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Polypharmacy and inappropriate prescribing in elderly patients: a retrospective study at Buriadah Central Hospital, Saudi Arabia

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Abstract. – OBJECTIVE: An increase in life expectancy has been attributed to better access to health care and viable treatment options for diseases where there were none before. However, a multiple-drug regimen increases the risk of inappropriate prescription and drug-related problems. This study aimed to investigate polypharmacy and inappropriate prescription among elderly patients in the Qassim region of Saudi Arabia.

PATIENTS AND METHODS: This was a retrospective study wherein the electronic files of patients aged ≥ 60 years were reviewed and investigated for polypharmacy and inappropriate drug prescription using Beer's criteria 2019.

RESULTS: The 1123 patients who met the eligibility criteria were between 60-102 years of age (mean age: 71.9 years). 387 patients (34.46%) used five medications, while the remaining patients used more than five medications. The prevalence of potentially inappropriate medications (PIMs) was 66.25%. The most commonly prescribed PIMs were non-steroidal anti-inflammatory drugs, baclofen, proton pump inhibitors, diuretics, and aspirin (11.3%, 10.6%, 10.1%, 8.46%, and 5.6%, respectively).

CONCLUSIONS: This study showed a high prevalence of polypharmacy, which consequently led to a high prevalence of PIMs. This is a serious health problem in the elderly population and should be prevented or tackled with caution.

Key Words:
Geriatric, Aging, Life-expectancy, Saudi Arabia, Retrospective study, Beer's criteria, Adverse drug events.

Introduction

Defining 'elderly' is not as straightforward as it seems. Global discussions and debates have taken place regarding the definition. There is global variation in the definition as there are no distinct signs or specific characteristics to look for while identifying someone as elderly[1]. Some countries have chosen the retirement age as the start for classifying the elderly population, while others have selected a specific age. In this research, 'elderly' refers to those aged 60 years and older.

With reference to the above definition, it is clear that the world population is aging, with an increase in the number of older adults worldwide[2]. It is predicted that the number of elderly people aged 60 years and older will double worldwide in the next three decades[3]. In Saudi Arabia, the number of people aged 60 years and over was 1.1 million in 2010, representing 3% of the total population. However, the percentage of the elderly population is expected to reach 9.5% and 18.4% by 2035 and 2050, respectively. In addition, by 2050, people aged 80 years, or more are projected to comprise 4% of the total population of Saudi Arabia[1]. This presents a real challenge as older people are a vulnerable group, often with co-morbidities and multiple prescriptions. Prescribing for older people becomes challenging considering the physical and functional changes related to aging and the accompanying health problems.

The increase in life expectancy has been associated with better access to health care and treatment for many diseases. This has resulted in more elderly patients with multidrug regimens prescription for different conditions. The use of many drugs (at least five types of drugs) in a single patient has been termed 'polypharmacy'. Although the term polypharmacy has variable definitions, the most commonly used is the previously mentioned definition[4].

Polypharmacy has become an issue in the majority of the elderly population. It is estimat-

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ed that 90% of people aged 60 years or over have one or more chronic conditions. Therefore, it can be argued that polypharmacy in the elderly is inevitable, given the existence of multiple medical conditions. With polypharmacy, prescribing cascades are more common as duplicative prescribing is prevalent within the same drug class. This may lead to the need to treat symptoms caused by unrecognized drug adverse effects with more drugs. Additionally, compliance becomes more challenging for older people with polypharmacy. This non-compliance with prescribed medicines may lower the therapeutic effectiveness of medication and lead to negative clinical consequences[5,6]. Often, when non-compliance is not recognized, the chance of potentially inappropriate prescribing (PIP) increases. Adverse drug reactions may occur as the physician may increase the dose of the currently prescribed medicines or prescribe an additional drug[7,8]. PIP is 82% in patients using seven or more drugs, 38% in those taking four, and 13% in those taking two simultaneously[9].

Despite growing evidence that polypharmacy increases drug-drug, drug-disease interactions risks and adverse drug reactions, treating multiple chronic diseases concomitantly using several drugs is in practice[10-12]. It is quite clear that older populations are more at risk of drug-drug interactions (DDIs) and PIP[13,14].

Inappropriate prescribing is the use of medications that carry more risk than benefit, especially when safer choices exist[15]. It encompasses the irrational use of dosing, dosage forms, or duration, and the prescription of medicines with serious drug-drug and drug-disease interactions[16]. PIP was reported to introduce a significant adverse drug-related event risk, with an equally or more effective alternative medication[17]. Studies show that PIP is becoming a major health burden, with global prevalence ranging from 13 to 35%[18]. This high prevalence rate poses serious health threats as well as drains limited health resources, especially in developing countries.

Unfortunately, despite all these facts, research focusing on this issue in Saudi Arabia is still limited[19]. This highlights the need for more research exploring PIP rates, especially considering the growing elderly population in Saudi Arabia. Therefore, this study was conducted to fill this important literature gap by assessing inappropriate prescribing in elderly patients at Buriadah Central Hospital (BCH).

Patients and Methods

Study Design and Participants

To tackle polypharmacy and inappropriate prescribing problems in the elderly, tools were developed to alert clinicians concerning patients at risk of drug-related problems[20]. Beer's criteria are one of the most common tools used to assess inappropriate prescriptions in the elderly. The Beer's Criteria is a list of potentially inappropriate medications (PIMs) to be avoided by older adults in most circumstances or under specific situations. It is a list of medications considered inappropriate in elderly patients because they are unnecessary, ineffective or bear a high risk for adverse events. In this study, Beer's criteria 2019 were used to determine the characteristics of inappropriate prescribing in elderly patients at BCH. All the medications found in patients' charts were checked against Beer's criteria. Any identified PIMs were examined for each patient, and their use was considered when a patient's record contained one or more. PIMs include drug-disease or drug-syndrome interactions that may exacerbate the disease or syndrome in older adults. They include drugs to be used with caution, drug-drug interactions and medications that should be avoided or have their dosage reduced with varying levels of kidney function and drugs with strong anticholinergic properties.

A retrospective study was conducted at BCH, and the BetaCare register database was used for data collection. BetaCare is a hospital electronic health record at BCH. A convenience sampling method was adopted for conducting this study. BetaCare was used to search for eligible patients. The inclusion criteria were patients aged $\geq$ 60 years who visited outpatient clinics in BCH with five or more medications during the study period. The search was conducted from November 1, 2017 to April 20, 2018. The search settings for BetaCare software were from November 1, 2017 to April 30, 2018, sex, nationality, and age $\geq$ 60 years. The exclusion criteria were any patients with missing demographic or medication data, patients < 60 years old, or using less than five medications. The study has received ethical approval from Qassim Research Ethics Committee, Saudi Arabia (No. 20181006 Dated: 11/10/2018).

Procedure

Data concerning drugs used per patient, sex, age, and diagnoses were extracted from the 1123 eligible medical records. The data were entered

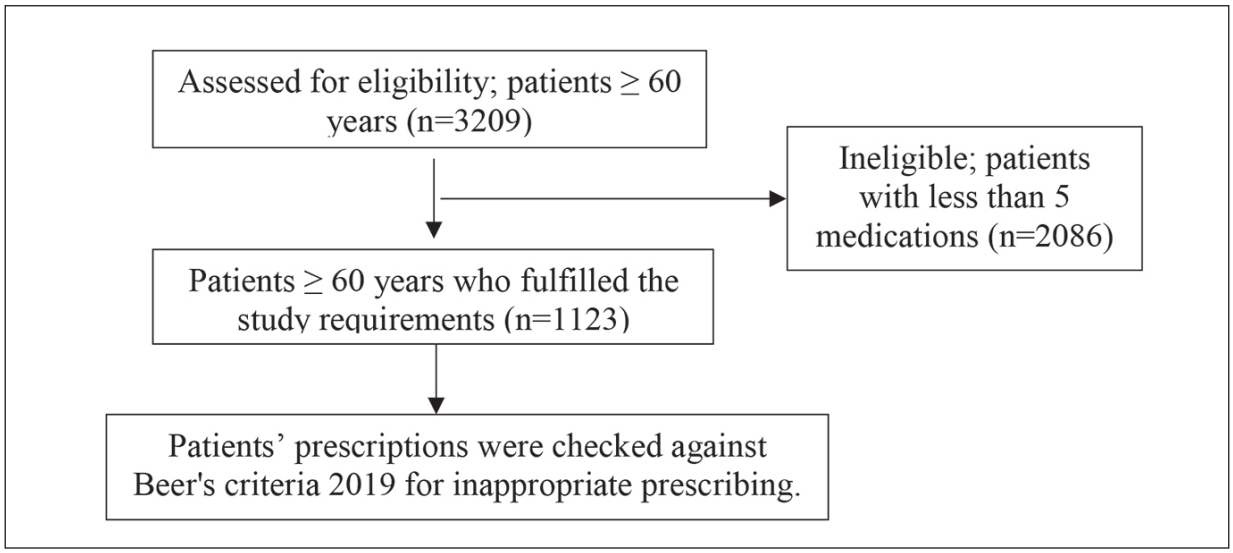

Figure 1. Sampling pathway.

into the data collection form, and polypharmacy frequency and the characteristics of inappropriate prescriptions in elderly patients were determined. The prescriptions of 1123 patients were evaluated for the occurrence of inappropriate medication prescriptions. The process was completed by checking the drugs written against Beer's criteria.

Statistical Analysis

The collected data were keyed into a database using MS Office Excel (2007) (Microsoft, Redmond, VA, USA) and exported to IBM SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Descriptive analysis of the demographic data, diagnoses, and number of drugs per prescription was conducted. A Chi-square test of independence was conducted between sex and the number of medications used. Somer's Delta (Somer's d) test was conducted to measure the association between the number of medications used, age categories, and the number of diseases. Statistical significance was defined as a two-sided $p<0.05$. All statistical analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA).

Results

The medical records of 3209 elderly patients indicated that 1123 patients were taking ≥ 5 medications (34.9%) (Figure 1), and the files of these patients were investigated. The following information was extracted: age, sex, diagnoses, and used medications.

The patients in this study were aged 60–102 years, with a mean age of 71.90 years. Women represented 53.07%, while the remaining patients were men (46.93%). 187 patients (34.46%) used five medications, while the remaining 736 patients used more than five medications (65.54%). The highest number of medications used by one patient was 11, with a mean of six medications per patient. Patient characteristics are shown in Table I.

The most common diagnoses were hypertension, osteoarthritis, diabetes, bronchial asthma, and osteoporosis. Cardiovascular diseases were predominant, followed by musculoskeletal, endocrine, and pulmonary disorders. The most common diagnoses are presented in Table II.

Inappropriate Prescribing as per Beers Criteria 2019

The prevalence of PIMs was 66.25%. The most frequently encountered PIMs prescribed were non-steroidal anti-inflammatory drugs (NSAIDs), baclofen, proton pump inhibitors, diuretics, and aspirin (17.1%, 16%, 15.2%, 12.8%, and 8.47%), respectively. The prevalence of PIMs is shown in Table III.

Table I. Patient characteristics for the retrospective phase of the study.

Category	Frequency	Percentage (%)
Age (Mean ± SD)	71.90 ±8.948	
60-70	551	49
71-80	387	34.5
81-90	138	12.3
91-105	47	4.2
Sex		
Female	596	53.1
Male	527	46.9
Number of medications per patient		
5	387	34.5
6	413	36.8
7	216	19.2
8	84	7.5
9	17	1.5
10	5	0.5
11	1	0.1
Number of diagnosed diseases per patient		
1	493	43.9
2	534	47.6
3	96	8.5

Moreover, some patients were prescribed medications that interacted with their health status. Examples of such interactions include medication prescriptions that are not recommended or include unadjusted doses for patients with renal, hepatic, or heart failure. NSAIDs comprised 36.9% and 15.36% of medications prescribed to patients with renal and heart failure, respectively. Details of the results are listed in Table IV.

In addition, some patients were prescribed medications that had clinically important drug-drug interactions. Most of these interactions involved NSAIDs and anticholinergics. The details are presented in Table V.

In addition, spironolactone 15%, ranitidine 18.8%, and pregabalin 18.2% orders were prescribed at unadjusted doses for patients with renal impairment. These details are presented in Table VI.

Inferential Statistics

Chi-square test of independence between sex and the number of medications used showed a value of $\chi 2 = 6.356$ (p=0.499). Somer's d test of the association between the number of medications used (as the dependent variable) and age categories showed d=0.01 (p=0.718). For the number of diseases, the value was d=0.295 (p<0.001). From the results mentioned above, a statistically significant association was observed between the number of diseases and the number of medications. Details of inferential statistics are presented in Table VII.

Discussion

Polypharmacy is a common phenomenon in elderly patients in BCH, and more than one-third of elderly patients were on polypharmacy regimens (35%). The average number of medications used by the patients was six[21]. The mean number of medications was low compared with other studies, because this study was conducted in a general hospital with limited specialized service scope.

There are many reasons for polypharmacy among the elderly. In this study, the most important risk factors were increased age and the presence of comorbidities. The greater the age and number of diseases, the more prescribed drugs. Thus, aging and comorbidities increase the likelihood of polypharmacy in the elderly. Diseases highly prevalent in the elderly, such as cardiovascular diseases, diabetes, renal failure, asthma, and musculoskeletal disorders, are significantly correlated with polypharmacy. Most of these diseases require multiple drugs for treatment or prophylaxis. Patients with diabetes, hypertension, heart failure, and osteoarthritis require a minimum of eight different drugs[22].

The findings support other studies[22-24] linking increased age and the number of medications with polypharmacy and drug-related problems after adjusting for age, sex, and comorbidity. Nonetheless, some studies have found that female patients had a marginally higher risk of polypharmacy and potentially inappropriate drug use than their male

Table II. The most common diagnoses obtained from patients' medical records.

Category	Frequency	Percentage (%)
Cardiovascular disorders	699	37.7
Musculoskeletal disorders	547	29.5
Endocrine disorders	268	14.4
Pulmonary disorders	182	9.81
Neurological disorders	51	2.75
Renal disorders	28	1.51
Genitourinary disorders	26	1.4
Haematological disorders	10	0.54
Gastrointestinal disorders	29	1.56
Dermatological disorders	6	0.32
Ent disorders	8	0.43
Eye disorders	2	0.11
Total	**1856**	**100**

Table III. The most encountered potentially inappropriate medications according to Beer's criteria.

PIMs	Frequency	Percentage (%)
NSAIDs	127	17.1
Baclofen	119	16
Proton Pump inhibitors	113	15.2
Diuretics	95	12.8
Aspirin (as antiplatelet)	63	8.47
Glibenclamide	47	6.32
Digoxin	36	4.84
Metoclopramide	31	4.17
Chlorpheniramine	28	3.76
Diphenhydramine	23	3.09
Hyoscine	18	2.42
Amiodarone	11	1.48
Amitriptyline	7	0.94
Nitrofurantoin	6	0.81
Haloperidol	5	0.67
Indomethacin	5	0.67
Dabigatran	4	0.54
Prazosin	2	0.27
Chlorzoxazone	2	0.27
Regular Insulin	1	0.13
Carbamazepine	1	0.13
Total	**744**	**100**

counterparts. However, the present study indicated no difference between the sexes[25].

Inappropriate prescribing exacerbates polypharmacy in the elderly. In this study, the prevalence of PIMs was 66.25% and NSAIDS 17.1%, baclofen 16%, proton pump inhibitors 15.2%, diuretics 12.8%, and aspirin 8.47%. The prevalence of PIMs was relatively high. Nonetheless, this rate is comparable to that reported in other studies[26,27]. Alturki et al[26] conducted a study at the Family and Community Medicine clinics in Riyadh, Saudi Arabia, to determine the prevalence of PIMs. The study reported that 60.7% of elderly patients use at least one PIM. They found that PPIs, diuretics, NSAIDs, and aspirin were the most common PIMs. Alhawassi et al[27] reported similar findings. They noted that the prevalence of PIMs to be avoided was 57.6%, while the prevalence of PIMs to be used with caution was 37.5%. The most commonly prescribed PIMs were diuretics, antidepressants, and gastrointestinal and endocrine agents[28].

Moreover, inappropriate prescriptions for patients with renal/heart failure, NSAIDS constituted 36.9% and 15.36% of the medications prescribed. NSAIDs are medications that are known to worsen heart/renal failure[26]. This scenario has been evident in patients with heart/renal failure who also had osteoarthritis. The prevalence of NSAID use in elderly patients is as high as 95% in general practice settings[27]. Therefore, caution should be exercised when prescribing this group of medications to patients with renal/heart problems.

Another common issue in prescribing for the elderly is the possibility of overdosing medications in patients with renal failure. The pharmacokinetics of many medications are worsened because of decreased renal function and age. Chronic kidney diseases affect renal elimination function. Thus, medications are not properly cleared, which results in a significant accumulation of them. When a drug accumulates, there is an increase in the risk of toxicity and side effects. Therefore, adjusting doses according to individual capacity to clear medications is essential for safe prescribing[29].

In this study, 33.5% of medications prescribed to patients with renal impairment were not adjusted according to the patients' creatinine clearance. The culprits were ranitidine, pregabalin, and spironolactone. The elimination half-life of ranitidine in patients with renal impairment is approximately three times greater than that in healthy patients. Therefore, ranitidine dose reduction is important

Table IV. Summary of potentially clinically important drug that should be avoided in older adults because they interact with their health status.

Disease	PIMs	Frequency	Percentage (%)
Renal Insufficiency	Ibuprofen	20	11.36
	Meloxicam	29	16.48
	Celecoxib	16	9
	Acyclovir	3	1.7
Total		**68**	**38.54**
Heart Failure	Naproxen	22	7.86
	Meloxicam	16	5.7
	Celecoxib	5	1.79
Total		**43**	**15.36**

Table V. Summary of potentially clinically important drug-drug interactions that should be avoided in older adults.

Drug	Interacting drug	Frequency	Percentage (%)
Baclofen	Hyoscine	23	19
Baclofen	Chlorpheniramine	18	15
Warfarin	Naproxen	15	13
Prednisolone	Ibuprofen	11	9.2
Prednisolone	Naproxen	12	10
Diphenhydramine	Chlorpheniramine	11	9.2
Meloxicam	Prednisolone	9	7.5
Warfarin	Meloxicam	8	6.7
Memantine	Amitriptyline	4	3.3
Warfarin	Amiodarone	4	3.3
Amitriptyline	Tolterodine	3	2.5
Memantine	Citalopram	2	1.7
Total		**120**	**100**

when renal function declines[30] In addition, pregabalin doses should be decreased by approximately 50% for each 50% decline in creatinine clearance to avoid drug accumulation and toxicity[31]. Similarly, high doses of spironolactone induce hyperkalaemia and can deteriorate renal functions[32].

Other studies[33,34] have reported similar findings. Cardone et al[33] found that 36% of elderly patients were prescribed medications at unadjusted doses based on the estimated glomerular filtration rate. Another study[35] was conducted on 573 patients with impaired renal function with a mean age of 80 years. They found that more than 30% of medications prescribed were either contraindicated, not recommended or at doses considered inappropriate.

Additionally, besides the importance of appropriate prescription in terms of drug selection and dosing, clinicians should be aware of any DDIs. Sometimes, drugs are carefully selected for the right patient at the right dose; however, interaction with other medications is often overlooked[33]. Considering comorbidities, the elderly is more susceptible to drug interactions because of age-related changes, an increased risk of diseases, and increased medication use[36]. Patients taking five or more medications had a four times higher risk of DDIs[37]. A study[38] from Brazil found that the risk of DDIs when patients were taking 2-3 medications was 39%. Also, they found that the risk reached 100% for patients taking 6-7 medications. One study[39] claimed that more than 30% of elderly hospitalized patients experienced at least one potential DDI. Another study by Teka et al[40] reported that, among 160 hospitalized patients, more than 200 DDIs were detected. Among them, 12% were major interactions, 7.5% were moderate interactions, and the remaining were minor interactions[37]. Although not every DDI is clinically important because not every interaction translates into clinical effect. Some interactions are very serious and require prompt intervention when the following medication groups are involved: NSAIDs, warfarin, amiodarone, and benzodiazepines[41].

In this study, NSAIDs and anticholinergics were the most frequently detected DDIs. NSAID interactions increase the risk of peptic ulcer disease or gastrointestinal bleeding, while anticholinergic interactions increase the risk of cognitive decline. Other interactions involved antidepressants and antipsychotics, which increased the risk of falls and fractures. In clinical practice, the effect of drug interactions often remains unidentified, as symptoms may be linked to underlying diseases rather than interactions[13].

Therefore, healthcare providers involved in medication orders should be vigilant when prescribing, monitoring, and dispensing medications to elderly patients. Inappropriate prescriptions can

Table VI. Summary of potentially clinically important drugs that should be avoided or their dosage reduced in older adults with varying levels of kidney function.

Drug	Creatinine Clearance	Frequency	Percentage (%)
Ranitidine	> 50 mL/min	32	15
Pregabalin	> 60 mL/min	19	18.8
Spironolactone	> 30 mL/min	8	18.2

Table VII. Inferential statistics.

Association	Value of test statistic	*p*-value (2-sided)
Age categories and number of medications (dependent variable)	d = 0.010	0.718
Number of diseases and number of medications (dependent variable)	d = 0.295	<0.001*
Gender and number of medications	$\chi^2 = 6.356$	0.499

* Statistically significant results.

be minimized by implementing double checks. Integrating interactions and dosing alerts through the hospital electronic system is an effective way to avert prescribing errors[40,42-44]. The hospital electronic system (BetaCare) enables physicians to revise all patients' medications to avoid unnecessary prescribing or at least prescribe the least harmful agents. However, the system is not efficiently utilised by the prescribers. One contributing factor is that patients are usually treated by different clinicians from different specialties. Thus, optimal multidisciplinary care for elderly patients requires effective physician–physician communication and efficient electronic medical records to avoid discrepancies in patient care[45].

It is worth noting that all patients enrolled in the cohort were Saudi. This can be attributed to the fact that non-Saudi residents are mainly in Saudi Arabia for employment. Hence, they are more likely to be younger than 60 to continue working. Another reason is that almost all non-Saudi workers are covered by medical insurance. Thus, their primary point of care is the private sector.

The data and findings of this study should be interpreted in the context of important limitations. One limitation of this study is its monocentric and time-limited study design. Furthermore, the study was conducted in a hospital that lacks cardiac, oncology, psychiatric, and obstetrics/gynaecology services. However, the patients' profiles did not differ from those visiting or enrolling in other tertiary care hospitals. Therefore, the sample is representative of this population.

Another limitation of this study is that we did not account for over-the-counter drugs and herbal medicines, which might be considered inappropriate or deemed responsible for DDIs.

Conclusions

In conclusion, this study showed a high prevalence of polypharmacy, leading to a high prevalence of PIMs in elderly patients. This serious health problem needs to be avoided or dealt with caution. Elderly patients are fragile and vulnerable to drug-related problems. Thus, their medications should be reviewed with the intention to de-prescribe. In addition, the prescribing pattern in this age group should be guided by evidence. Evidence-based tools should be used to alert clinicians to patients at risk of drug-related problems.

Conflict of Interest

The authors declare that they have no conflicts of interest to disclose.

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Informed Consent

Informed consent was obtained from all individual participants included in the study.

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Authors' Contributions

Conceptualization, S.A., Y.A., and A.A.; Data curation, S.A., and Y.A.; Formal analysis, S.A.; Methodology, S.A., Y.A., and A.A; Supervision, Y.A., and A.A.; Writing—original draft, S.A.; Writing—review and editing, Y.A., and A.A. All authors have read and agreed to the published version of the manuscript.

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Data Availability Statement

The data that support the findings of this study are available from the corresponding author, Y.A., upon reasonable request.

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