such finding could be due to number of reasons including that these medications are the only drugs available to physicians to prescribe as they should be following the institutional drug formulary list for prescribing and low cost of these medications compare to other alternatives such as second-generation antihistamines and new classes of antiemetics (e.g, ondansetron and aprepitant). Another retrospective study was conducted in Jordan, which demonstrated that the most common PIMs identified among outpatients were drugs to be used with caution (69%),[20] consistent with a study in Qatar where 65% of PIMs were drugs to be used with caution.[19] Different findings between our study and other studies may be due to cancer patients' need for special medications considerations and complex regimens different from other patient categories·

A significant predictor of PIM prescribing in this cohort was found to be polypharmacy (P<0.001). Eighty-three percent of patients received ≥5 concurrent medications, and 54.2% received ≥10 concurrent medications. Other studies of elderly cancer patients have found that the prevalence of polypharmacy varies from 2% to 80%, depending on the group studied and how polypharmacy is defined.[24] This is expected due to cancer patients being prescribed various groups of medications including analgesics, antiemetics, supplements, and comorbidity medications, in addition to their chemotherapy treatment. Polypharmacy, which has been established as a predictor of PIMs use among participants, can partially explain the inappropriate prescribing attitude reported by this study.

Our results confirm those of prior studies that demonstrate the significant correlation between polypharmacy and PIMs.[25,20,5]

After polypharmacy was considered, age was not found to be a significant predictor of PIM use in the current investigation. Multi-comorbidity and subsequent polypharmacy may play a role in mediating the relationship between age and PIM prescribing in the elderly. This result is in line with a prior study conducted in Kuwait.[12] Female gender and PIM use were not significantly associated in this study, due to the fact that cancer treatment is based on a complex regimen regardless of gender. Findings from a study conducted in Jordan demonstrated that female gender was significantly associated with PIM use, as females generally are at higher risk for developing comorbidities than males, consequently being more susceptible to more inappropriate prescribing.[20]

The study found that medication that should be avoided or whose dosage should be adjusted due to older persons' renal function accounted for nearly 14.8% of the total potentially inappropriate medications (PIMs) encountered. This result highlights the importance of considering an older person's renal function when prescribing medications, as renal function decreases with age and can affect medication clearance.

One common example of a medication that can cause PIMs in older adults with reduced renal function is enoxaparin, a low-molecular-weight heparin used to prevent blood clots. The study found that prescribing enoxaparin when the patient's creatinine clearance (CrCl) was below 30 ml/min was a common cause of PIMs in this category. Enoxaparin is primarily cleared by the kidneys, and reduced renal function can result in decreased clearance and increased risk of bleeding. Thus, it is essential to adjust the dose of enoxaparin or consider alternative therapies in patients with reduced renal function.[23]

The findings from this study are consistent with prior research that has demonstrated the importance of considering renal function when prescribing medications to older adults. The American Geriatrics Society Beers Criteria and other tools provide guidance on medication use in older adults, including recommendations for dose adjustments based on renal function. These guidelines can help prevent PIM use in older adults with reduced renal function and reduce the risk of adverse drug events.[16,23,26] In conclusion, medications that should be avoided or whose dosage should be adjusted due to older persons' renal function is a significant contributor to PIMs encountered in older adults. Prescribing enoxaparin when the patient's CrCl is below 30 ml/min is a common cause of PIMs in this category. Clinicians should consider renal function when prescribing medications to older adults and adjust the dose or consider alternative therapies as needed to prevent PIM use and adverse drug events.

Study strengths and limitations

Our study had utilized the most updated version of Beer's criteria (AGS 2019) to evaluate the PIMs prevalence among study participants.

The study was limited by the retrospective cross-sectional nature. However, all measurements related to PIMs were attentively evaluated for the specified patients. Also, This study was a unicenter study, thus our results might not be generalized to other healthcare facilities including cancer centers in Jordan.

CONCLUSION

This study found that inappropriate prescribing is common among geriatric oncology and PIM is a concern in geriatric oncology. There is a need for more attention to this population. Patients with polypharmacy are found to have significantly higher prevalence of PIMs compared to those patients with non-polypharmacy category. Plans to avoid the prescribing of inappropriate medications should be implemented in the future.

CONFLICTS OF INTEREST

All authors declare no conflicts of interest is encountered.

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