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Association between potentially inappropriate prescribing, polypharmacy, and functional/cognitive impairment among Egyptian geriatric patients

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Background and aims. Potentially inappropriate medications (PIM) use is common among seniors and could be related to various geriatric syndromes. The objective was to determine association between PIM use, polypharmacy, and functional/cognitive impairment among Egyptian geriatric patients.

Methods. A cross-sectional study included 251 older adults (aged ≥ 60 years), admitted at the geriatrics hospital of Ain Shams University, Egypt, between March and September 2022. Patients underwent taking of the medical history including age, sex, chronic diseases, geriatric syndromes, pre-hospitalization medications intake, and geriatric assessment; functional status by activities of daily living (ADL) and instrumental activities of daily living (IADL) and cognitive status by mini-mental state examination (MMSE). Multi-morbidity assessed by charlson comorbidity index (CCI). Polypharmacy identified as receiving ≥ 5 medications daily. PIM use defined by the American Geriatrics Society Beers criteria-2019 (AGS Beers criteria-2019). Logistic regression and Pearson correlation were applied.

Results. PIM use occurred in 126 (50.2%) patients. Polypharmacy, CCI, having diabetes mellitus, hypertension and a cardiac disease had significant association with PIM use. Polypharmacy (OR 5.514; 95% CI: 2.776- 10.952; P .000) and having a cardiac disease (OR 2.359; 95% CI: 1.239-4.490; P . 009) were independent predictors of PIM use. Number of PIM use had a significant negative correlation with MMSE scores. Use of diuretics, proton-pump inhibitors (PPIs) and digoxin were the most frequent PIM.

Conclusions. Polypharmacy and having a cardiac disease were predictors of PIM use. The total number of the used PIM negatively correlated with MMSE scores. Medications review and de-prescribing are essential for geriatric patients.

Key words: polypharmacy, potentially inappropriate medications, geriatric syndromes

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INTRODUCTION

Geriatric patients are more likely to have multi-morbidity with subsequent multiple medications usage and polypharmacy [1]. Aging is associated with an increased risk of adverse drug events (ADEs) due to reduced

medication clearance and age-related metabolic changes [2]. Polypharmacy could be associated with prescribing cascades which occurs when an adverse effect is misinterpreted as a recent medical issue, with the subsequent prescription of another potentially inappropriate medications (PIM) [3].

ADEs could be a serious complication of PIM use [1]. It is significantly associated with the presence of common geriatric syndromes [4], such as frailty, cognitive impairment, and functional dependence [5]. Accordingly, PIM use should be avoided because of the high risk of medication related harm in seniors [6].

In clinical practice, PIM could be identified through implicit and explicit methods [7]. Implicit methods target defining PIM for a particular patient based on an expert opinion, which is a timely process [7]. Explicit methods are criteria-based with a well-defined inventory of medications described as PIM that requires less time and has a higher benefit [8].

The American Geriatrics Society Beers criteria (AGS Beers criteria) are a widely used explicit list of PIM since 1991. It has been published by the AGS for practitioners to guide them towards safer prescribing for geriatric patients [6]. For the AGS Beers criteria-2019 update, an interdisciplinary expert group reviewed the evidence published in 2015 to dictate if recent criteria should be added or if existing criteria should be deleted or modified [9].

This study aims to determine association between PIM use, polypharmacy, and functional/cognitive impairment and to describe pre-hospitalization prescribing patterns among Egyptian geriatric patients.

PATIENTS AND METHODS

A cross-sectional study included 251 older adults (aged ≥ 60 years), admitted at the geriatrics hospital of Ain Shams University, Egypt, between March and September 2022. Exclusion criteria involved patients/proxies who refused participation in the study and patients with missing medication history.

Patients underwent taking of the medical history including age, sex, co-morbidities, pre-hospitalization medications intake and geriatric syndromes including dementia, polypharmacy, falls, fractures, pressure ulcers, and urinary/fecal incontinence besides geriatric assessment including mini-mental state examination (MMSE) for cognitive assessment [10] and activities of daily living (ADL) [11] and instrumental activities of daily living (IADL) [12] for determination of functional status.

The total number of medications intake before hospitalization was determined for each patient. Polypharmacy was identified as receiving ≥ 5 medications per day [13]. Multimorbidity was determined by charlson comorbidity index (CCI) [14]. PIM use was identified in accordance with the AGS Beers criteria-2019 [9]. Patients were classified into 2 groups either with or without PIM use.

Statistical analysis

Values were presented as numbers and proportions for qualitative variables or mean and standard deviation for quantitative variables. Quantitative variables were checked for normality by Shapiro-Wilk test. Unadjusted odds ratio (OR) was calculated to detect variables with potential association with PIM use. Outcomes with significant un-adjusted OR were then entered into logistic regression analysis to detect significant predictors for PIM use. Pearson correlation was performed to test correlation between number of PIM and geriatric assessment domains.

All tests were bilateral and a P-value of 5% was the limit of statistical significance. Analysis was performed by statistical package software IBM- SPSS version 24.

RESULTS

A total of 251 geriatric patients were included with a mean age of 73.31 ± 8.368 years. PIM use occurred in 126 (50.2%) patients. Participant's characteristics were compared between those with and without PIM use. Univariable analysis was done to detect potential association between various variables and PIM use. The following variables were found to have a significant association with PIM use: polypharmacy, CCI, having a cardiac disease, hypertension, and diabetes mellitus. Having polypharmacy would increase the odds of PIM use by 6.750 times. By 95%, having polypharmacy would increase the odds of PIM use from 3.669 to 12.420 as described in Table I.

The significant variables were entered into multivariate regression analysis. Significant predictors for PIM use were polypharmacy (OR 5.514; 95% CI: 2.776-10.952; P .000), and presence of a cardiac disease (OR 2.359; 95% CI: 1.239-4.490; P. 009). The model was able to explain 28.8% of the variability of PIM use as indicated by Nagelkerke R Square value. It was able to correctly predict PIM use by 72.8%. The results showed that with polypharmacy, the odds of PIM use would increase by 5.51 times and with the presence of a cardiac disease, the odds of PIM use would increase by 2.35 times. The 95% CI means that by 95% we are confident that taking ≥ 5 medications daily would increase the odds of PIM use from 2.776 to 10.952 times. While, having a cardiac disease would increase the PIM use odds from 1.239 to 4.490 times as described in Table II.

Based on AGS Beers criteria PIM were subdivided into 6 groups: PIM, drugs to be avoided, PIM use due to drug-syndrome interaction, PIM; drugs to be used with

Table I. Association between participant's characteristics and potentially inappropriate medications use.

Participant's characteristics	Total N = 251 (100%)	No PIM use N = 125 (49.8%)	PIM use N = 126 (50.2%)	Univariate analysis	
				OR 95% C.I.	P value
Age Mean ± SD	73.31 ± 8.368	73.13 ± 8.423	73.49 ± 8.342	1.005 (.976-1.035)	.730
Male/female	99 (39.4)/152 (60.6)	47 (47.5)/78 (51.3)	52 (52.5)/74 (48.7)	1.166 (.703- 1.936)	.552
Charlson comorbidity index	6.30 + 2.119	5.99 ± 2.012	6.61 ± 2.188	1.152 (1.007-1.319)	**.039**
Co-mordidities					
Hypertension	160 (63.7)	72 (45.0)	88 (55.0)	1.705 (1.013 - 2.868)	**.044**
Diabetes mellitus	125 (49.8)	54 (43.2)	71 (56.8)	1.697 (1.030- 2.796)	**.038**
Chronic hepatic disease	58 (23.1)	33 (56.9)	25 (43.1)	.690 (.382- 1.247)	.219
Chronic kidney disease (CKD/ESRD)	54 (21.5)	25 (46.3)	29 (53.7)	1.196 (.654- 2.187)	.561
Malignancy	41 (16.3)	18 (43.9)	20 (56.1)	1.327 (.677 - 2.603)	.410
Old stroke	56 (22.3)	25 (44.6)	31 (55.4)	1.305 (.718- 2.371)	.382
Cardiac disease (CHF/AF/ISHD)	106 (42.2)	39 (36.8)	67 (63.2)	2.504 (1.496- 4.193)	**.000**
Respiratory disease	37 (14.7)	17 (45.9)	20 (54.1)	1.199 (.595-2.414)	.612
Thyroid disease	25 (10.0)	11 (44.0)	14 (56.0)	1.284 (.559- 2.950)	.556
Geriatric syndromes					
Falls	51 (22.7)	26 (51.0)	25 (49.0)	.918 (.492- 1.714)	.789
Fracture	37 (18.3)	19 (51.4)	18 (48.6)	.959 (.470- 1.957)	.908
Pressure ulcer	46 (21.1)	18 (39.1)	28 (60.9)	1.789 (.921- 3.474)	.086
Incontinence (urinary/fecal)	45 (24.5)	21 (46.7)	24 (53.3)	1.127 (.574- 2.209)	.729
Polypharmacy	85 (33.9)	18 (21.2)	67 (78.8)	6.750 (3.669-12.420)	**.000**
Dementia	43 (19.0)	23 (53.5)	20 (46.5)	.842 (.432- 1.637)	.611
Geriatric assessment					
MMSE Mean ± SD	23.98 ± 6.933	24.85 ± 7.206	23.23 ± 6.680	.965 (.904 - 1.030)	.285
ADL Mean ± SD	3.60 ± 2.412	3.51 ± 2.467	3.69 ± 2.369	1.032 (.912 -1.168)	.615
IADL Mean ± SD	3.87 ± 3.073	3.76 ± 3.257	3.98 ± 2.900	1.023 (.928 -1.127)	.647

PIM: Potentially Inappropriate Medications; CKD: Chronic Kidney Disease; ESRD: End-Stage Renal Disease; CHF: Congestive Heart Failure; AF: Atrial Fibrillation; ISHD: Ischemic Heart Disease; MMSE: Mini-Mental State Examination; ADL: Activities of Daily Living; IADL: Instrumental Activities of Daily Living.
*Bold numbers mean significant value.

caution, potentially clinically important drug-drug interactions, medications need adjustment according to renal function, and use of drugs with strong anticholinergics effects. Diuretics, proton-pump inhibitors (PPIs) and digoxin were the most frequently used PIM among 62 (24.7), 38 (15.1), and 15 (6.0) participants, respectively. The frequency, distribution and ranking of PIM among participants are described in Table III and Figure 1.

Number of PIM showed a negative correlation with MMSE, ADL and IADL scores, but only significant correlation was found between the number of PIM and MMSE scores (r -.252, P .019) as described in Table IV.

The ranking and frequencies of pre-hospitalization medications use among geriatric patients is described in Table SI.

DISCUSSION

There is a paucity of data regarding PIM use among geriatric patients in developing countries that make not only defining these medications essential but also avoiding them to mitigate ADEs [15]. The study utilized the AGS Beers criteria-2019 to define PIM [9]. PIM use was common in older patients, it occurred in 126 (50.2) patients. The association between PIM use and every other variable was assessed by logistic regression analysis. Factors associated with PIM use were polypharmacy, CCI, and chronic diseases including diabetes mellitus, hypertension and cardiac disease. After multivariate analysis, polypharmacy and the presence

Table II. Predictors of potentially inappropriate medications use.

Risk factors of PIM use	Multivariate analysis	
	OR 95% C.I.	P value
Polypharmacy	5.514 (2.776-10.952)	**.000**
Charlson comorbidity index	1.105(.945-1.292)	.212
Hypertension	1.444 (.725- 2.873)	.296
Diabetes mellitus	1.294 (.667-2.511)	.447
Cardiac disease (CHF/AF/ISHD)	2.359 (1.239-4.490)	**.009**

PIM: Potentially Inappropriate Medications; CHF: Congestive Heart Failure; AF: Atrial Fibrillation; ISHD: Ischemic Heart Disease.
*Bold numbers mean significant value.

Table III. Description of potentially inappropriate medications defined by AGS Beers criteria-2019.

PIM defined by AGS Beers criteria-2019	Total No.	%
PIM; drugs to be avoided	**80**	**31.9**
Antipsychotics (quitapine/olanzapine)	3	1.2
Anticholinergics (clomipramine, olanzapine, benztropine, dimenhyrinate, paroxitine)	4	1.6
Glimepiride	14	5.6
Digoxin	15	6.0
Insulin, sliding scale	3	1.2
Glibenclamide	3	1.2
Diclofenac	6	2.4
Methyldopa	6	2.4
Metoclopramide	1	.4
Chlorzoxazone	1	.4
Proton-pump inhibitors (pantoprazole/lansoprazole)	38	15.1
PIM due to drug-syndrome interactions	**9**	**3.6**
Dementia or cognitive impairment with anticholinergics	3	1.2
Dementia or cognitive impairment with antipsychotics	4	1.6
Falls or fractures with antidepressants (venlafaxine, escitalopram, mirtazapine)	4	1.6
Falls or fractures with opioids (tramadol)	1	.4
PIM; drugs to be used with caution	**76**	**30.3**
Selective serotonin reuptake inhibitors (escitalopram/vortioxetine)	8	3.2
Serotonin-norepinephrine reuptake inhibitors (duloxetine/venlafaxine)	2	.8
Mirtazapine	3	1.2
Rivaroxaban	3	1.2
Aspirin	1	.4
Tramadol	3	1.2
Oxcarbazepine	1	.4
Diuretics (hydrochlorothiazide, bumetanide, torsemide, furosemide, spironolactone)	62	24.7
Potentially clinically important drug-drug interactions	**17**	**6.8**
Inhibitors of the renin-angiotensin system with potassium-sparing diuretics (enalapril/ramipril with spironlactone)	7	2.8
Corticosteroids with a non steroidal anti-inflammatory drug	4	1.6
Combination of ≥ 3 central nervous system-active drugs	3	1.2
Anticholinergic with anticholinergic	1	.4
Warfarin with a non steroidal anti-inflammatory drug	2	.8
Medications need adjustment according to renal function	**3**	**1.2**
Spironolactone with creatinine clearance < 30 mL/min	2	.8
Apixaban with creatinine clearance < 25 mL/min	1	.4
Medications with strong anticholinergic effects		
(clomipramine, olanzapine, benztropine, dimenhyrinate, paroxitine)	4	1.6

PIM: Potentially Inappropriate Medications; AGS Beers criteria-2019: American Geriatrics Society Beers criteria-2019.

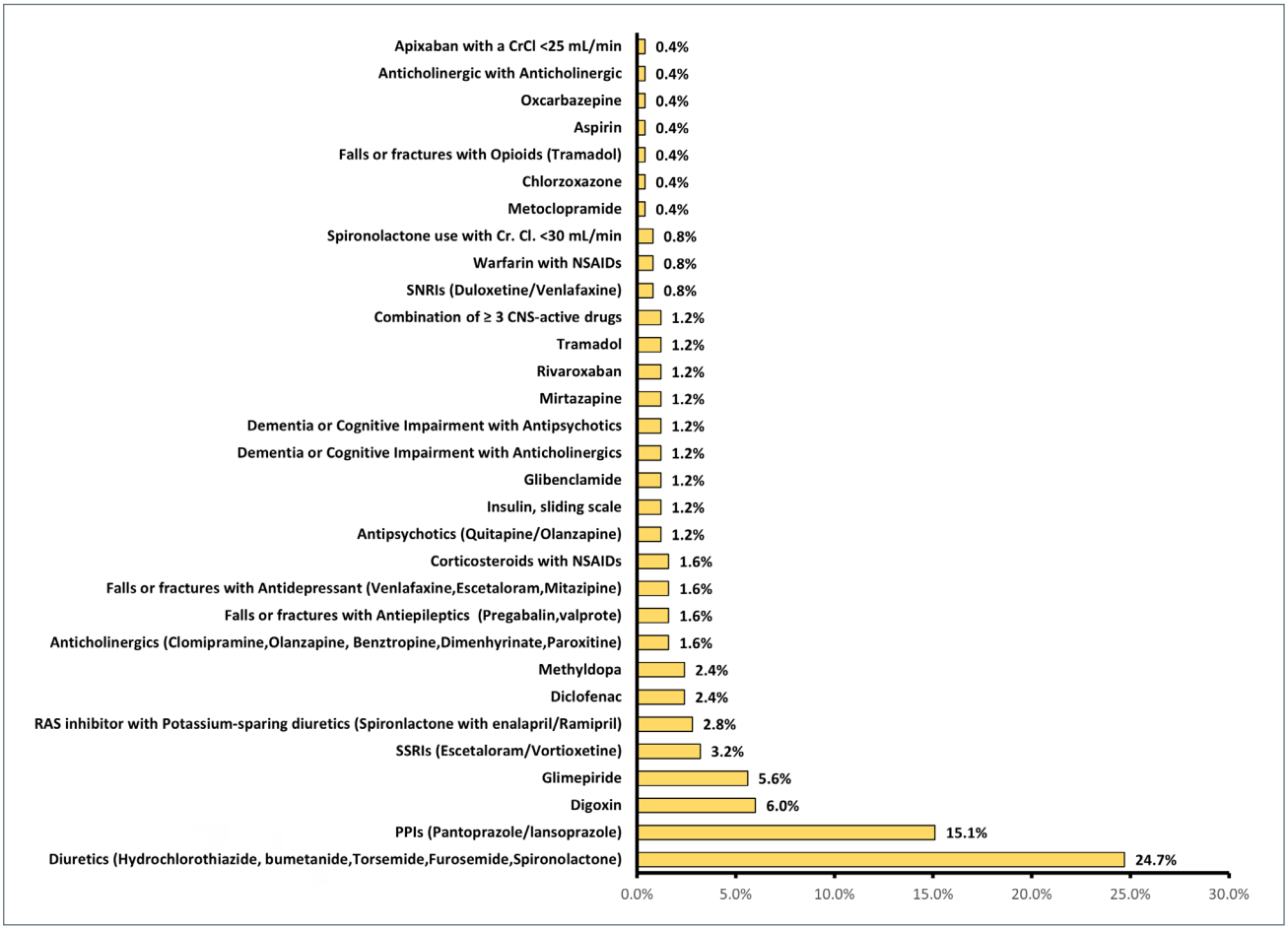

Figure 1. Ranking and frequencies of potentially inappropriate medications used before hospitalization among participants.

Table IV. Correlation between number of potentially inappropriate medications and geriatric assessment domains.

			MMSE	ADL	IADL
Whole sample	**Number of PIM**	r	-.252	-.048	-.043
		P-value	**.019**	.529	.571
		No.	87	175	174

PIM: Potentially Inappropriate Medications; MMSE: Mini-Mental State Examination; ADL: Activities of Daily Living; IADL: Instrumental Activities of Daily Living.
*Bold numbers mean significant value.

of a cardiac disease were independent predictors of PIM use. These data coincide with a recent study that included 496 older adults in Kuwait applying the same explicit criteria that revealed PIM use among 58.4% of patients and polypharmacy as the most likely predictor of PIM use [16]. This high prevalence of PIM use could be related to the complexity of the management of geriatric patients and ill-defined approaches in a given nation [16]. Multimorbidity is significantly related to polypharmacy [1]. Multimorbidity, as assessed by CCI, was significantly associated with PIM use in our study and previous studies [16]. In this study, polypharmacy was defined as use of ≥ 5 medications per day, it occurred in 85 (33.9) patients. Polypharmacy pooled prevalence was 49% (95% CI: 42-56; P < 0.01) in a previous meta-analysis including 27 studies in India [17]. The variability of the prevalence of polypharmacy could be related to different settings and cut-offs for defining polypharmacy among various studies.

The current study also highlighted the significant relationship between cognition and PIM use as patients with lower scores on the MMSE used more PIM (r -.252, P value .019) in line with other studies reporting that geriatric patients with lower scores on the MMSE

took more medications and utilized more PIM [18]. However, the results did not show a significant association between functional impairment as assessed by ADL/IADL and PIM use compared to other studies reporting a significant association between functional dependence and PIM use [19]. This discrepancy in data further supports the thought of context-specific risk factors as they could be affected by the criteria to detect PIM, as well as the setting of the study.

Based on applying the AGS Beers criteria-2019 on participants' prescriptions before hospital admission [9], PPIs were the most commonly prescribed PIM; drugs to be avoided. The most commonly prescribed PIM that should be used with caution were diuretics. The most frequently reported potential drug-drug interaction was an inhibitor of the renin-angiotensin system (RAS) with potassium-sparing diuretics. The most frequently involved drug-syndrome interactions were dementia/cognitive impairment with antipsychotics and falls/fractures with antidepressants. The most commonly prescribed PIM in the category of "renal dose adjustment" was spironolactone. Strong anticholinergics included clomipramine, olanzapine, benztropine, dimenhyrinate and paroxitine. These findings correlate to a great extent with another similar study [16]. Here is a further discussion of the reported PIM use among participants in the study.

First, PIM; drugs to be avoided

It occurred in 80 (31.9) patients. PPIs were the most frequently reported PIM in this category of PIM. The excessive use of PPIs is related to reduced bone mineral density, fracture, vitamin B-12 deficiency, pneumonia and colon cancer [20]. The study highlights the widespread use of PPIs among geriatric patients with non-evidence-based need [21].

Glimepiride and glibenclamide were used in 14 (5.6) and 3 (1.2) patients, respectively. These medications are associated with a higher risk of hypoglycemia among seniors. Methyldopa was reported in 6 (2.4) patients. It has poor effects on the central nervous system (CNS) and should be avoided as the first-line medication for hypertension in seniors [9].

Diclofenac use had occurred in 6 (2.4) patients, it is a non steroidal anti-inflammatory drug (NSAID) with multiple ADEs in geriatric patients such as hypertension, cardiovascular disease (CVD), gastrointestinal disease, and renal disease [22]. Pain management via physical therapy and acetaminophen are preferable choices [22]. A previous study showed that more than 30% of geriatric patients in general practice were taking a NSAID on a regular basis [23]. A previous study also compared the effects of various painkillers on blood pressure in hypertensive patients. Compared with patients on acetaminophen, NSAID users had a higher proneness to blood pressure elevation [24].

Regular human insulin (sliding scale) use had reported in 3 (1.2) patients. Its use is inappropriate when it is not used concomitantly with long-acting insulin due to the higher risk of hypoglycemia and poor control of hyperglycemia [9]. Antipsychotic use had been reported in 3 (1.2) patients. It is related to increased risk of cognitive decline, cerebrovascular accidents, and mortality in patients with dementia [9].

Metoclopramide was reported in 1 (0.4) patient. It is related to the risk of extrapyramidal manifestations such as dystonia, secondary parkinsonism, and tardive dyskinesia [25]. Chlorzoxazone use occurred in 1 (0.4) patient. It is a skeletal muscle relaxant with anticholinergic consequences [9]. The study highlighted the potentially inappropriate use of anticholinergics among older adults. Anticholinergics could be associated with a higher risk of delirium and in-hospital mortality in frail seniors [26].

PIM use due to drug-syndrome interactions

It occurred in 9 (3.6) patients. Medications may interact with geriatric syndromes by having a role in deteriorating these conditions [27]. Dementia and falls/fractures were the observed geriatric syndromes with PIM use. Demented patients were on anticholinergics and antipsychotics among 3 and 4 cases, respectively. Falls with a coexisting use of antidepressants and opioids were reported among 4 and 1 patient, respectively. These data alarm physicians towards screening for geriatric syndromes and the eminent need to de-prescribe PIM in frail elders.

PIM; drugs to be used with caution

Despite the acceptable use of these medications, careful observation is mandatory because of the high risk of ADEs. The study showed that 76 (30.3) patients utilized these medications. Diuretics were the most frequent medications among 62 (24.7) patients. Diuretics cause electrolyte imbalance and pre-renal azotemia. Also, certain antidepressants such as selective serotonin reuptake inhibitors (SSRI), serotonin-norepinephrine reuptake inhibitors (SNRI) and mirtazapine had been reported in 8 (3.2), 2 (0.8), and 3 (1.2) patients, respectively. These medications could induce hyponatremia in seniors [9].

Rivaroxaban use had been reported in 3 (1.2) patients. It is a new oral anticoagulant (NOAC) with a higher risk of hemorrhage compared to other NOAC [9].

Tramadol use had been reported in 3 (1.2) patients. It should be used cautiously for pain control due to the high risk of syndrome of inappropriate antidiuretic hormone secretion (SIADH). Similarly, oxcarbazepine may be related to SIADH [9].

Aspirin for primary prevention of CVD reported in 1 (0.4) patient. Aspirin is preferable for secondary prevention in geriatric patients with settled CVD [9].

Potentially clinically important drug-drug interactions

It occurred in 17 (6.8) patients. Inhibitors of the RAS with potassium-sparing diuretics represented the most frequent interaction with high risk of hyperkalemia. Also, concomitant use of corticosteroids with NSAID had reported in 4 (1.6) patients with subsequent high risk of bleeding [9].

A combination of ≥ 3 CNS-active medications appeared in 3 (1.2) patients. Simultaneous use of CNS-acting medications is frequent among elders and commonly associated with several ADEs such as respiratory tract infections, serotonin syndrome, falls and fractures [28].

Use of warfarin with a NSAID occurred in 2 (0.8) patients. The risk of hemorrhage is higher with the simultaneous use of warfarin and a NSAID as compared with utilizing warfarin alone [29].

An anticholinergic use with another anticholinergic reported in 1 (0.4) case. This combination is deleterious as taking several medications with anticholinergic consequences for different diseases is common in older adults and could be under-evaluated [30]. The total burden could be summated in the anticholinergic burden (ACB) to estimate the risk of getting ADEs such as constipation, and cognitive decline [30]. Recently, multiple scales have been used to help practitioners in estimating ACB [31]. But little evidence of ascendancy of one scale over the other has been found [32].

Medications need adjustment according to renal function

PIM use with the need for renal dose adjustments occurred in 3 (1.2) patients. Medication dose adjustment according to creatinine clearance (Cr.Cl.) is an integral part of the proper management of geriatric patients, as aging induces reduced glomerular filtration rate (GFR) that necessitates dose reduction and meticulous follow-up of renal function [33]. Spironolactone and apixaban were the reported medications in this category. Cr.Cl. according to the Cockcroft-Gault equation is a preferable estimate of renal function as GFR could overestimate kidney function in geriatric patients [33]. Accordingly; Cr.Cl. should be recognized during prescribing for geriatric patients [34].

Medications with strong anticholinergic effects

Anticholinergics antagonize the action of acetylcholine, a key neurotransmitter with prominent effects on the nervous system [30]. Geriatric patients are more vulnerable to anticholinergics [35]. Strong anticholinergics use had been occurred in 4 (1.6) patients; the culprit medications were clomipramine; tricyclic antidepressant (TCA), paroxetine; SSRI, dimenhydrinate; a first-generation H1 receptor antagonist, benztropine; an antiparkinson and olanzapine; a second-generation antipsychotic [36].

It is worth reporting that; clomipramine has stronger anticholinergic adverse effects than paroxetine. But, paroxetine has a higher affinity for muscarinic acetylcholine receptors than other SSRI [37]. Accordingly, classical TCAs should be prohibited as SSRI are safer alternatives in older adults. De-prescribing should be an integral part of the comprehensive medication management of seniors [38].

On the other side of our analysis, the study showed pre-hospitalization prescribing patterns among geriatric patients. Beta-blockers were the most frequently prescribed, followed by acetylsalicylic acid, Insulin Isophane (NPH), PPIs, loop diuretics, angiotensin-converting enzyme (ACE) inhibitors, atorvastatin, amlodipine, metformin, nitroglycerin, and hydrochlorothiazide/metolazone. These results showed that the top ten prescribed drugs were to treat CVD and metabolic disorders in line with previous studies [39,40].

Cardiovascular-acting drugs were the most commonly used drugs. It could be explained by the predominance of hypertension among 160 (63.7) patients and supported by describing heart disease as the leading cause of death in older adults worldwide [41,42]. The ranking for all the used medications among participants seemed logical and followed the prevalent chronic conditions in the study. The differences between various studies are related to socioeconomic factors and changes in the prescribing patterns of different times and settings.

Strengths and limitations

It is the first study conducted in Egypt to assess PIM use and describe prescribing patterns among older adults. The study provided a thorough description of both PIM and prescribing patterns among geriatric patients before hospitalization. It highlighted the association between PIM use and common geriatric syndromes. The study supports the international attempts to combat ADEs through promoting pharmacovigilance [43]. Limitations include its limited generalizability because of the involvement of geriatric patients at a single institute in Egypt with the inclusion of relatively small sample size, especially for particular variables such as MMSE and ADL/IADL. Also, the study was conducted on patients admitted to the hospital and did not include patients from outpatient clinics. Patients admitted to the hospital usually have more comorbidities with more polypharmacy compared to outpatients. That is why including outpatients may minimize the percentage of PIM use.

Finally, the study lacked frailty assessment and the duration of PIM use.

CONCLUSIONS

PIM use is common among geriatric patients. Polypharmacy and having a cardiac disease are predictors of PIM use. The study provides an overview of the culprit PIM and common prescribing patterns among geriatric patients. Careful medication review and de-prescribing are essential to mitigate ADEs and prescribing cascades among geriatric patients.

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Conflict of interest statement
The authors declare no conflict of interest.

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Author contributions
Both authors have considerably contributed to the study through data analysis, interpretation and manuscript writing. Khalid Elsayed Elsorady has also contributed to the study's design/conceptualization, participant's selection, data gathering/processing and manuscript drafting. Both authors read and approved the final manuscript.

Ethical consideration
The study's protocol got an approval code: FMASU R 52/2022 on 23/3/2022 from the Research Ethics Review Committee at the faculty of Medicine, Ain Shams University. The study protocol was also revised and approved by the ethical committee in the geriatrics hospital of Ain Shams University where the study was conducted.

References

1 Loddo S, Salis F, Rundeddu S, et al. Nutritional status and potentially inappropriate medications in elderly. J Clin Med 2022;11:3465. https://doi.org/10.3390/jcm11123465

2 Kucukdagli P, Bahat G, Bay I, et al. The relationship between common geriatric syndromes and potentially inappropriate medication use among older adults. Aging Clin Exp Res 2020;32:681-687. https://doi.org/10.1007/s40520-019-01239-x

3 Rochon PA, Gurwitz JH. The prescribing cascade revisited. Lancet 2017;389:1778-1780.

4 Bolt J, Park E, Wong K, et al. Retrospective cross-sectional analysis of potentially inappropriate medication use in ambulatory seniors with geriatric syndromes. Drugs Ther Perspect 2022;38:156-163. https://doi.org/10.1007/s40267-022-00904-y

5 Muhlack DC, Hoppe LK, Stock C, et al. The associations of geriatric syndromes and other patient characteristics with the current and future use of potentially inappropriate medications in a large cohort study. Eur J Clin Pharmacol 2018;74:1633-1644. https://doi.org/10.1007/s00228-018-2534-1

6 Beers MH, Ouslander JG, Rollingher I, et al. Explicit criteria for determining inappropriate medication use in nursing home residents. UCLA division of geriatric medicine. Arch Intern Med 1991;151:1825-1832.

7 Spinewine A, Schmader KE, Barber N, et al. Appropriate prescribing in elderly people: how well can it be measured and optimised? Lancet 2007;370:173-184. https://doi.org/10.1016/s0140-6736(07)61091-5

8 Kaufmann CP, Tremp R, Hersberger KE, et al. Inappropriate prescribing: a systematic overview of published assessment tools. Eur J Clin Pharmacol 2014;70:1-11. https://doi.org/10.1007/s00228-013-1575-8

9 By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. J Am Geriatr Soc 2019;67:674-694. https://doi.org/10.1111/jgs.15767

10 Folstein MF, Folstein SE, McHugh PR.'Mini mental state'. A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189-198.

11 Katz S, Ford AB, Moskowitz RW, et al. Studies of illness in the aged: the index of ADL: a standardized measure of biological and psychosocial function. JAMA 1963;185:914-919. https://doi.org/10.1001/jama.1963.03060120024016

12 Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. The Gerontologist 1969;9(3 Part 1):179-186. https://doi.org/10.1093/geront/9.3_Part_1.179

13 Assis DL, Chagas VO, Valente M, et al. Uso de medicamentos inapropriados em idosos institucionalizados: lições ainda não aprendidas. Geriatr Gerontol Aging 2016;10:126-131.

14 Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373-383. https://doi.org/10.1016/0021-9681(87)90171-8

15 de Oliveira RMA, Gorzoni ML, Rosa RF. Potentially inappropriate medication use in hospitalized elderly patients. Rev Assoc Med Bras 2022;68:797-801.

16 Alshammari H, Al-Saeed E, Ahmed Z, et al. Prevalence and predictors of potentially inappropriate medications among patients aged ≥ 65 years on hospital admissions in Kuwait. Clin Interv Aging 2022;17:1025-1036. https://doi.org/10.2147/CIA.S328693

[17] Bhagavathula AS, Vidyasagar K, Chhabra M, et al. Prevalence of polypharmacy, hyperpolypharmacy and potentially inappropriate medication use in older adults in India: a systematic review and meta-analysis. Front Pharmacol 202112:685518. https://doi.org/10.3389/fphar.2021.685518

[18] Caçador C, Teixeira-Lemos E, Oliveira J, et al. The prevalence of polypharmacy and potentially inappropriate medications and its relationship with cognitive status in portuguese institutionalized older adults: a cross-sectional study. Int J Environ Res Public Health 2022;19:2637. https://doi.org/10.3390/ijerph19052637

[19] Ramsdale E, Mohamed M, Yu V, et al. Polypharmacy, potentially inappropriate medications, and drug-drug interactions in vulnerable older adults with advanced cancer initiating cancer treatment. The Oncologist 2022;27:E580-E588. https://doi.org/10.1093/oncolo/oyac053

[20] Maes ML, Fixen DR, Linnebur SA. Adverse effects of proton-pump inhibitor use in older adults: a review of the evidence. Therap Adv Drug Safety 2017;8:273-297.

[21] Eshetie TC. Potentially inappropriate prescribing before and after initiation of medicines for dementia: an Australian population-based study. Geriatr Gerontol Int 2019;19:654-659.

[22] Liantonio JJ, Brent Simmons ŸB. NSAIDs and the geriatric patient: a cautionary tale (https://www.consultant360.com/articles/nsaids-and-geriatric-patient-cautionary-tale, accessed on 13/10/2022).

[23] Pilotto A, Franceschi M, Leandro G, et al. NSAID and aspirin use by the elderly in general practice: effect on gastrointestinal symptoms and therapies. Drugs Aging 2003;20:701-710.

[24] Aljadhey H, Tu W, Hansen RA, et al. Comparative effects of non-steroidal anti-inflammatory drugs (NSAIDs) on blood pressure in patients with hypertension. BMC Cardiovasc Disord 2012;12:93.

[25] Klotz U. Pharmacokinetics and drug metabolism in the elderly. Drug Metab Rev 2009;41:67-76. https://doi.org/10.1080/03602530902722679

[26] Luukkanen MJ, Uusvaara J, Laurila JV, et al. Effects of anticholinergic drugs on delirium and mortality. Dement Geriatr Cogn Disord Extra 2011;1:43-50. https://doi.org/10.1159/000322883

[27] Onder G, Giovannini S, Sganga F, et al. Interactions between drugs and geriatric syndromes in nursing home and home care: results from Shelter and IBenC projects. Aging Clin Exp Res 2018;30:1015-1021. https://doi.org/10.1007/s40520-018-0893-1.

[28] Musich S, Wang SS, Slindee LB, et al. Concurrent use of opioids with other central nervous system-active medications among older adults. Popul Health Manag 2020;23:286-296. https://doi.org/10.1089/pop.2019.0128

[29] Villa Zapata L, Hansten PD, Panic J, et al. Risk of bleeding with exposure to warfarin and nonsteroidal anti-inflammatory drugs: a systematic review and meta-analysis. Thromb Haemost 2020;120:1066-1074. https://doi.org/10.1055/s-0040-1710592

[30] Woodford HJ, Stevenson JM. Anticholinergic drugs and dementia: time for transparency in the face of uncertainty. Cochrane Database System Rev 2021;9:ED000154. https://doi.org/10.1002/14651858.ED000154

[31] Durán CE, Azermai M, Vander Stichele RH. Systematic review of anticholinergic risk scales in older adults. Eur J Clin Pharmacol 2013;69:1485-1496. https://doi.org/10.1007/s00228-013-1499-3

[32] López-Álvarez J, Sevilla-Llewellyn-Jones J, Agüera-Ortiz L. Anticholinergic drugs in geriatric psychopharmacology. Front Neurosci 2019;13:1309. https://doi.org/10.3389/fnins.2019.01309

[33] Wood S, Petty D, Glidewell L, et al. Application of prescribing recommendations in older people with reduced kidney function: a cross-sectional study in general practice. Br J Gen Pract 2018;68:E378-E387. https://doi.org/10.3399/bjgp18X695993

[34] Sharma R, Bansal P, Garg R, et al. Prevalence of potentially inappropriate medication and its correlates in elderly hospitalized patients: a cross-sectional study based on Beers criteria. J Family Community Med 2020;3:200-207. https://doi.org/10.4103/jfcm.JFCM_175_20

[35] Riedel WJ, van Praag HM. Avoiding and managing anticholinergic effects of antidepressants. CNS Drugs 1995;245-259. https://doi.org/10.2165/00023210-199503040-00002

[36] Chew ML, Mulsant BH, Pollock BG. Anticholinergic activity of medications. J Am Geriatr Soc 2008;56:1333-1341. https://doi.org/10.1111/j.1532-5415.2008.01737.x

[37] Fujishiro J, Imanishi T, Onozawa K, et al. Comparison of the anticholinergic effects of the serotonergic antidepressants, paroxetine, fluvoxamine and clomipramine. Eur J Pharmacol 2002;454:183-188. https://doi.org/10.1016/s0014-2999(02)02557-8

[38] Page AT, Clifford RM, Potter K, et al. The feasibility and effect of deprescribing in older adults on mortality and health: a systematic review and meta-analysis. Br J Clin Pharmacol 2016;82:583-623.

[39] Mizokami F, Koide Y, Noro T, et al. Polypharmacy with common diseases in hospitalized elderly patients. Am J Geriatr Pharmacother 2012;10:123-128.

[40] Guisado-Clavero M, Roso-Llorach A, López-Jimenez T, et al. Multimorbidity patterns in the elderly: a prospective cohort study with cluster analysis. BMC Geriatr 2018;18:16.

[41] Jackson CF, Wenger NK. Cardiovascular disease in the elderly. Rev Española Cardiol (English Ed) 2011;64:697-712.

[42] Guisado-Clavero M, Violán C, López-Jimenez T. et al. Medication patterns in older adults with multimorbidity: a cluster analysis of primary care patients. BMC Fam Pract 2019;20:82. https://doi.org/10.1186/s12875-019-0969-9

[43] Reporting and learning systems for medication errors: the role of pharmacovigilance centres, 2014 (https://www.who.int/publications/i/item/9789241507943).

SUPPLEMENTARY MATERIALS

Table SI. Ranking and frequencies of medications used before hospitalization among participants.

Rank	Drug	%
1	Beta blockers (bisoprolol/carvidilol/propranolol/atenolol/nivolol)	33.9
2	Acetylsalicylic acid	22.3
3	Insulin isophane/NPH	16.7
4	Omeprazole/pantoprazole/lansoprazole	15.9
4	Furosemide/torasemide	15.9
5	ACEIs (enalapril/captopril/ramipril)	14.3
6	Atorvastatin	11.2
7	Amlodipine	10.8
8	Metformin	10.4
9	Nitroglycerin	9.6
10	Hydrochlorothiazide/metolazone	9.2
10	Clopidogrel	9.2
11	Vitamin B12	8.4
11	Gliclazide	8.4
12	Formoterol/salbutamol	7.2
13	Glimepiride	6.8
13	ARBs (valsartan/losartan/olmisartam/irbisartan)	6.8
14	Spironolactone	6.4
14	Calcium and vitamin D	6.4
15	Apixaban	6
15	Digoxin	6
15	Levothyroxine	6
16	Doxazosin/tamsulosin	5.6
17	Warfarin	5.2
18	Trimetazidine	4.8
18	Sitagliptin/vildagliptin	4.8
19	Memantine	3.6
20	SSRIs (escitalopram/vortioxetine/paroxetine/sertraline)	2.8
20	Paracetamol	2.8
21	Prednisolone/dexamethasone	2.4
21	Amantadine	2.4
21	Enoxaparin/heparin	2.4
21	Itopride	2.4
22	Laxatives	2
22	Ivabradine	2
22	Valproate	2
23	Theophylline	1.6
23	Gabapentin/pregabalin	1.6
23	Diclofenac topical	1.6
23	Methotrexate	1.6
23	Methyldopa	1.6
24	Rivaroxaban	1.2
24	Rapid-acting insulin	1.2
24	Carbimazole	1.2
24	Iron supplements	1.2
24	Finasteride	1.2
24	Mebeverine	1.2
24	Pentoxifylline	1.2

Table SI. *continues*.

Rank	Drug	%
24	Mertazipine	1.2
24	Cerebrolysin	1.2
24	Tramadol	1.2
24	Ursodeoxycholic acid	1.2
25	Glibenclamide	0.8
25	Insulin glargine	0.8
25	Carbidopa/levodopa	0.8
25	Risperidone	0.8
25	Levetiracetam	0.8
25	Dapagliflozin	0.8
25	Allopurinol	0.8
25	Verapamil	0.8
25	Venlafaxine/duloxetine	0.8
25	Diclofenac	0.8
25	Nicorandil	0.8
25	Quitapine/olanzapine	0.8
25	Famotidine/rebamipide	0.8
26	Colchicine	0.4
26	Donepezil	0.4
26	l-ornithine-l-aspartate	0.4
26	Betahistine	0.4
26	Multi amino acids chelated antioxidant	0.4
26	Ginkgo biloba	0.4
26	Chloroxazone	0.4
26	Nystatin	0.4
26	Sotalol	0.4
26	Loratadine	0.4
26	Fexofenadine	0.4
26	Chymotrypsin	0.4
26	Denosumab	0.4
26	Benzatropine	0.4
26	Cilostazol	0.4
26	Eplerenone	0.4
26	Diltiazem	0.4
26	Verapamil	0.4
26	Venlafaxine	0.4
26	Duloxetine	0.4
26	hydroxyurea	0.4
26	Montelukast	0.4
26	Leflunomide	0.4
26	Oxcarbazepine	0.4
26	Lithium	0.4
26	Erythropoitin	0.4
26	Propafenone	0.4
26	Dimenhydrinate	0.4
26	Cinnarizine	0.4
26	L carnitine	0.4
27	Pramipexol	0