Pre-Admission Administration of Potentially Inappropriate Medications in Geriatric Patients Admitted to a Tertiary Care Teaching Hospital

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Abstract

Background: The global population of older adults is increasing. Considering the differences in the pharmacokinetics and pharmacodynamics of medications in this population, some medications are considered potentially inappropriate. This study examined the pre-admission use of potentially inappropriate medications (PIM) in hospitalized geriatric patients and investigated drug-drug interactions (DDI) among these individuals.

Methods: This cross-sectional study was conducted at a tertiary care teaching hospital in Tehran, Iran. The Beers criteria were utilized to identify PIM. All medications taken by eligible patients prior to admission, including over-the-counter drugs, herbal remedies, and dietary supplements, were documented along with the patients' diseases and health conditions.

Results: Among the patients, 56.8% were men, and their ages ranged from 65 to 95 years. We found that 39% of patients received at least one PIM. Out of 1406 pre-admission medications, 132 (9.3%) and 26 (1.84%) were classified as PIM based on drug-to-avoid and drug-disease criteria, respectively. In 4.4% of patients, selected DDI was noted, and polypharmacy was observed in 151 (60.4%) patients. The most frequent PIM in drug-to-avoid criteria belonged to the nervous system (46.46%), followed by the alimentary tract and metabolism (26.1%). Based on the drug-to-avoid and drug-disease criteria, the average number of underlying diseases in patients with PIM was significantly higher than those without PIM (p-value = 0.014 and p-value = 0.001, respectively).

Conclusion: The prevalence of PIM in the present study was similar to that of previous studies conducted with the same criteria and setting. Polypharmacy and a higher number of comorbidities significantly increased PIM utilization. With the growing elderly population, healthcare providers must be more vigilant about the varied medication needs of this population.

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Keywords: Beers Criteria; Potentially Inappropriate Medications; Polypharmacy, Drug-Drug Interactions

Introduction

The term "elderly" typically refers to individuals who are 65 years old or older (1). By 2050, it is estimated that the elderly population will make up about 16% of the global population, which was 10% in 2022 (2). According to the 2016 census data, 9.2% of the population in Iran was elderly (3). As the elderly population has significantly increased, their use of health services has also risen notably (4). Additionally, their growing population highlights their health needs.

Due to the alteration of the pharmacokinetics and pharmacodynamics of medications, multi-morbidity, and polypharmacy, geriatric patients are at a higher risk for

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the development of adverse drug events (ADEs) (4). Some medicines may be considered potentially inappropriate for this age group, presenting more risks than benefits (5). The prevalence of potentially inappropriate medication (PIM) in geriatric patients has been reported in two meta-analyses. Tian et al. reported a prevalence of PIM at 36.7% among 371.2 million participants in studies on outpatient geriatrics (6). Similarly, Ming Liew et al. reported 33.3% PIM among 5.054 million participants in studies on primary care geriatric patients (7).

It was shown that 25 to 56% of inpatients, and half of the nursing home residents, were prescribed at least one regular PIM (8). Prescribing PIM to the elderly is crucial to consider due to their prevalence and associated consequences. These include hospitalization (9), increased healthcare costs (8, 9, 10), a higher risk of adverse effects (8, 11), decreased quality of life (8, 12), an elevated risk of falls, poor medication adherence (8), and increased mortality (8, 11).

The American Geriatric Society (AGS) Beers criteria are popular and the most broadly used explicit criteria to detect PIM in geriatrics (13). It was first developed in 1991 by geriatrician Mark H. Beers (14). This tool can be used in various clinical settings, including outpatient, acute hospital care, and institutions (15).

Regarding prescribing inappropriate medications for geriatrics, several studies have been conducted in Iran (16-18). To the authors' knowledge, none of the studies have examined the frequency of PIM in patients admitted to the hospital. In Tehran, it has been documented that 31.2% of ambulatory geriatric patients visiting pharmacies had at least one PIM among their latest prescribed medications (19). However, due to the unavailability of medical histories and lab data, the study could not assess the PIMs that might exacerbate the disease or syndrome due to drug-disease or drug–syndrome interactions (19). Therefore, this study focused on pre-admission PIM administrations based on the Beers criteria in patients admitted to a referral hospital in Tehran.

Methods

Study design and population

This cross-sectional study was conducted as part of a research project that comprehensively evaluated medications of hospitalized geriatric patients. We enrolled 250 patients aged 65 years or older admitted to Shariati Hospital affiliated with Tehran University of Medical Sciences (TUMS) between April 2016 and January 2017. The hospital is a referral teaching hospital among the major tertiary care hospitals in Tehran, Iran. The study was approved by the ethics committee of TUMS (Ethics Code: 12739).

A researcher used reports from the hospital information system to determine admissions on the previous day and screened the patients. Patients qualified for the study if they were 65 years old or older, admitted to inpatient wards (including the emergency department) for at least 24 hours, and no more than 72 hours had elapsed since their admission. Exclusion criteria included admission to the ICU, intubation, or death during the study, as well as discharge from the hospital before the second assessment of patients on the third day of hospitalization.

Data collection

Demographic information (age, gender, etc.) and past medical and medication histories were recorded separately. In terms of medication history, all outpatient prescription medications, over-the-counter medicines, dietary supplements, and herbal medications were recorded. Medication and medical histories were obtained using charts and patient interviews. We also consulted the patient's family member and caregiver, wherever available, especially in cases where the patient could not communicate.

Medications were classified using the World Health Organization-Anatomical Therapeutic Chemical (WHO-ATC), available from https://atcddd.fhi.no/atc_ddd_index/. Medical conditions were classified using the International Statistical Classification of Diseases and Related Health Problems (ICD-10).

Sample size calculation

The required sample size was calculated to determine the prevalence of PIM in this population. Based on the literature, the prevalence of PIM in this population was 32% (20). Using this estimate and allowing for a maximum margin of error (d) of 6%, the calculated sample size needed was 232 patients. To accommodate a potential 10% attrition rate, the final adjusted sample size was increased to 258 patients.

Assessment of PIM utilization

We used the AGS Beers criteria 2015 to determine the PIM (21). We investigated PIM for the participants regardless of their medical conditions (drug-to-avoid list or general criteria). Additionally, we assessed PIM that may deteriorate disease or syndromes due to drug-disease or drug–syndrome interactions (drug-disease criteria).

Notably, not all the medications listed in the above-mentioned tables of the Beers criteria are considered entirely inappropriate. The criteria define specific circumstances

under which prescribing these medications can be appropriate. For example, first-generation antihistamines are among the drugs to be generally avoided. However, the use of diphenhydramine for the acute treatment of severe allergic reactions is acceptable. In assessing PIM, we considered this issue to avoid overestimating inappropriate prescribing. Based on the assessments, we categorized medication into three classes:

- Category 0: inappropriate medications
- Category 1: medicines in the Beers criteria that are considered appropriate under certain conditions (as noted above).
- Category 2: appropriate medications not among the two main Beers criteria lists.

Moreover, we evaluated patients' medications to detect potentially clinically meaningful non-anti-infective drug-drug interactions (DDI) that should be avoided in older adults. Polypharmacy was defined as taking five or more medications daily (22).

In the current study, we did not document the utilization of medications that need caution in older adults because we could not judge whether the physicians had prescribed the medications cautiously or not. Moreover, these medications were not supported by sufficient evidence to be categorized as PIM by AGS (23).

Statistical analysis

Data were analyzed using SPSS software (version 24 for Windows). Descriptive statistics were reported for essential variables. The chi-square test was used to compare the polypharmacy in patients who received at least one PIM with that of those who did not. The nonparametric Mann-Whitney test was used to compare the number of medications, the number of PIM, and the number of underlying diseases in groups. The significance level was considered 0.05.

Results

During the study period, 340 patients were evaluated, and based on the study criteria, the medical records of 250 elderly patients were examined. The mean age of patients (±SD) was 74.42 ± 6.67 years, with an age range of 65 to 95 years. Most patients were men (n = 142, 56.8%).

Medical conditions

The most common underlying disease classes were diseases of the circulatory system, followed by endocrine, nutritional, and metabolic diseases, and mental and behavioral disorders. Table 1 shows characteristics of the study population.

Table 1. Descriptive Statistics of the study patients

Characteristics of patients		N (%)
Sex	Male	142 (56.8)
	Female	108 (43.2)
Underlying diseases	Hypertension	144 (57.6)
	Diabetes	81 (32.4)
	Ischemic heart disease	71 (28.4)
	Insomnia	51 (20.4)
Underlying diseases (ICD-10)	Diseases of the circulatory system	262 (45.8)
	Endocrine, nutritional, and metabolic diseases	97 (16.9)
	Mental and behavioral disorders	58 (10.1)

ICD-10: International Statistical Classification of Diseases and Related Health Problems, 10th revision

Medications

Patients received an average of 5.62 ± 3.31 medications before admission. In total, 1406 medications were recorded among medication histories. According to the ATC classification, the most commonly used medicines were those related to the cardiovascular system, followed by alimentary tract and metabolism medications. The most frequent medications were aspirin (n=121, 8.6% out of 1406), losartan (n=83, 5.9%), atorvastatin (n=79, 5.6%), nitroglycerin pearl (n=62, 4.4%), furosemide (n=55, 3.91%), and metoprolol (n=48, 3.4%), respectively.

We found that women took a significantly higher mean number of medications (6.15±3.19) than men (5.22±3.3) (p-value=0.009).

PIM

We found that 37.2% (n=93) and 7.2% (n=18) of patients received PIM based on the drug-to-avoid and the drug-disease criteria, respectively. In total, 98 patients (39%) received at least one PIM before the hospital admission based on both lists of the Beers criteria.

Among the medications, 319 (22.68%) agents were included in the drug-to-avoid criteria, of which 132 (9.3%) agents were prescribed inappropriately (category 0). The remaining 187 (13.3%) medications were prescribed for acceptable situations based on the criteria (category 1). Additionally, 294 (20.91%) medications were listed in the drug-disease criteria; among them, 26 (1.84%) medications were inappropriately prescribed (category 0). Classification of PIM based on the ATC classification is summarized in Table 2.

Table 2. Medications and their appropriateness based on ATC classification

ATC index	Number of medications	Drug-to-Avoid Criteria† Categories€ N§ (%*), [n$]			Drug-Disease Criteria¥ Categories€ N§ (%*), [n$]		
		0	1	2	0	1	2
Cardiovascular system	559	9 (1.6), [3]	18 (3.2), [3]	532 (95.1), [28]	0, [0]	9 (1.6), [3]	550 (98.4), [28]
Alimentary tract and metabolism	245	64 (26.1), [6]	32 (13.1), [5]	149 (60.8), [28]	1 (0.4), [1]	20 (8.2), [7]	224 (91.4), [30]
Blood and blood-forming organs	203	1 (0.5), [1]	121 (59.6), [1]	81 (39.9), [7]	0, [0]	121 (59.6), [1]	82 (40.4), [8]
Nervous system	118	55 (46.6), [18]	0, [0]	63 (53.4), [28]	19 (16.1), [14]	75 (63.5), [31]	24 (20.3), [11]
Respiratory system	117	3 (2.6), [2]	0, [0]	114 (97.4), [16]	0, [0]	12 (10.2), [3]	105 (89.7), [15]
Genitourinary system and sex hormones	51	0, [0]	3 (5.9), [1]	48 (94.1), [5]	0, [0]	5 (9.8), [3]	46 (90.2), [3]
Musculoskeletal system	39	0, [0]	13 (33.4), [4]	26 (66.6), [7]	6 (15.4), [3]	10 (25.6), [5]	23 (59), [6]
Others	74	0	0	74 (100)	0	16 (21.62)	58 (78.37)
Total	1406	132	187	1087	26	268	1112

ATC: Anatomical Therapeutic Chemical Classification

† Drug-to-avoid Criteria identify potentially inappropriate medications (PIM) regardless of patients' medical condition.

¥ Drug-disease Criteria identify PIM that may deteriorate preexisting disease or syndromes due to the disease/syndrome interactions.

€ Categories: 0: PIM, 1: appropriate based on the existing condition (although the medication was listed in the Beers criteria, it was considered appropriate due to meeting the exceptional conditions of those criteria, and 2: appropriate medications (not included in the Beers criteria). For more explanation please refer to the method section.

§ Number of medications: sum of the medications, including the same medication for different patients.

* The percentages in parenthesis were calculated by using the value in the column of "number of medications" as the denominator.

$ Number of distinct medications: The same medication for different patients was only calculated once.

As shown in Table 2, the most common PIM in drug-to-avoid criteria belonged to the nervous system (n=55, 46.46%), followed by the alimentary tract and metabolism (n=64, 26.1%).

As for the drug-to-avoid criteria, the top three PIM among the pre-admission medications were pantoprazole (n=26, 19.7% from 132 inappropriate medications), glibenclamide (n=21, 15.9%), and alprazolam (n=15, 11.3%). Regarding the drug-disease criteria, the most frequent PIMs were diclofenac (n=4, 15.38%) followed by alprazolam (n=3, 11.53%). Most medications in the drug-disease criteria were inappropriate considering patients' history of falls or fractures and dementia. Figure 1 shows the percentage of patients receiving different numbers of PIM based on both criteria.

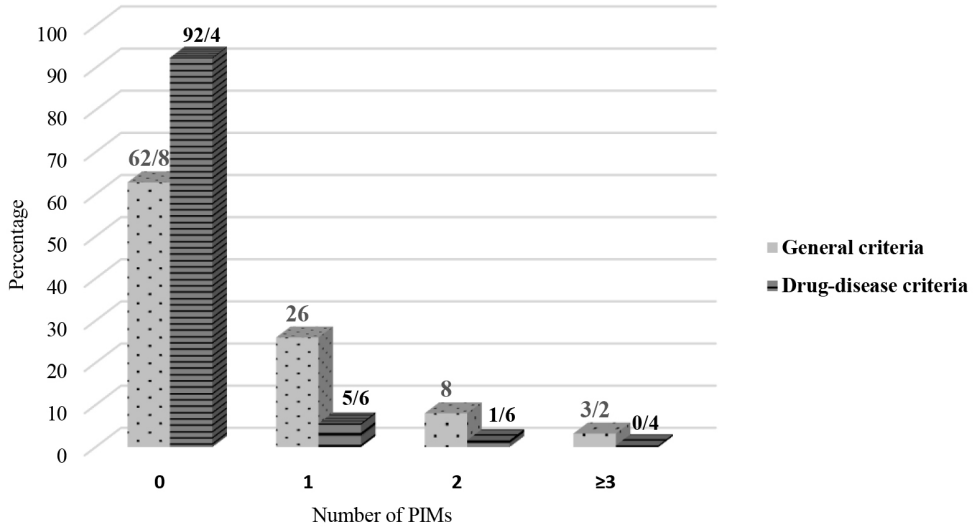

Figure 1. Percentage of patients who received different numbers of potentially inappropriate medications in their per-admission medication history based on the two Beers criteria

PIM: Potentially Inappropriate Medications

The prevalence of PIM based on the drug-to-avoid criteria in men and women was 32.39% (n=46) and 43.51% (n=47), respectively. Based on the drug-disease criteria, the PIM was administered to 7% (n=10) and 7.4% (n=8) of men and women, respectively. As shown in Table 3, the mean ± SD of the number of PIM received by men and women was not significantly different. The mean number of underlying diseases in patients with and without PIM based on the drug-to-avoid criteria was 2.7±1.4 and 2.2±1.4, respectively, which was statistically significant (p-value=0.014).

Table 3. The mean (SD) number of potentially inappropriate medications among pre-admission medicines based on patients' sex

Beers criteria	Sex	PIM Mean ± SD	P-value
Drug-to-avoid criteria	Men	0.46 ± 0.80	0.059
	Women	0.62 ± 0.83	
Drug-disease criteria	Men	0.11 ± 0.52	0.716
	Women	0.10 ± .36	

PIM: Potentially inappropriate medications; SD: Standard Deviation

Similar findings were noted regarding the drug-disease criteria. The mean number of underlying diseases in patients with and without PIM was 3.4 ± 1.4 and 2.3 ± 1.4, respectively (p-value=0.001).

Drug-drug interactions

Using the list of potentially clinically important non-antimicrobial drug interactions between medications, we found 11 DDIs (4.4%). Four were interactions between antidepressants and other CNS-active drugs, and three were interactions between benzodiazepines and non-benzodiazepines with CNS-active drugs.

Polypharmacy

We noted that 151 (60.4%) patients received five or more drugs in their drug histories. Table 4 shows that patients who received fewer than five drugs received significantly less PIM. Polypharmacy was observed in 53% (n=75) of men and 70.4% (n=76) of women, indicating a significant difference (Pearson Chi-Square=5.27, p-value=0.02). However, the mean age of patients with and without polypharmacy was not significantly different (Mann-Whitney Z=-0.354, p-value=0.72).

Table 4. Frequency of receiving potentially inappropriate medication in patients with and without polypharmacy

Beer Criteria	Presence of PIM	Medications <5	Medications ≥5	Pearson Chi-Square	P-value
Drug-to-avoid Criteria	No	80 (80.8)	77 (51)	22.75	<0.001
	Yes	19 (19.2)	74 (49)		
Drug-disease Criteria	No	98 (99)	133 (88.1)	10.13	0.001
	Yes	1 (1)	18 (11.9)		

PIM: Potentially Inappropriate Medications

Discussion

The current study evaluated the medical and medication histories of geriatric patients admitted to a tertiary care teaching hospital to find the PIM among their pre-admission medications. To the best of our knowledge, this is the first study to investigate the pre-admission PIM of patients in a hospital setting in Iran.

We found that 39% of patients had at least one PIM among their pre-admission medications based on Beers' drug-to-avoid and drug-disease criteria. The prevalence of patients with PIM at admission in our study was close to that of a similar study. In a retrospective study conducted on patients admitted with eight medical conditions in Japan, 47.9% of patients had at least one PIM based on the drug-to-avoid and drug-disease lists of Beers criteria (2015) (24).

We noted that 37.2% of patients received PIM according to the drug-to-avoid criteria. This finding was similar to a study conducted on patients admitted to a geriatric hospital in Egypt. Elsorady and El-Mohsen reported that PIM based on the drug-to-avoid criteria (Beers 2019) was detected in 31.9% of patients (25). However, the results of a study on patients referred to the ambulatory care service of a tertiary care hospital in Saudi Arabia showed that 57.6% received a PIM based on drugs-to-avoid criteria (Beers 2015)(26), which was higher than our study's In another study on the data of the American cohort of geriatric admissions to hospital due to heart failure, Jaber et al. demonstrated that 61.1% of patients had a PIM among their medications based on the drug-to-avoid list of the 2019 Beers criteria (27). However, the inclusion of patients with a specific disease and several comorbid conditions (median of eight) may explain their high rates. Additionally, retrospective studies may overestimate the prevalence of PIM. As shown in Table 2, the frequency of medication classified as category 1 was considerable. This category belongs to the medications that, despite being listed among the Beers criteria, were appropriately prescribed (see method section for details). We noted that among all the medications, 319 (22.68%) agents were included in the drug-to-avoid list, of which 9.3% were considered as PIM. In the case of retrospective studies and the unavailability of detailed patient conditions, such medications may be misclassified as PIM.

Elsorady and El-Mohsen noted that the most frequent PIMs were PPI and glimepiride (25), which were similar to the two most frequent medications in our study (pantoprazole and glibenclamide). PPIs were also the leading PIM medications in the study by Di Martino et al. However, their second most frequent agents were peripheral alpha-1 blockers (28). In a study conducted in the US, PPIs (32.6%) were the most frequently administered PIM, whereas benzodiazepines (14.2%) and analgesics (8.6%) were the other high-ranking agents (27). A review article on studies indexed in PubMed demonstrated that the long-term use of PPIs in the elderly was associated with various adverse effects in observational studies and meta-analyses (29). Vitamin B12 deficiency, osteoporotic fractures, dementia, Clostridium difficile infection, community-acquired pneumonia, and renal diseases were also noted (29). The inappropriate use of PPIs has been widely reported (30). A study on the health claims database of the elderly in British Columbia during 10 years reported that 62% and 42% of the study population had cumulatively two years and more than five years of PPI utilization, respectively (31).

In our study, drug-disease interaction contributed to the use of PIMs in 7.2% of patients. This percentage was higher than the findings of Elsorady and El-Mohsen, who noted that a PIM due to drug-disease interaction was found in 3.6% of patients (25). Similarly, the study by Di Martino et al. reported a prevalence of PIMs at 4% (28). However, the findings regarding this part of the criteria clearly depend on the prevalence of comorbidities in the study population.

In our study, drug-drug interactions (DDIs) was noted in 4.4% of patients. This finding aligns with studies by Elsorady and El-Mohsen, who identified DDIs in 6.8% of patients at admission (25), and Di Martino et al., who reported a rate of 5% (28). However, this DDI prevalence belonged only to the medications in the Beers criteria, while total DDIs were much higher in these patients (32).

We identified 9.3% of the pre-admission medications of patients among the drugs-to-avoid list of the Beers criteria. This rate was considerably lower than that reported in a retrospective study in Italy (28). Using the 2015 Beers criteria, Di Martino et al. reported that 56% of medications used by 1800 patients at admission were among the drug-to-avoid list of the Beers criteria. This considerable difference was noted despite the similarity in the mean number of medications (5.39 ± 3.00 vs. 5.62 ± 3.3 in the study by Di Martino et al. and ours, respectively). The variation in medication availability and administration patterns in different countries may explain this finding.

In this study, the proportions of patients with one, two, and three or more PIMs according to the drug-to-avoid list were 26%, 8%, and 3.2%, respectively. However, in the study by Jaber et al. in the United States, the percentages of the mentioned prevalence were 36.7%, 18.1%, and 6.3%, respectively (27), which were higher than the current study.

Polypharmacy was observed in 60.4% of the participants. Additionally, similar studies (33) demonstrated that patients with polypharmacy received significantly higher PIM either based on the drug-to-avoid criteria or the drug-disease criteria, compared with those with less than five medications in their drug history. Moreover, polypharmacy was the most significant factor determining potentially harmful prescribing patterns, which were defined as cases where PIM was initiated at admission or continued

through hospitalization (27). Similarly, Alhawassi et al. showed that the probability of receiving a PIM based on the drugs-to-avoid list increased sevenfold in patients with polypharmacy compared with those without polypharmacy (26). Our results demonstrated that women took significantly more medications than men. However, the mean number of PIM was not significantly different between the two groups. The inconsistency between the latter finding and the highlighted role of polypharmacy in increasing PIM can be explained by the fact that the mean number of medications in both men and women was more than five. Similarly, Alhawassi et al. found that sex was not significantly associated with PIM (26).

A fundamental point to consider while comparing the prevalence of the PIM in different studies is to ensure that similar components of the Beers criteria were investigated. Unfortunately, several studies that report PIM do not clearly define this issue, which may lead to misjudgments.

One of the advantages of the current study was that we collected data prospectively. This approach helped us obtain the required data from various sources in addition to the medical charts. Moreover, in contrast to several previous studies, we included patients admitted to different wards, and we did not exclusively include patients with special medical conditions. These measures could have increased the generalizability of the results to similar settings.

When addressing the challenge of PIM administration, it is essential to consider various strategies that can help mitigate this risk. For example, Rodrigues et al., in a systematic review, concluded that medication review is a useful strategy for hospitalized patients (34). Deprescribing medications can be a beneficial approach for elderly individuals living in the community (35). Additionally, in the primary care setting, educational strategies were effective (34).

Limitations

This study was a single-center study. Moreover, considering the hospital that admits patients with severe diseases or morbidities, it is expected that the participants generally suffer from several diseases, and polypharmacy can be more common compared to nonreferral settings. Moreover, the inclusion and exclusion criteria were based on the whole project rather than pre-admission medications. As a result, some patients not included in the study might have been evaluated if we had considered the criteria for this part of the project. We used the 2105 version of the Beers criteria. However, the 2015 and 2019 versions agree well in detecting PIM at admition to hospital (36).

Conclusion

More than a third of patients admitted to the hospital received at least one PIM among their pre-admission medications. Polypharmacy was prevalent and was significantly associated with PIM utilization. The study determined the most frequent PIM in geriatrics. Physicians and pharmacists should be more vigilant regarding geriatric medications to prevent harms associated with PIMs.

Conflicts of Interest

The authors have nothing to declare.

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