

Original Research

Potentially inappropriate medications prescribing according to Beers criteria among elderly outpatients in Jordan: a cross sectional study

Ahmad AL-AZAYZIH , Rawan ALAMOORI , Shoroq M. ALTAWALBEH 

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Abstract

Background: Due to aging, along with its associated physiological changes, older adults are extremely vulnerable to be afflicted with multiple chronic conditions (multimorbidity). Accordingly, prescribing a large number of drugs to older adults would be inevitable. Resulted complex drug regimens can lead to prescribing of Potentially Inappropriate Medications (PIMs) with subsequent negative health and economic outcomes.

Objectives: The main objective of this study is to investigate the prevalence and predictors of PIMs prescribing among Jordanian elderly outpatients, using the last updated version of the American Geriatrics Society (AGS) Beers Criteria (2015 version).

Methods: A Unicenter, cross-sectional study were data was assessed using medical records of included study subjects conducted over three months period from beginning of October to the end of December 2016 at King Abdullah University Hospital, Al Ramtha, Jordan. Our study included patients aged 65 years or above who visited the outpatient clinics at King Abdullah University hospital (KAUH) and were prescribed at least one oral medication during the study period. PIMs were identified for these patients and further classified according to the 2015 AGS Beers Criteria. We measured the prevalence of PIMs prescribed among elderly outpatients in Jordan.

Results: A total of 4622 eligible older adults were evaluated in this study, of whom 62.5% (n=2891) were found to have at least one PIM prescribed during the three months study period. 69% of identified PIMs were medications to be used with caution in elderly, 22% were medications to avoid in many or most older adults, 6.3% were medications to be avoided or have their dosage adjusted based on kidney function in older adults, 2.04% medications were to avoid in older adults with specific diseases/syndromes, and 1.6% were potentially clinically important non-anti-infective drug-drug interactions to be avoided in older adults. Female gender and polypharmacy were found to be significant predictors of PIMs use among elderly.

Conclusions: Potentially Inappropriate Medication prescribing is common among Jordanian elderly outpatients. Female gender and polypharmacy are associated with more PIMs prescribing and so need further attention.

Keywords

Potentially Inappropriate Medication List; Inappropriate Prescribing; Polypharmacy; Aged; Outpatients; Risk Factors; Pharmacists; Cross-Sectional Studies; Jordan

INTRODUCTION

Potentially inappropriate medications (PIMs) among elderly is defined as “medications or medication classes which generally should be avoided in patients aged 65 years or older because of being either ineffective or pose potential high risk for such age group while safer alternatives are available”.¹ PIMs use, where adverse effects exceed its health benefits, is a highly witnessed issue among older adults ranging from a prevalence of 11.5 - 85.1% among community dwelling and hospitalized elderly patients in various countries.²⁻¹⁴ Data from numerous studies performed at various settings revealed PIM prescribing with prevalence of up to 40% in nursing home residents and up to 28% among community-based older patients.¹⁵⁻²³ Healthcare utilization, including: hospitalizations, healthcare visits (Inpatient, Outpatient and Emergency Department), re-admissions and length of stays, was shown to be significantly associated with PIM use among elderly

patients.²⁴

Detecting adverse drug reactions among geriatric patients is challenging, as they often exhibit non-specific symptoms such as constipation, lethargy, lightheadedness, confusion, falls and depression.²⁵ Nonetheless, adverse drug reaction rates among elderly patients are at least three-times that of the younger as well as general population.²⁵ Several studies performed in order to investigate the association between PIMs use and developing unwanted Adverse Drug Reactions (ADRs) and Adverse Drug Events (ADEs) among elderly patients at different settings (hospitalized, outpatient and even nursing home residents) concluded that using PIMs is significantly associated with an increased risk of developing ADRs and ADEs.²⁶⁻²⁸

Screening tools for PIMs use have been developed over the past two decades, with the latest updated version of the Beers Criteria was released by the American Geriatrics Society (AGS) in October, 2015.²⁹ In addition to updating existing criteria (i.e., 2012), the 2015 version has come up with two new major aspects: 1) Drugs for which dosage adjustment is required based on the patient's kidney function, and 2) Drug-Drug Interactions (DDIs).²⁹ The goal of the 2015 update of AGS Beers Criteria continues to be improving geriatric care by reducing their exposure to PIMs. Prudent application of the criteria as a non-punitive

Ahmad AL-AZAYZIH. Department of Clinical Pharmacy, Faculty of Pharmacy, Jordan University of Science and Technology. Irbid, (Jordan). aaazayzih@just.edu.jo

Rawan ALAMOORI. Department of Clinical Pharmacy, Faculty of Pharmacy, Jordan University of Science and Technology. Irbid, (Jordan). rammouri53@gmail.com

Shoroq M. ALTAWALBEH. Department of Clinical Pharmacy, Faculty of Pharmacy, Jordan University of Science and Technology. Irbid, (Jordan). smaltawalbeh@just.edu.jo

educational tool and quality improvement measure is intended to achieve a closer monitoring of medication usage among older adults.²⁹

Overall, PIM use among geriatric patients has become a global concern, and studies were conducted in many countries using globally developed tools for screening this phenomenon.^{2,30-32} However, no study has yet systemically examined PIMs prescribing among Jordanian elderly patients. Accordingly, this study is aiming to investigate the prevalence and predictors of PIM prescribing among Jordanian elderly outpatients, using the last updated version of the American Geriatrics Society (AGS) 2015 Beers Criteria. The main objective of this study is to investigate the prevalence and predictors of PIMs prescribing among Jordanian elderly outpatients, using the last updated version of the American Geriatrics Society (AGS) Beers Criteria (2015 version).

METHODS

Ethics Approval

This study was approved by the Institutional Review Board (IRB) of King Abdullah University Hospital (KAUH). (Approval Number: 16/100/2016)

Study design and population

This study was a cross-sectional study where data was assessed using medical records of included study subjects. In this study, patients aged 65 years and older who visited the King Abdulla University Hospital (KAUH) located at Al-Ramtha, Jordan, and were ordered at least one outpatient

prescription containing at least one prescribed medication during the period from October 1, 2016 to December 31, 2016 were identified as the study population. Electronic outpatient medical records were reviewed and data including demographics and clinical characteristics including age, gender, comorbidities related to AGS Beers Criteria, medications prescribed, and the latest measured serum Creatinine level were extracted. Latest measured serum creatinine level for each patient was used to calculate creatinine clearance using Jelliffe equation, which could be used and reasonably accurate when height and weight are not available in average-sized patients.³³ Polypharmacy was investigated and defined as simultaneous use of five or more different prescribed medications.³⁴

Primary outcomes

Potentially Inappropriate Medications (PIMs) among participants were identified and further classified according to the 2015 American Geriatrics Society (AGS) Beers Criteria in the following classes:²⁹

- 1) Medications to avoid in many or most geriatrics (Class I). Prescribing any of the listed medications among the study population was considered as a PIM.
- 2) Medications to avoid in older adults with certain diseases/syndromes (Class II). Drug-disease interactions were evaluated for each patient who was ordered any of the listed medications. All related conditions/diseases have been investigated and confirmed for those patients using their medical records. Subsequently, patients exposed to PIM were

Table 1. Potentially inappropriate medications to avoid in many or most older adults (22% of total PIMs)

Class/Medication	% of total	QOE	SOR
Pain medications Orphenadrine Non-COX-Selective NSAIDs	31.2	Moderate Moderate	Strong Strong
Gastrointestinal PPIs Metoclopramide	25.3	High Moderate	Strong Strong
Antispasmodics Clidinium-Chlordiazepoxide Scopolamine (Hyoscine butylbromide)	13.5	Moderate Moderate	Strong Strong
Endocrine Glyburide (Glibenclamide) Estrogens with or without progestins	10.8	High High	Strong Strong
Central Nervous System (CNS) Benzodiazepines Antidepressants Antipsychotics	9.8	Moderate High Moderate	Strong Strong Strong
Cardiovascular Digoxin Central alpha blockers (Methyldopa) Amiodarone Nifedipine, IR Peripheral alpha blockers (Doxazosin)	5.4	Moderate Low High High Moderate	Strong Strong Strong Strong Strong
Anticholinergics (1st generation antihistamines) Chlorpheniramine Meclizine	2.6	Moderate Moderate	Strong Strong
Antithrombotics Dipyridamole, SA	1.2	Moderate	Strong
Genitourinary Desmopressin	0.15	Moderate	Strong

Non-COX-Selective NSAIDs: non-cyclooxygenase selective non-steroidal anti-inflammatory drugs, PPIs: Proton Pump Inhibitors, QOE: Quality of Evidence, SOR: Strength of Recommendation

Object System/Disease	Interacting class/Medication	% of total	QOE	SOR	
Central Nervous System (CNS)	-	81.3	-	-	
History of falls or fractures	Anticonvulsants	-	Moderate	Strong	
	Antipsychotics	-	Moderate	Strong	
	Benzodiazepines	-	Moderate	Strong	
	TCA's	-	Moderate	Strong	
	SSRIs	-	Moderate	Strong	
	Dementia or cognitive impairment	Anticholinergics	-	Moderate	Strong
		Benzodiazepines	-	Moderate	Strong
		Antipsychotics	-	Moderate	Strong
	Chronic seizures or epilepsy	Tramadol	-	Low	Strong
	Insomnia	Theophylline	-	Moderate	Strong
Kidney and Urinary tract		10.6			
Lower Urinary Tract Symptoms, BPH	Anticholinergics (Strong)	-	Moderate	Strong	
Cardiovascular		8.1			
Heart failure	NSAIDs	-	Moderate	Strong	
	Syncope	Anticholinergics	-	Moderate	Strong

TCA's: Tri-Cyclic Antidepressants, SSRIs: Selective Serotonin Reuptake Inhibitors, BPH: Benign Prostatic Hyperplasia, NSAIDs: Non-steroidal Anti-inflammatory Drugs, QOE: Quality of Evidence, SOR: Strength of Recommendation

then highlighted based on related recommendation. (e.g., patients ordered the oral decongestant pseudoephedrine were evaluated for the presence of insomnia; if such drug-disease interaction was confirmed then the patient was considered to have been exposed to a PIM).

- 3) Medications that should be used with caution among elderly patients (Class III). Prescribing any of the listed medications among the study population was considered as a PIM.
- 4) Potentially clinically important non-anti-infective drug-drug interactions (Class IV). Interacted medications were identified and highlighted for each subject.
- 5) Medications to avoid or their dosage should be adjusted based on patient kidney function (Class V). Using at least one of the listed medications along with patient creatinine clearance below indicated thresholds was considered as a PIM (e.g. patient with creatinine clearance <30ml/min and was concurrently prescribed enoxaparin was considered to have a PIM).
- 6) Medications belong to more than one class of the above were counted as more than one PIMs (for example, if a drug belong to class I and II, it will be considered as two PIMs)

The quality of evidence (QOE) and strength of recommendation (SOR) for each encountered Beers PIM or criterion were also reported according to The Grades of Recommendation, Assessment, Development and Evaluation (GRADE: "a common, sensible and transparent approach to grading quality or certainty of an evidence as well as strength of recommendation").³⁵

Statistical analysis

Descriptive statistics, such as percentages and arithmetic means, were used to describe patient characteristics and to estimate the prevalence of PIM use among studied population. Multivariable logistic regression model was conducted to investigate potential risk factors associated with PIM use. P value of less than 0.05 was considered statistically significant. All analyses were conducted using Stata v14 (StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP).

RESULTS

Eligible 4,622 geriatric patients were included in the study. Mean age (standard deviation) of studied population was 73.2 (SD 6.3) years, and 50.6 % (n=2340) of subjects were females. After excluding over the counter products, 4,356

Class/Medication	% of total	QOE	SOR	
Diuretics	45.1	Moderate	Strong	
Aspirin for primary prevention of cardiac events	38.8	Low	Strong	
Vasodilators	12.3	Moderate	Weak	
Antidepressants	1.7			
	SSRIs*	-	Moderate	Strong
	TCA's*	-	Moderate	Strong
	SNRIs*	-	Moderate	Strong
Antipsychotics	1.1	Moderate	Strong	
Carbamazepine	0.63	Moderate	Strong	
Chemotherapy	0.19			
	Carboplatin	-	Moderate	Strong
	Cyclophosphamide	-	Moderate	Strong
	Cisplatin	-	Moderate	Strong
	Vincristine	-	Moderate	Strong

SSRIs: Selective Serotonin Reuptake Inhibitors, TCA's: Tri-cyclic Antidepressants, SNRIs: Serotonin-Norepinephrine Reuptake Inhibitors, QOE: Quality of Evidence, SOR: Strength of Recommendation

Object Drug/Class	Interacting Drug/Class	% of total	QOE	SOR
Anticholinergic	Anticholinergic	91.5	Moderate	Strong
CNS-active drug*	≥ 2 other CNS-active drugs	4.3	High	Strong
ACEIs	Amiloride	2.1	Moderate	Strong
Peripheral Alpha-1 blockers	Loop diuretics	1.1	Moderate	Strong
Corticosteroids, oral or parenteral	NSAIDs	1.1	Moderate	Strong

CNS-active drugs: SSRIs, TCAs, Antipsychotics, Benzodiazepines, Opioids, ACEIs: Angiotensin-Converting Enzyme Inhibitors, NSAIDs: non-steroidal anti-inflammatory drugs

patients were found to be prescribed at least one medication, with average of 5.6 (SD 3.9) prescribed medications per patient. Overall, 53.7% of women and 51.7% of men aged 65 years and older were ordered at least five prescription medications (i.e. exposed to “polypharmacy”).

Of the total geriatric sample evaluated, 2891 subjects (62.5%) were prescribed at least one PIM according to 2015 Beers Criteria. The majority of these subjects were prescribed one (39.6%) or two (23.3%) PIMs, however, prescribing of three (15.8%) or four (7.6%) PIMs were also not uncommon. Of the identified PIMs, 69% were medications to be used with caution in older adults (class III), whereas 22% were medications to avoid in many or most older adults (class I), 6.3% were medications to avoid or their dosage should be adjusted based on the kidney function (class V), 2.1% were medications to avoid for older adults with specific diseases/syndromes (class II), and 1.6% were potentially clinically important non-anti-infective drug-drug interactions (class IV).

Most commonly prescribed medication classes considered as PIMs to avoid in majority of elderly patients were pain medications (31.2%), followed by gastrointestinal medications (25.3%) and antispasmodics (13.5%), Table 1.

Potential drug-disease/syndrome interactions were 2.04% of total identified PIMs. Subjects diagnosed with Central Nervous System (CNS)-related conditions (including history of falls or fractures, dementia, chronic seizures or epilepsy and insomnia) were most commonly prescribed PIMs (81.3%) in this class, Table 2.

The majority (69%) of total PIMs prescribed were medication classes to be used with caution among elderly. Diuretics (45.1%), aspirin for primary prevention of cardiac events among older adults aged ≥80 years (38.8%) and vasodilators (12.3%) were most commonly prescribed PIMs in this class, Table 3.

Only (1.6%) of total prescribed PIMs were due to drug-drug interactions (the 1st newly added component by the 2015 AGS Beers Criteria). Almost (91.5%) of detected interactions resulted from the simultaneous prescribing of at least two different medications with anticholinergic properties including first generation antihistamines

(chlorpheniramine and triprolidine), antimuscarinic (oxybutynin), antispasmodics (clidinium-chlordiazepoxide and hyoscyamine), Table 4.

Drugs to be avoided or have their dosage adjusted based on varying levels of kidney function in older adults (the 2nd newly added component by the 2015 AGS Beers Criteria) have contributed to almost 6.3% of total PIMs encountered. Prescribing gabapentin when CrCl <60 ml/min was responsible for the majority of PIMs in this class, Table 5.

Having at least one identified PIM was significantly associated with female gender (adjusted OR: 1.33, 95% CI: 1.14-1.55) and polypharmacy (adjusted OR: 28.39, 95%CI: 23.83-33.81), Table 6.

DISCUSSION

To the best of our knowledge, this is the first study examining PIM prevalence using Beers Criteria as a screening tool among geriatric patients in Jordan. Moreover, it considered the first study investigating and presenting the 2015 AGS Beers Criteria PIM classes in details among elderly outpatients.

Results from this study showed a high prevalence of PIM prescribing among Jordanian elderly outpatients (62.5%) according to the most updated version of the AGS Beers Criteria (2015). Female gender and polypharmacy were identified as significant predictors of PIM prescribing in this population. Previous iterations of Beers Criteria were used by a wide variety of studies examining the prevalence of PIM prescribing among older adults at various populations and settings with estimated ranges between 11.5% and 85.1%.^{2,4-14,36,37} A good number of these studies have assessed prevalence of PIM prescribing based on Beers Criteria (mostly 2012 update) among community-dwelling elderly patients (outpatients) with total prevalence ranges between (23% and 81%).^{4,7,8,11,13,38} The updated AGS Beers Criteria were released in 2015 and so still less thoroughly used in the available literature. In the United States, a study was conducted using Medicare Current Beneficiary Survey (MCBS) data set to identify PIMs according to 2015 AGS Beers Criteria.²⁹ Findings from this study showed that around 57% of older adults with dental care visits were

Medication	CrCl (ml/min)	Action Required	QOE	SOR	% of total
Gabapentin	<60	Reduce dose	Moderate	Strong	71.7
Levetiracetam	≤80	Reduce dose	Moderate	Strong	13.9
Ranitidine	<50	Reduce dose	Moderate	Strong	5
Pregabalin	<60	Reduce dose	Moderate	Strong	5
Famotidine	<50	Reduce dose	Moderate	Strong	4.5

CrCl: Creatinine Clearance (ml/min), QOE: Quality of Evidence, SOR: Strength of Recommendation

Table 6. Predictors of potentially inappropriate medications prescribing among elderly patients.		
Variable	OR (95% CI)	P-value
Age	0.99 (0.98-1.0)	0.14
Gender (Female)	1.33(1.14-1.55)	*<0.001
Polypharmacy #	28.39 (28.83-33.81)	*<0.001
*p-value is significant at <0.05 #: Polypharmacy was defined as ≥ 5 prescribed medications CI, confidence interval; OR, odds ratio; PIM, potentially inappropriate medication		

prescribed at least one Beers Criteria medication.³⁹ Another study conducted in Brazil found that 50% of community-dwelling elderly patients were prescribed at least one PIM according to the 2015 update of AGS Beers Criteria.⁴⁰ Accordingly, PIM prevalence in the current study (62.5%) is relatively comparable with available literature which investigated geriatric PIMs using the updated Beers Criteria in the outpatient settings. Nevertheless, it is an apparently high prevalence in Jordan. The vast majority of PIMs identified in the current study were drugs to be used with caution (69%). This finding is consistent with recent study in Qatar where 65% of PIMs were drugs to be used with caution.¹²

Female gender was significantly associated with PIM use. This finding is consistent with various published studies.^{8,13,39} Females generally are at higher risk for developing multiple chronic conditions than males, consequently being more susceptible for drug-disease and drug-drug interactions which will lead to more inappropriate prescribing.^{34,41} Polypharmacy is consistently shown to be a significant risk factor of PIM use.^{8,13,42,43} Polypharmacy was the most significant predictor of PIM prescribing in the current study. Increasing age was reported by some studies as a significant risk factor of PIM use.^{4,5,8} However, others have found no association between age and PIM use.⁴⁴ In the current study, age was not a significant predictor of PIM use after adjusting for polypharmacy and gender. The effect of age on PIM prescribing in older adults may be mediated by the multi-comorbidity and the resultant polypharmacy in this population.

This study has some limitations. As this was a retrospective study, all data were obtained from patient medical records and were as accurate as available documentation. Due to the large study sample, some patients' characteristics (for example, patients' weight and height) and clinical indicators were not extracted and so their association with PIM prescribing was not evaluated in this study. Similarly, complete comorbidity profiles were not obtained for all

patients, however, all conditions related to PIMs were carefully evaluated for the relevant patients. In addition, because of the retrospective nature of the study, we were not able to capture the dose reduction if happened; however, we considered all those on regular maintenance dose with varying kidney functions to have potential inappropriate use. This was challenging since Beers criteria did not provide a cut off dose for these meds to be considered as PIMs. Finally, all identified PIMs are not conclusive without the clinical judgment, the criteria serve only as a warning light to raise attention to clinical evaluation that further assess risks and benefits associated with these PIMs. Overall, this study has the strength of evaluating a large number of elderly patients, enabling generalizability and reliability of findings. In addition, this is the first study-examining trend of prescribing among elderly patients in Jordan using the most updated version of Beers Criteria (2015) for PIMs identification.

CONCLUSIONS

This study demonstrates that PIM prescribing is common among Jordanian elderly outpatients. Female patients and those with polypharmacy are the most vulnerable groups that need further attention. Strategies to monitor, review, and prevent inappropriate prescribing should be supported.

CONFLICT OF INTEREST

The authors declare no conflict of interest does exist.

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