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Prevalence and Assessment of Potentially Inappropriate Medications among Lebanese Elderly inpatients

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Abstract

Background: Potentially inappropriate medications (PIMs) prescribing in older increases the risk of hospitalization, drug-related problems, and other adverse health outcomes by two to three folds (Lu WH, 2015) (WHO, 2018). Hence several regulations have been implemented in geriatric clinical practice to improve drug appropriateness. This study aimed to assess the prevalence of PIMs identified by the Beers 2019 criteria among Lebanese elderly inpatients, and to identify the factors that may influence such inappropriateness. **Methods:** This observational study was conducted among elderly patients of 3 hospitals in Lebanon. Data were collected from patients using a questionnaire based on the 2019 Beers criteria. Descriptive statistics and multivariable logistic regression were used to describe and identify the predictors of PIMs use. Statistical analysis was carried out using the SPSS software version 22.0. **Results:** A total of 110 in-patients aging 65 years and older were analyzed. 80% of patients were taking drugs that are considered PIMs to be avoided; The most commonly prescribed PIM was proton pump inhibitors (PPIs) (60%). PIMs use was significantly associated with polypharmacy and other comorbid conditions (p-value <0.05). The prevalence of PIMs to be used with caution was 78.2%, those having drug-disease interactions were 22.7% and those having clinically important drug-drug interactions were 15.5%. **Conclusion:** A high prevalence of PIMs use in Lebanese hospitalized patients was observed, and was significantly associated with polypharmacy and other CNS conditions. This study supports the need for the implementation of clinical guidelines and staff to improve drug prescribing in older adults. **Trial registration:** retrospectively registered.

Key words: PIMs, pharmaceutical care, elderly, Beer's criteria, geriatrics

Main Text

Introduction

It is well documented that the worldwide proportion of older people aging 65 years or more is expected to nearly double from 12% to 22% by 2050, causing an increased shift in the overall health cost and demand for services (WHO, 2018). A major patient safety concern in elderly is the increased risk of adverse drug reactions, which is manifested as falls, orthostatic hypotension, delirium, renal failure, gastrointestinal and intracranial bleeding (Lavan AH, 2016). Many factors may contribute to such risks including age-related changes in pharmacokinetics and pharmacodynamics, increasing burden of comorbidity, polypharmacy, use of potentially inappropriate medications (PIMs) and suboptimal monitoring of drugs (Lavan AH, 2016). PIMs are defined as “drugs for which use among older adults should be avoided due to the high risk of adverse reactions for this population and/or insufficient evidence of their benefits when safer and equally or more effective therapeutic alternatives are available” (American Geriatrics Society, 2019). PIMs prescribing in older adults is a common cause of increased risk of hospitalization, drug-related problems, and other adverse health outcomes (Lu WH, 2015) (Alhawassi T, 2019). To prevent PIMs use, different criteria have been set by experts including the Beers criteria, a compendium of medications worth discussing with health professionals because they may not be the safest or most appropriate options for older adults (American Geriatrics Society, 2019). Recently, it has been adopted by the American Geriatric Society (AGS) to provide guidance regarding medication selection, educate clinicians and patients, and reduce adverse drug events (American Geriatrics Society, 2019). Many trials have been conducted in various countries to study the use of PIMs in different settings including ambulatory primary care, community, hospital, and nursing homes. In Lebanon, no studies have studied the prevalence of PIMs identified by the updated 2019 version of the Beers criteria in hospitalized elderly patients. Thus, the aim of this study was to assess the prevalence of PIMs identified by the American Geriatrics Society Beers Criteria among Lebanese hospitalized elderly patients, and to explore risks that may influence such inappropriateness.

Methods

This cross-sectional observational study was conducted in three main Hospitals in Bekaa/ Lebanon within 8-weeks duration. Data was collected from patients’ profiles using the hospital’s systems, and directly from patients or caregivers. Subjects were assessed by officially licensed Lebanese pharmacists who were trained to present and collect data in order to maintain its uniformity. Ethical approval was obtained from the School of Pharmacy at the Lebanese International University, and verbal informed consent was taken from the patients/ caregivers and from the 3 hospitals’ administrations. A written informed consent was also obtained.

The questionnaire used was based on the 2019 Beers criteria, and was divided into three main parts: Demographic properties, Comorbidities/ disease states, and medications taken. Medications and co-morbidities were then classified into categories based on Beers’ criteria division also, for example, medications were classified as: (1) medications to be avoided, (2) medications to be used with caution, (3) medications having drug-disease or drug syndrome interaction that

may exacerbate the disease or syndrome, and (4) medications having clinically important drug-drug interactions that should be avoided. PIMs use also was classified into two categories: PIMs use, and no PIMs use. Data were coded and entered for analysis. Descriptive testing was used to summarize and describe subjects' related information; frequencies and percentages were used to describe demographic properties of patients and primary outcomes. Fisher exact test was used to determine statistical significance in the bivariate analysis between PIMs use and subjects' characteristics and comorbidities, while logistic regression was used in the multivariable analysis. The 95% confidence intervals (CI) were based on likelihood. All reported p-values were 2-sided and considered significant if they were less than <0.05. Data were entered and analyzed using software IBM Statistical Package for Social Science (SPSS) version 20.

Results

During the eight-week study, 110 subjects were enrolled in the study by convenient sampling. Average age was 36.9 ± 13.5 (range between 18 and 85 years), and the majority were females. Subjects above 65 years were divided according to age group, with 40 subjects aging between 65 and 69 years, 17 aging between 70 and 74 years, 13 aging between 75 and 79 years, and 38 aging more than or equal to 80 years. The majority of the study population had chronic conditions, particularly hypertension and diabetes [Figure 1]. The prevalence of polypharmacy was high among subjects (73.6%) with significant associations. Detailed participants' socioeconomic data are presented in [Table 1].

The prevalence of PIMs in the tested population was 105 out of 110 (95.5%) - one subject may have more than one type of PIM-, and was divided as follow: PIMs to be avoided (80%), followed by PIMs to be used with caution (78.2%), PIMs having drug-disease or drug syndrome interaction that may exacerbate the disease or syndrome (22.7%) and PIMs having clinically important drug-drug interactions that should be avoided (15.5%) [Table 2]. The most commonly prescribed PIMs to be avoided were gastrointestinal agents (particularly PPIs) followed by CNS acting drugs [Table 3]. The most commonly prescribed PIMs to be used with caution were antipsychotics (48.2%), followed by diuretics (30.9%), while aspirin and SSRIs were in equal proportions (15.5%) [Table 4]. In regards to drug-disease interactions, the most commonly encountered drug-disease interactions were: 1) Falls with SSRIs (4.5%), antipsychotics (3.6%), BZDs (3.6%), 2) Dementia with BZDs (4.5%), antipsychotics (4.5%), 3) Delirium with antipsychotics (3.6%). Two main drug-drug interactions were noticed: the use of 3 or more CNS active drugs with a proportion of 14.5%, followed by the concomitant use of 2 anticholinergics with a proportion of 1.8%.

The prevalence of PIMs to be avoided was associated with different variables like marital status and polypharmacy, and conditions like hypertension, diabetes mellitus, falls and bipolar. Detailed percentages and P values are presented in [Table 5]. In the multivariate analysis, older adults with polypharmacy, and conditions like dementia, falls, insomnia, and schizophrenia were associated with PIMs. For example, 88.9% of patients who were taking more than or equal 5 drugs have a PIM to be avoided, while 11.1% don't (P value= 0.001) [Table 6]. Another example is in the case of falls, where 94.7% of patients suffering from this condition have PIMs to be used with caution, while 5.3% don't (P value = 0.05). Adjusted odds ratios and 95% confidence intervals (CI) for factors associated with PIMs use are presented in [Table 6].

160 Discussion

161 It is well known that PIMs use among older patients is associated with negative health consequences and can impact
162 patients' quality of life, with increased hospitalization risk, drug related problems and cost burden on the healthcare
163 system (Alhawassi T, 2019). Clinical studies show there is high prevalence of PIMs among elderly, ranging between
164 53.5% to 58.4%, which is consistent with the results of this study (Zhang X, 2017) (Ní Chróinín D, 2016) (Endres H,
165 2016). The prevalence of PIMs in this sample of the Lebanese population was apparently higher than that in other
166 countries, especially for the PIMs to be avoided (80%), and the PIMs to be used with caution (78.2%). Reasons behind
167 these results may intersect, where the absence of specific in-patient criteria to assess the use of medications for elderly
168 patients in the assessed Lebanese hospitals could be the main one. The absence of clinical pharmacists in the assessed
169 hospitals may have contributed to these results, where the comprehensive medication reviews clinical pharmacists do, has
170 been shown to improve overall patient health and alleviate health care burdens (Nemes S, 2009). Previous studies
171 strongly support the clear role for pharmacists in working directly or collaboratively to improve medication use and
172 management in older population (Lee J, 2015). Pharmacist integration into a multidisciplinary team has been shown to
173 have a positive impact in the management of a variety of different disease states. Different assessment tools or versions
174 may also contribute to such difference. Also, a marked difference in the prevalence of PIMs was shown when applying
175 two versions of beers criteria (2003 and 2012) on the same population, as results varied by a 9% increase (48% versus
176 59% respectively), which could be another cause for the results variation (Baldoni ADO, 2014).

177 Being the most prevalent PIM to be avoided (60%), proton pump inhibitors (PPIs) are among the most used medications
178 in hospitals, while antipsychotics (48%) and diuretics (31%) are among the most common PIMs to be used with caution.
179 Long term use of PPIs without a specific clinical indication is considered a PIM in older adults, increasing the risk of C.
180 diff infection, bone loss, or fractures, and should be carefully prescribed and monitored (Trifan A, 2017) (Zhou B, 2015)
181 especially that age-related bone loss with marked increase in bone resorption is evident in both genders, along with a
182 reduction in bone formation and initial fall in bone mineral density (Demontiero O, 2012). These findings are consistent
183 with other studies conducted in different countries, showing that PPI's are among the most prevalent PIMs (Zhang X,
184 2017) (Bhatt A, 2019), while antipsychotics and diuretics are among the most common PIMs to be used with caution
185 (Vieira de Lima T, 2013) (Mann E, 2009). CNS active drugs taken by elderly in this sample were mainly SSRIs,
186 antipsychotics, BZD, TCAs and opioids, while two main drug-drug interactions were noticed, which may be alarming.
187 First, the administration of 3 or more CNS active drugs concomitantly (ex: SSRIs, TCAs, BDZ) can increase the risk of
188 falls/fractures (Hanlon J, 2017). Second, the use of 2 anticholinergics at the same time (ex: amitriptyline, trihexyphenidyl,
189 hyoscyamine) which can increase the risk of cognitive decline (Dauphinot V, 2017). CNS active drugs are highly
190 associated with increased risk of falls in nursing home residents especially with older population (Hanlon J, 2017), and
191 thus precaution measures should be taken into consideration.

192 The most important independent predictor for having a PIM in the tested population was found to be polypharmacy,
193 especially when the majority of patients suffer from concomitant chronic conditions. It is an area of concern for elderly
194 due to the greater risk for adverse drug reactions, drug-drug interactions, prescribing cascades and risk of falls (Dagli R J,
195 2014) and can lead to decreased medication compliance, poor quality of life and unnecessary drug expenses

(Abdulraheem I, 2013). A strong association between polypharmacy and different types of PIMs has been reported in this study and in other studies (Alhawassi T, 2019) (Napolitano F, 2013). Patients with multiple comorbid conditions, recent hospitalizations and counseled by multiple physicians are more likely to be on multiple medications, and thus increased opportunities to have a prescribed PIM (Bao Y, 2011). A systematic review aiming to quantify the extent of inappropriate prescription to elderly persons in the primary care setting concluded that one in five prescriptions to elderly is inappropriate, despite the attention that has been directed to the quality of prescription (Opondo D, 2012). The findings in this study sheds the light more on the importance of reducing the number of prescribed drugs for which there is no clinical need, to diminish the prevalence of drug inappropriateness in elderly patients. The association between PIM use and certain pathologies could be an important marker of incorrect disease management and increased tendency for irrational prescriptions (Wawruch M., 2018) Several medical conditions found to be directly related to prescribed PIMs, such as insomnia, schizophrenia, dementia and falls.

The need to adopt different interventions by all healthcare professionals to reduce the tendency of prescribing PIMs in elderly is essential. An overview aiming to identify and critically evaluate systematic reviews addressing the effectiveness of such interventions showed the potential benefits of different strategies (Santos N, 2019). Those interventions included: computerized systems to support drug prescription and dispensing, training on the use of validated tools for the detection of PIMs, procedures and explicit routines for medications review, continuing education for health professionals and geriatric medicine services; combined interventions reveal better results than isolated ones.

To our knowledge, this is the first study in a developing country like Lebanon that investigates the prevalence of PIMs for in-patients, and particularly in Bekaa area, where no university hospitals are found. Thus, it was essential to assess the prevalence of such inappropriateness in areas where medications' safety and efficacy protocols are uncommon, underestimated in practice, or even absent. A validated and updated criterion adopted by the American Geriatric Society (AGS) was used in assessment, which gives the study more strength and validity. The primary limitation of this study is the small sample size. Data was collected during the Covid-19 pandemic, where approaching patients and files was low. Small sample sizes usually lead to the overestimation of odds ratio and to the reduction in the statistical power of a study (Deziel C, 2020). Also, only hospitalized patients were included which is not representative of community-based aged patients who were recently discharged. The last limitation is related to the nature of the study; it is cross sectional which doesn't allow us to determine the presence or absence of a temporal link between PIMs use and its determinants.

Conclusion

High prevalence of potentially inappropriate medications in the Lebanese hospitalized elderly population was shown to be evident. There was a strong association between potentially inappropriate medications use and polypharmacy, which is considered a serious challenge in the geriatric healthcare sector. These findings underscore the need to improve the medication prescription quality for the elderly by implementing clinical guidelines, reducing the number of unnecessary prescribed medications when possible, and assisting physicians in delivering appropriate medications. Pharmacists, working in a multidisciplinary team can play a significant role in reducing PIMs use among elderly, and thus their absence may affect the overall clinical outcomes, safety, and efficacy of the prescribed drugs. This role can be illustrated in

reviewing the patients’ prescriptions, detecting PIMs and recommending appropriate drug use, and creating changes in prescribing practices in accordance with guidelines from the literature.

Declaration

Ethics approval and consent to participate

This study design and methods were carried out in accordance with relevant guidelines and regulations under Ethics approval and consent to participate. Ethical approval was obtained from the School of Pharmacy at the Lebanese International University and the hospitals’ administrations. Written informed consent was also obtained.

Consent of publication

Not applicable

Availability of Data and Material

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study

Conflicts of interest

The authors declare that they have no competing interests

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None

Authors' contributions

The authors confirm contribution to the paper as follows: study conception and design: M.H, M.H, A.C, S.Y, M.R. Data collection, analysis and interpretation of results: M.H, M.H, A.C, M.M, N.M. Draft manuscript preparation and revision: all authors: M.H, M.H, A.C, S.Y, N.M, M.M, M.R.

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List of tables and figures:

Characteristics	N (%)
Age	
65-69	40 (37%)
70-74	17 (15.7%)
75-79	13(12%)
>=80	38(35.2%)
Gender	
Male	19 (17.4%)
Female	90 (82.6)
Marital status	
Single	3 (3.1%)
Married	92 (93.8%)
Widowed/separated	3 (3.1%)
Bedridden	
No	89 (82.4%)
Yes	19 (17.6%)
Smoking status	
No	59 (55.7%)
Yes	47 (44.3%)
Alcohol status	
No	103 (99%)
Yes	1 (1%)
Polypharmacy	
No	29 (26.4%)
Yes	81 (73.6%)

Table 1: Participants’ socioeconomic data

Figure 1: Participants’ comorbidities

Type of PIM	N (%)
PIMs in total	105 (95.5%)
PIMs to be avoided	88 (80%)
PIMs to be used with caution	86 (78.2%)
PIMs having drug-disease or drug syndrome interaction that may exacerbate the disease or syndrome	25 (22.7%)
PIMs having clinically important drug-drug interactions that should be avoided	17 (15.5%)

Table 2: PIMs

PIMs	N (%)
Anticholinergics	
First generation antihistamines	13 (11.8%)
Antiparkinsonian agents	
Trihexyphenidyl	14 (12.7%)
Antispasmodics	
Scopolamine	2 (1.8%)
Cardiovascular	
Peripheral alpha-1 blockers for the treatment of hypertension	1 (0.9%)
Digoxin	1 (0.9%)
Central nervous system	
Antidepressants	2 (1.8%)
Antipsychotics, first (conventional) and second (atypical) generations	6 (5.5%)
Benzodiazepines	14 (12.7%)
Endocrine	
Insulin	4 (3.6%)
Sulfonylureas, long acting	4 (4.5%)
Gastrointestinal	
Proton-pump inhibitors	66 (60%)
Metoclopramide	2 (1.8%)
Pain medications	
Meperidine	1 (0.9%)
Non-cyclooxygenase-selective NSAIDs, oral	1 (0.9%)

Table 3: PIMs to be avoided

PIMs to be used with caution	N (%)
Diuretics	34 (30.9%)
SSRIs	17 (15.5%)
Antipsychotics	53 (48.2%)
Aspirin	17 (15.5%)
Carbamazepine	1 (0.9%)
TCAs	3 (2.7%)
Opioids	1 (0.9%)
Rivaroxaban	1 (0.9%)

405

Table 4: PIMs to be used with caution

406

	With PIMs to be avoided		Without PIMs to be avoided		P-value
	N	%	N	%	
Total	88	80	22	20	
Gender					0.4
Male	17	89.5	2	10.5	
Female	70	77.8	20	22.2	
Age					0.2
65-69	31	77.5	9	22.5	
70-74	11	64.7	6	35.3	
75-79	12	92.3	1	7.7	
>=80	33	86.8	5	13.2	
Marital status					0.07
Single	29	69	13	31	
Married	24	82.8	5	17.2	
Widowed/separated	28	90.3	3	9.7	
Smoking					1
No	47	79.7	12	20.3	
Yes	38	80.9	9	19.1	
Alcohol					1
No	84	81.6	19	18.4	
Yes	1	100	0	0	
Polypharmacy					<0.001
No	16	55.2	13	44.8	
Yes	72	88.9	9	11.1	
Bedridden					1
No	72	80.9	17	19.1	
Yes	15	78.9	4	21.1	
HF					0.3
No	85	81	20	19	
Yes	3	60	2	40	
HTN					0.002
No	38	67.9	18	32.1	
Yes	50	92.6	4	7.4	
DM					0.02
No	46	71.9	18	28.1	
Yes	42	91.3	4	8.7	
Seizure					1
No	83	79.8	21	20.2	
Yes	5	83.3	1	16.7	
Delirium					1
No	85	79.4	22	20.6	
Yes	3	100	0	0	
Dementia					1
No	73	80.2	18	19.8	
Yes	15	78.9	4	21.1	
Falls					0.01
No	69	75.8	22	24.2	
Yes	19	100	0	0	
Insomnia					0.1

No	71	77.2	21	22.8	
Yes	17	94.4	1	5.6	
Parkinson					0.4
No	87	80.6	21	19.4	
Yes	1	50	1	50	
Alzheimer's Disease					0.5
No	80	80.8	19	19.2	
Yes	8	72.7	3	27.3	
Bipolar					0.03
No	87	82.1	19	17.9	
Yes	1	25	3	75	
Schizophrenia					0.09
No	58	85.3	10	14.7	
Yes	30	71.4	12	28.6	
BPH					0.6
No	82	78.8	22	21.2	
Yes	6	100	0	0	

Table 5: Variables and conditions associated with PIMs

	Type of PIM	With PIM		Without PIM		Multivariable Analysis	
		N	%	N	%	OR (95% CI)	P-value
Age	PIMs to be avoided						0.04
	65-69	31	77.5	9	22.5	Reference	
	70-74	11	64.7	6	35.3	0.11(0.01,0.92)	
Polypharmacy	PIMs to be avoided						0.001
	No	16	55.2	13	44.8	Reference	
	Yes	72	88.9	9	11.1	16.82(2.97,95.18)	
	PIMs to be used with caution						0.05
	No	17	58.6	12	41.4	Reference	
	Yes	69	85.2	12	14.8	3.46(1.01,11.81)	
	PIMs of Drug-disease interaction						0.04
	No	3	10.3	26	89.7	Reference	
	Yes	22	27.2	59	72.8	12.91(1.09,152.41)	
Dementia	PIMs of Drug-disease interaction						0.01
	No	14	15.4	77	84.6	Reference	
	Yes	11	57.9	8	22.1	40.88(3,556.71)	
Falls	PIMs to be used with caution						0.05
	No	68	74.7	23	25.3	Reference	
	Yes	18	94.7	1	5.3	8.92(1,79.55)	
	PIMs of Drug-disease interaction						<0.001
	No	12	13.2	79	86.8	Reference	
	Yes	13	68.4	6	31.6	48.94(7.75,308.87)	
Insomnia	PIMs to be avoided						0.04
	No	71	77.2	21	22.8	Reference	
	Yes	17	94.4	1	5.6	15.80(1.16,215.18)	
	PIMs to be used with caution						0.02
	No	76	82.6	16	17.4	Reference	
	Yes	10	55.6	8	44.4	0.14(0.03,0.69)	
Schizophrenia	PIMs to be avoided						0.03
	No	58	85.3	10	14.7	Reference	
	Yes	30	71.4	12	28.6	0.14(0.03,0.79)	
	PIMs to be used with caution						0.003
	No	45	66.2	23	33.8	Reference	
	Yes	41	97.6	1	2.4	28.75(3.10,266.93)	
	PIMs of Drug-disease interaction						0.002
	No	2	2.9	66	97.1	Reference	
	Yes	15	35.7	27	64.3	13.54(2.55,71.81)	

Table 6: Combined significant results of the multivariate analysis

Figures

Figure 1

Participants' comorbidities