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Patterns of drug-prescribed and drug-related problems among hospitalized elderly patients

Mustafa A. Alssageer [1] *, **Fathi M. Sherif** [2] , **Esraa S. Mohammed** [1] and **Soaad A. Abd Alsalm** [1]

[1] Department of Pharmacology and Clinical Pharmacy, Faculty of Pharmacy, Sebha University, Sebha, Libya
[2] Department of Pharmacology and Clinical Pharmacy, Faculty of Pharmacy, University of Tripoli, Tripoli, Libya
*Author to whom correspondence should be addressed

Abstract: Prescribing drugs for elderly patients is not an easy task since elderly patients frequently have comorbid conditions. In Libya, there are no guidelines for the management of medications used in elderly patients and no specialized geriatric health institutions. This study aims to assess the pattern of medication use among hospitalized elderly patients in Sebha Medical Centre and the drug-related problems associated with these patterns. This report is a descriptive and retrospective cross-sectional study conducted at Sebha Medical Center in 2021. Potential drug-related problems were assessed based on the classification of Hepler and Strand. In this study, out of 195 participants, most patients have been given antibiotics (92.0%). The majority of patients have been prescribed anti-gastric agents, vitamins and anti-thrombotic agents which accounted for 75.0%, 62.0% and 55.0%, respectively. To a lesser extent, anti-hypertensive agents, analgesics and antihyperlipidemic were reported by 45.0%, 43.0% and 38.0%, respectively. Almost all the patients have at least one event of drug-related problem and more than three-quarters of the patients had more than one event of drug-related problems. The highest rate was untreated indications which were reported for 77.0% then followed by drug use without indication in nearly half of the events 48.0%. To fewer extent rates were reported: "in improper drug selection", "drug interaction" and "adverse effects" which were reported for 25.0%, 23.0% and 18.0% of the total events, respectively. Almost all elderly patients have been prescribed antibiotics, analgesics and vitamins. Drug-related problems are predominantly prevalent in the clinical practice at the center. This study highlights the importance of activation of clinical pharmacist interventions at hospitals which can contribute to reducing the chance of risk of drug-related problems events among hospitalized elderly patients and ensuring rational drug prescribing in the geriatric clinical settings.

Introduction

Pharmacotherapy is one of the essential components of geriatric care and management of elderly comorbidity diseases. Several characteristics of aging can influence the medication prescribing for them and making the appropriate selection process of their medications is an uneasy task. The study reports that elderly people use a substantial number of drugs between 4-6 drugs a day per person. Particularly for the treatment of chronic diseases, elderly patients were found to use about three times more drugs than younger patients [1]. In Libya, the first part of the present study that has been published showed that nearly two-thirds of the patients had three to five comorbidity diseases at the same time and almost all elderly patients have polypharmacy [2]. The treatment of multiple comorbidities and symptoms of elderly patients requires understanding how drugs affect the aging pharmacodynamic and pharmacokinetic aspects [3]. Optimizing the treatment based on medical guidelines in the presence of many comorbid conditions is not an easy task since elderly patients with comorbid conditions are frequently excluded from clinical trials [4] and as a consequence, the evidence coming from these studies may not be generalizable to this population [5]. Many unplanned admissions are medication-related [6] and a considerable number could be prevented [7]. The geriatric population is at high risk of drug-related problems (DRPs) due to age-related pharmacokinetic and pharmacodynamic changes, chronic disease conditions and poly-pharmacy may make elderly people respond differently than expected [8]. Inappropriate prescribing can cause substantial morbidity and represents a clinical and economic burden to patients and society [9]. Medication-related problems have been identified as the third or fourth cause of death among the elderly and can cause disability, gait disturbance and falls [10]. Therefore, drug-related problems (DRPs) are significant for the pharmaceutical care practitioner and they can occur in any phase of the medication use process. The essential element of DRPs is the impact of the problem on the health outcome of the pharmacotherapy. Thus, a DRP can be defined as an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes [11]. DRP originated from Hepler and Strand [12] who defined eight problems that could result in poorer health outcomes in an attempt to categorize DRP (**Table 1**). Inappropriate prescribing is one of the major challenges faced the physicians and it is a major concern particularly in developing countries where effective infrastructure health is often not well established. Rational drug prescribing is necessary for the elderly's health care since they are a vulnerable group of people because of the increased prevalence of comorbidities and poly-pharmacy [2]. Examining patterns of drug prescribing and identification of prescribing problems can contribute to drawing successful policies to improve the quality of prescribing and ensure medication safety. A previous Libyan study evaluated 106 elderly prescriptions from different community pharmacies according to Beers criteria and revealed that about 15.0% of the total drugs prescribed are inappropriate [13]. However, there is limited data on the pattern of drugs prescribed to elderly hospitalized patients in Libya, therefore, the aim was to assess the pattern of medication use among the hospitalized elderly patients and drug-related problems associated with such patterns.

Materials and methods

This study is a descriptive and retrospective cross-sectional study that was conducted at Sebha Medical Centre (SMC) located in the South region of Libya in 2021. A convenient sampling technique was used to select the sample size from patients records who fulfilled the inclusion criteria and were enrolled. Patient records were eligible for inclusion if the patient's age is 65 years and above. Patients with more than 24 hours of length of stay

in the hospital were included. A letter of ethical clearance was obtained from the ethical review committee of Sebha University (1/2021). Permission was also obtained from the SMC office for cooperation from the Department of Medical Records at SMC. Two independent data collectors "senior pharmacy students" were well-trained to retrieve the documentation of the medication review from the medical records. We used the standardized data extraction sheet to collect relevant information from patient medical records and data collected by trained pharmacy students using a pre-tested data collection checklist. They review the medications, medical records and laboratory data to identify and address DRPs. The sheet had three main sections patient demographics, medical history and laboratory data. The following data were recorded for each patient: age, gender, body weight, family and social histories, history of drug allergies, relevant medical and medication history, vital signs, drugs used at admission, drugs started during the hospital stay and at discharge reports, results of routine laboratory tests and the diagnosed diseases which are important for identification of drug therapy problems. Potential DRPs were assessed based on the classification of Hepler and Strand [12] as shown in this study. However, the failure to receive drugs category could not assessed since this study was s retrospective study. Two senior trained students of pharmacy for all medications used on the data of inclusion and documented on a standardized report form. The researchers were trained by professional a clinical pharmacist (principal investigator).

Table 1: Classification of drug-related problems [12]		
	Drug-related problems	**Description**
1	Untreated indication	Does the patient have an untreated medical condition or indication that may benefit from drug therapy?
2	Drug use without indication	Is the patient taking a drug for which there is no valid indication?
3	*Failure to receive drugs**	*Does the patient have a medical condition that is the result of him/her not receiving a drug*
4	Improper drug selection	Does the patient have a medical condition for which the incorrect drug is being taken?
5	Adverse drug reactions	Does the patient have a medical condition that is the result of an adverse drug reaction?
6	Drug interactions	Does the patient have a medical condition that is the result of a drug-drug or drug-food interaction?
7	Sub-therapeutic dosage	Does the patient have medical condition for which too small of the correct drug is being taken?
8	Overdosage	Does the patient have a medical problem for which too much amount of the correct drug is being taken?
* Failure to receive drugs category could not assessed since this study was a retrospective study.		

All data with prescribed medications and identification of potential DRPs by the individual researchers were reviewed, documented, categorized and entered into a data collection sheet and when necessary, adjusted by the principal investigator. Each documented drug therapy was evaluated for the presence of DRPs using standard textbooks as a pathophysiologic approach applied therapeutics: The clinical use of drugs. Medscape website is also used which provides access to medical information for clinicians. The reliability and accuracy of each drug therapy problem were assessed by the supervisor clinical pharmacist.

Statistical analysis: All data from the recorded collection sheet were classified and coded, then were fed into the computer and tabulated by using Microsoft Excel and IBM. Statistical Package for the Social Sciences (SPSS-20 software) was used and analyzed. DRPs were then classified according to Hepler and Stand classification (1990) as mentioned above in the introduction.

Results

Pattern of drug prescribed: As shown in **Table 2**, a total of 2223 prescribed drugs were dispensed to 195 elderly patients recruited in the study, corresponding to 12 drug categories. In **Table 2**, the three major groups of medications used by elderly inpatients are antibiotics (n=179, 92.0%), anti-gastric agents (n=146, 75.0%) and vitamins and minerals (n=120, 62.0%). Regarding to anti-gastric agents, the highest rate was proton-pump inhibitors (PPIs) which accounted for 65.5% (n=127) followed by metoclopramide by 29.3% (n=57) while ranitidine accounted for 06.6% (n=13). More than half of the patients (n=65, 55.0%) use antithrombotic agents and just less than half of the patients (45.0%) use anti-hypertension drugs and 43.0% use analgesics. Over one third of the patients use anti-hyperlipidemic drugs (38.0%), 37.0% use fluid supplements and 34.0% for diuretics. However, less than one-third (31.0%) use hematinic agents. The lowest types of drugs that used among elderly patients are calcium supplements (19.0%) and anti-diabetics (08.0%).

Table 2: Pattern of drug use among Libyan participants			
Drugs	Male patient	Female patient	**Total**
Antibiotics	97 (95%)	82 (88%)	**179 (92%)**
Anti-gastric agents	77 (75%)	69 (74%)	**146 (75%)**
Vitamins	70 (69%)	50 (54%)	**120 (62%)**
Anti-thrombotic agents	35 (34%)	30 (32%)	**65 (55%)**
Anti-hypertension agents	42 (41%)	46 (49%)	**88 (45%)**
Analgesics	44 (43%)	40 (43%)	**84 (43%)**
Anti-hyperlipidemic	36 (35%)	39 (41%)	**75 (38%)**
Fluid supplements	45 (44%)	27 (29%)	**72 (37%)**
Diuretics	35 (34%)	32 (34%)	**67 (34%)**
Hematinic agents	36 (35%)	25 (27%)	**61 (31%)**
Ca supplements	14 (04%)	18 (19%)	**32 (16%)**
Anti-diabetics	11 (11%)	07 (08%)	**18 (09%)**
Total	102 (52%)	93 (47.6%)	**195**
Patients may have more than one drug			

Table 3: Frequency of patients who have drug-related problems			
DRP	Male patient	Female patient	**Total**
3 - 4	34 (33%)	41 (44.0%)	**75 (38%)**
1 - 2	32 (31%)	24 (26.0%)	**56 (29%)**
5 - 6	22 (22%)	18 (19.0%)	**40 (21%)**
> 6	07 (07%)	05 (05.0%)	**12 (06%)**
00	07 (07%)	05 (05.0%)	**12 (06%)**
Total	102 (52%)	93 (47.6%)	**195**

Drug-related problem: Regarding to frequency of DRP among elderly inpatients, as is shown in **Table 3**, more than one-third of the participants (38.0%) had 3-4 DRP events. Female elderly patients have more prevalence (44.0%) compared to male patients (33.0%), followed by 29.0% of the patients who had 1-2 DRPs. Just over one-fifth of the patients held 5-6 DRPs. The lowest rate (n=12, 06.0%) was reported for having more than six DRPs. Only 06.0% (n=12) of the participants were not exposed to any event of DRPs. Moreover, nearly two-thirds of the participants (n=127, 65.0%) had at least three DRPs. In general, the mean number of DRPs was 2.9 which nearly close to three events per patient.

Drug-related problems: **Table 4** shows the most commonly identified DRPs. From 195 participants, there were 407 events of DRPs and nearly equal ratio between genders. The highest rate was untreated indications which was found in 155 patients (77.0%) from the total events of untreated indications (306). In this category, over one-third of the events 113 (37.0%) were untreated electrolyte imbalances followed by untreated anima in (18.3%) of untreated indication conditions. Over one tenth of untreated conditions (n=33, 10.7%) were diabetic patients. Minority of untreated conditions reported with hypertension (n=18, 05.8%), thrombocytopenia (05.5%), fever (03.5%) and hypotension (n=10, 03.2%). The second highest DRP category was drug use without indication which was reported in about half of the patients 48%. Prescribing of antibiotics without clear indication was the majority which was represented by 157 patients (84.4%) of the total events (n=186) of this category (**Table 5**).

Table 4: Drug-related problems identified by the patients			
Drug-related problems	**Male patients**	**Female patients**	**Total**
Untreated indication	83 (81%)	68 (73%)	**151** (77%)
Drug use without indication	57 (56%)	36 (39%)	**93** (48%)
Improper drug selection	25 (25%)	24 (26%)	**49** (25%)
Drug interaction	13 (13%)	31 (33%)	**44** (23%)
Adverse reaction	11 (11%)	25 (27%)	**36** (18%)
Overdosage	10 (10%)	09 (10%)	**19** (10%)
Subtherapeutic dosage	07 (07%)	08 (09%)	**15** (08%)
Failure to receive drugs	00 (00%)	00 (00%)	**00** (00%)
Total	206 (50.6%)	20 (49.4%)	407 events

In **Table 5**, to a lesser extent rates of cases under the category of improper drug selection (n=54, 17.6%) were reported from the total drug-related problems. Out of these 54 cases, 15 cases represent prescribing ranitidine and five cases use oral hematinic agents. Potential drug interaction cases accounted with 54 patients (17.6%) of total DRP events including 45 cases where a potential risk of bleeding due to the use combination of anti-platelet agents. For category adverse effect cases, they were found to be 12.7% (n=39). Hyponatremia or a dry cough (n=15) and hypotension (n=09) cases could be associated with angiotensin-converting enzyme inhibitors and furosemide, respectively. Minority events were represented among overdosage (23, 07.5%) as prescribing aspirin 300 mg as a tablet represented seven cases or metoclopramide eight cases. Similarly, the rate of sub-therapeutic dosage was reported by 03.2% (n=10) for instance normal doses for end-stage renal failure and three cases of low doses of atorvastatin based on lipid profile data.

Table 5: Types of drug-related problems associated with their causes			
Drug-related problem	**Example**	**n**	**Details**
Drug without indication	Antibiotics	157	Mostly ciprofloxacin & metronidazole
	Others	11	Tranexamic acid, diazepam & nystatin
	Total	**186**	
Inappropriate drug selection	Ranitidine	15	Outdate regime
	Oral hematinic agents	05	Must be replaced by blood transfusion
	Others	24	Metformin & ACE
	Total	**54**	
Untreated diseases	Anemia	56	
	Hyponatremia	45	
	Hypocalcemia	34	
	Diabetes mellitus	33	
	Hypokalemia	21	
	Hypertension	18	
	Hypotension	10	
	Fever	11	
	Thrombocytopenia	17	
	CVA	09	
	Infection	06	
	Hyperkalemia	05	
	Hypernatremia	05	
	IHD	05	
	Diarrhea	05	
	Prostatic hyperplasia	04	
	Others	16	Constipation & hypercalcemia
	Total	**306**	
Adverse effect	ACEIs	15	Causes hyponatremia or dry cough
	Furosemide	09	Causes hypotension
	Others	15	Thrombocytopenia
	Total	**39**	
Drugs interaction	Risk of bleeding	45	Due to more than an anti-platelet
	Others	09	Risk of bradycardia when given carvidol with bisoprolol & digoxin
	Total	**54**	
Overdose	Aspirin	07	Aspirin dose needs to be adjusted
	Metoclopramide	08	Metoclopramide needs to be decreased in dose according to GFR
	Others	08	Insulin, azithromycin & ciprofloxacin
	Total	**23**	
Subtherapeutic doses	Furosemide	07	
	Atorvastatin	03	Needs to be adjusted
	Total	**10**	

Discussion

Evidence suggests the use of drugs in elderly people is often inappropriate partly because of the complexities of prescribing, patient, provider, and health-system factors. Antibiotic is frequently prescribed among hospitalized elderly patients [14]. Consumption of antibiotics by the elderly population is up to 45.0% with a significant rise over the past decades [15]. Accordingly, this study revealed the highest category compared with other drugs with the majority of elderly patients prescribed antibiotics. The high rate of antibiotic use observed may be due to the

absence of standard protocols or guidelines for antibiotic use. PPIs class exerts a greater acid-suppressing effect than other traditional therapies [16]. There has been a significant increase in the use of PPIs over the last 15 years, particularly, in the older population [17]. This suggests a high number of drugs per prescription led to an increased prescription of these gastrointestinal drugs to avoid gastric irritation. In this study, nearly two-thirds of the patients had received PPIs during their stay. However, inappropriate PPI use is of great concern, especially in the elderly, who are often affected by multiple comorbidities and polypharmacy. Thus, this long-term PPI among the elderly can increase the risk of adverse outcomes and DDIs [18]. Previously, the main inappropriate indication of PPIs was prophylaxis of gastrointestinal bleeding in low-risk patients [19]. As the use of drugs with potential gastrointestinal toxicity is associated with the prescribing of various drugs, it is perhaps not surprising that PPI is associated with polypharmacy, appropriate or inappropriate. The elderly are at a high risk of developing nutritional deficiencies due to low dietary intake or impairment in the mechanism of absorption or failure to convert to active forms [20]. This trend of deficiency of vitamins could be consistent with the high prescribing rate of vitamins for two-thirds of the population.

Positive correlation between dyslipidemia and heightened CVD risk [21, 22] which increases significantly with the increase of age [23]. Currently, 15.0% of the population have hyperlipidemia, 35.0% with heart disease and a similar rate for patients receiving antihyperlipidemic. Certain studies demonstrated that treatment with statins reduces CVD events and mortality rates with well-tolerated in the elderly [24, 25]. 40.0% of elderly patients have diabetes mellitus [2]. In contrast, the patients who documented taking anti-diabetic oral hypoglycemic agents or insulin were low. This can be justified by the fact that diabetic inpatients are always under direct surveillance and treatment. Health practitioners usually suppose patients were already taking diabetes drugs even though the medical records miss this information in the file. This inconsistency may reflect the non-observance of the complete recording of all medical information among clinicians. Missing information on pharmacotherapy will negatively influence patients' therapy and expose them to DRPs and medication errors.

The elderly population is at greatest risk for DRPs due to age-related pharmacological changes, multi-comorbidity and poly-pharmacy [8, 26]. Any symptom in a patient should be considered as a drug side effect until proven otherwise [27]. In this study, most patients have one DRP and every patient had an average of two which is in line with other studies [28-30]. DRPs are associated with increased healthcare costs and hospital admission, prolonged hospital stays and reduced quality of life with increased mortality [31, 32]. The most common DRP is an untreated condition accounting for 50.0% out of the total DRPs with a prevalence rate of 75.0%. A similar trend of incidence of inappropriate treatment that required additional therapy has been reported [33] with less extent in India's study [34]. This high prevalence rate can be explained by a high burden of comorbidity and could be illustrated that physicians are more likely to focus on major conditions and give less attention to minor conditions. As mentioned, 35.0% of the patients have an infection. About half of the antimicrobial agents prescribed to hospital in-patients are considered inappropriate [35]. The inappropriate use of antibiotics contributes to the emergence and spread of antimicrobial resistance [36]. Patients with hyperlipidemia and on statins are in line with others [37]. It is important that elderly patients establish successful plans for prevention and reducing risk factors or need intensive treatment of dyslipidemia to prevent recurring complications [38].

Drug use without indication phenomenon was stated in developing countries [39]. The unnecessary drug therapy problems frequently tend to be overlooked in polypharmacy prescribing. In Jimma University's specialized hospital, polypharmacy was the only independent predictor for unnecessary drug therapy [40]. The prevalence rate of drug use without indication is more frequent than problems due to the prescribing of drugs for elderly patients [41]. Drug use without indication was the second DRP occurrence among our population. Nevertheless,

health practitioners are often not fully updated with their patient's actual medication use [42, 43]. Physician prescribing errors can arise from the choice of the wrong or improper drug selection when prescribing ineffective drugs where more effective drugs available. In this study, prescribed drugs were under improper drug selection and its prevalence rate is 25.0%. Evidence found that omeprazole is significantly more effective than ranitidine in gastritis and heartburn [44] and normalized physiological well-being [45]. Thus, older drugs tend to be less expensive and this may be a factor in drug selection. Inappropriate polypharmacy occurs when patients use or are prescribed more medicines than are clinically indicated [46]. Beer's criteria provide evidence-based recommendations on medications that healthcare providers should pay attention to, as these medications are probably not the most appropriate, safest or best choice for patients of 65 years and above [47].

In this study, 25.0% of the patients have potential DDI between their prescribed drugs during hospitalization. This is in line with studies that reported 25-50% clinically relevant potential DDIs in elderly patients [42, 48]. DDIs present unfavorable outcomes causing 03.0% of all hospitalizations of older patients and costing the healthcare system more than U$ one billion [49, 50]. Concomitant administration of anticoagulant and antiplatelet therapies increases the risk of bleeding [51]. COMPASS study indicated that dual antiplatelet combination therapy significantly reduces the incidence of adverse CVD events. The bleeding events that occurred is significantly more among the patients who treated with combination therapy [52]. It is especially difficult to obtain therapeutic benefit that outweighs the risk of bleeding from the concurrent use of antithrombotic drugs, since the tendency of bleeding increases with advanced age. DDIs are more likely to happen in the elderly because they tend to use multiple medications and have altered pharmacokinetic aspects [53]. Evidence shows an increasing risk of potential DDIs with increasing use of prescribed medication [53]. Advanced age is associated with increased risk of acquiring ADR [54], more than half of all the hospitalizations due to ADR occurred in elderly patients [55]. Polypharmacy increases the risk of DDIs and ADRs [56], thus, increasing with number of drugs used [57]. Currently, 20.0% of the patients have potential adverse effects from their drug received in hospital and from all drugs prescribed. However, even adherence to these guidelines of treatments still may cause reactions particularly in patients with hypotension [58]. Accomplishing full understanding the adverse effects by using why, how and where could help clinicians choose appropriate interventions to reduce occurring and preventable side effects. One possible cause of complications of preventable side effects is that once the medication is initiated, it is not always regularly reviewed and titrated to adjust prescribed drugs for physiological changes in the elderly and DDI of concurrent drugs [59].

Based on fact that renal function falls with increasing age [60], the elderly should be considered as renal insufficient patients. Unsuitable dosing or frequency of administration is considered to be responsible for medication errors with overdosing being a significant problem [61]. In this study, 10.0% of the patients have over-therapeutic doses. The over-therapeutic doses in metoclopramide in patients needed to be decreased to 50.0-75.0% according to the patient's GFR. Drug dosing in renal insufficiency needs to be individualized whenever possible to optimize therapeutic outcomes and minimize toxicity. The use of aspirin to prevent the development of CVD is associated with the development of gastrointestinal ulcers [62]. Indeed, a systemic review study reported that low-dose aspirin increases the risk of major bleeding [63]. In Iran, most prescribing errors happened during selecting drug dose and frequency [64]. The disquiet from prescribing overdose to the patient leads to under-dosing of the drug which undermines and exploit the full potential of the particular drug. Unnecessary decreases in dosage may result in under-treatment or changing to an alternate drug with a narrower therapeutic index and lower efficacy. In this study, 10.0% of the patients have sub-therapeutic doses. Out of half of these cases, seven patients with advanced CKD, were taken the furosemide dose that is normally given to patients with

normal GFR. The threshold dose of intravenous furosemide is 10 mg in a population with normal renal function. This increases to 80-160 mg in patients with declining renal function [65]. Hence, furosemide doses lower than 80 mg are not effective in advanced CKD patients.

In Libya, there are no active local guidelines for the management of medications for elderly patients, no specialized geriatric health institutions and no specialized physicians in geriatric medicine. The traditional relationship between physicians and pharmacists is no longer to ensure rational prescribing and adherence to clinical guidelines of therapy particularly in clinical settings. Pharmacist interventions are nowadays considered valuable input in the elderly care process by rationalizing pharmacotherapy and reducing medication errors [66]. Pharmacists can improve the quality of drug prescribing [29, 67]. However, Libyan pharmacists as health providers represent potential, currently underused for optimizing drug use. Professional healthcare in certain developing countries lacks local working guidelines assessing the potential of inappropriate drugs. Palestine study demonstrates that physicians and pharmacists have relatively low awareness about appropriate medications for elderly patients [68]. This study highlighted the importance that clinical pharmacists should be enabled to engage in hospital medical teams for the treatment of geriatric inpatients to optimization pharmacotherapy. The optimizing of clinician prescribing can be achieved as a result of the physician accept recommendations introduced by clinical pharmacists and scientifically dealing with these suggestions in his/her medical practice. Professional cooperation between all healthcare providers is essential to the delivery of personalized and effective patient services [69].

Conclusion: Antibiotics, analgesics, and vitamins are the commonly prescribed medications for Libyan elderly patients. DRP predominant prevalence in clinical practice in Libya. Pharmacists should actively participate and intervene in clinical activities to reduce the incidence of DRPs in clinical settings. Clinical pharmacists can reduce the chances of experiencing DRPs and ensure patients receive effective, safe and efficient drug therapy. The hospital committee should encourage pharmacists to make an effort regarding medication use. This study can serve as a data-base for researchers and academic institutions for geriatric medication appropriateness. It may also help different healthcare providers to minimize the burden of DRPs and their consequences.

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