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Potential drug-drug interactions in elderly patients in a renal ward: a single-center retrospective study in Pakistan

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ABSTRACT

Background: The increasing prevalence of kidney disease among elderly populations has led to a rise in potential drug-drug interactions (pDDIs), particularly due to widespread polypharmacy use in this demographic.

Objective: This study aims to retrospectively analyze pDDIs and identify their prevalence and associated factors among elderly patients in a renal ward.

Methods: This retrospective observational study was conducted at Saidu Group of Teaching Hospital in Swat, Pakistan, from January to December 2022. Data were obtained from the Patients Records Office using a conventional paper-based record system. A sample of 43 elderly patients (age ≥60 years) was selected through consecutive sampling. Drug interactions were assessed using freely available online tools: Drugs.com and Medscape Drug Checker, selected for their user-friendly accessibility and suitability in resource-limited settings.

Results: Among the 43 elderly subjects with balanced gender distribution, the mean age was 66.53 ± 7.68 years. Comorbidities were present in 74.4% of patients, and each patient was prescribed an average of 4.58 medications. According to Medscape, 62.79% of patients experienced one or more potential drug interactions, while Drugs.com identified interactions in 67.44% of cases. Notably, 15% of these interactions were classified as high-risk by both tools. Logistic regression analysis indicated a significantly higher risk of potential drug interactions with increasing numbers of prescribed medications (OR = 4.515, p = 0.033).

Conclusion: This study identified a high prevalence of pDDIs among elderly patients with kidney disease in Pakistan. The majority had comorbidities necessitating multiple medications, thereby increasing the risk of adverse drug reactions (ADRs). Mitigating these risks requires accurate prescribing practices, reliable electronic surveillance systems, and clinical pharmacist support.

Keywords: drug-drug interactions, elderly patients, kidney disease, polypharmacy

Introduction

The global elderly population is rapidly expanding, with projections indicating an increase from 10% in 2022 to 16% in 2050 for individuals aged 65 years or older [1]. This demographic shift coincides with a growing prevalence of multimorbidity, defined as the concurrent presence of multiple chronic conditions. In Germany, for example, 24% of individuals above 75 years have five or more coexisting diseases [2]. Beyond advanced age (>60 years), other factors such as urbanization, non-communicable diseases, increased body mass index, and tuberculosis contribute to comorbidity burden [3]. This presents the challenge of patients concurrently using multiple medications, leading to potential drug interactions. The occurrence of potential drug-drug interactions (pDDIs) is strongly correlated with individuals aged 60 and above,

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those prescribed more than five drugs, and patients undergoing extended hospitalization [4].

Kidney diseases play a crucial role in the context of drug-drug interactions (DDIs) because alterations in renal function contribute to diminished clearance of water-soluble drugs and prolonged plasma elimination half-life. Concurrently, significant pharmacodynamic shifts occur, generally increasing drug sensitivity [5]. The global prevalence of chronic kidney disease (CKD) is estimated at approximately 10% of the world's population [6]. In Pakistan, the general prevalence of kidney disease is 16.6%, with 8.6% of participants exhibiting mild kidney disease and 8% having moderate kidney disease. Notably, age showed a significant association with kidney disease ($p < 0.0001$) [7]. However, a recent study revealed a higher prevalence of 23.3% for CKD, demonstrating an upward trend with advancing age [8]. This complex interplay between kidney diseases and pDDIs highlights the need for increased vigilance in prescribing medications for elderly patients with kidney disease in Pakistan.

As the global population ages, the intricate interplay between multimorbidity, pharmacokinetic changes, potential drug interactions, and CKD becomes increasingly evident. In resource-limited settings where electronic monitoring and clinical pharmacist support may be lacking, adopting a proactive approach is crucial to reduce the risks of drug-related problems and preventable adverse outcomes. Understanding these dynamics is essential for shaping effective healthcare strategies that address the complex healthcare needs of the aging population. The importance of establishing collaboration with clinical pharmacists and implementing electronic surveillance is particularly pronounced in developing countries like Pakistan, where these resources are currently lacking.

Methods

Research design

This was a retrospective observational study conducted in the renal ward of Saidu Group of Teaching Hospital (SGTH), a tertiary healthcare facility located in Swat, Pakistan, spanning from January to December 2022.

Population and sample

The study included elderly patients admitted to the renal ward at SGTH Swat. All patients meeting the inclusion criteria during the study timeframe (January to December 2022) were included using consecutive sampling technique to avoid selection bias.

Inclusion criteria: Patients aged 60 years or above (as defined by the United Nations) [9], admitted to the hospital for at least 24 hours, and with complete medical profiles.

Exclusion criteria: Patients aged less than 60 years and those with incomplete medical profiles that hindered data retrieval.

Ethical approval

Data were acquired from the Patients Records Office utilizing a conventional paper-based record-keeping system. Ethical approval for the study was obtained from SGTH Swat under reference number 15491-92/0-3. This study was conducted following the ethical principles outlined in the Declaration of Helsinki, and all patient data were handled with strict confidentiality and anonymity.

Data analysis

The investigation into potential drug interactions utilized two freely accessible online drug checker websites: Drugs.com and the Medscape Drug Checker. These tools were chosen because they are user-friendly, readily accessible at no cost, do not require technical expertise, and are suitable for resource-limited settings.

Both tools categorize pDDIs into three levels based on their clinical significance, although the nomenclature differs slightly between platforms. Medscape classifies interactions as: (i) *minor/significance unknown*, which includes interactions with limited or uncertain clinical impact; (ii) *use caution/monitor closely*, referring to interactions that may require dosage adjustments, closer monitoring, or specific clinical judgment; and (iii) *avoid or use alternate drug*, indicating combinations that pose significant risk and should generally be avoided unless no suitable alternatives exist.

Conversely, Drugs.com categorizes interactions as minor, moderate, and major. These correspond respectively to interactions that are minimally clinically significant, requiring little or no intervention; those that should usually be avoided or used with caution, possibly necessitating monitoring or adjustments; and those that should always be avoided, as the risk of adverse outcomes clearly outweighs any potential benefit.

Table 1. Sociodemographic characteristics (n=43)

Variables		n	%
Age (years)	Mean ± SD	66.53 ± 7.68	
Sex	Males	21	48.8%
	Females	22	51.2%
Level of education	Not formally educated	22	51.2%
	Formally educated	21	48.8%
Location	Urban	16	37.2%
	Rural	27	62.8%
Co-morbidities	Yes	32	74.4%
	No	11	25.6%
	Diabetes mellitus	14	32.6%
	Hypertension	25	58.1%
	COPD	2	4.7%
	Others	10	23.3%

COPD: Chronic Obstructive Pulmonary Disease

Statistical analysis

Descriptive statistics using cross-tabulations were employed to summarize and analyze data according to the classification of different variables. For continuous variables, means and standard deviations were calculated to provide measures of central tendency and variability, while frequencies and percentages were reported for categorical variables. Logistic regression was employed to identify factors associated with pDDIs. Statistical analyses were conducted using IBM SPSS Statistics version 22, 64-bit edition for Windows.

Results

Sample characteristics

Table 1 provides a comprehensive overview of sociodemographic characteristics and comorbidities within our study sample of 43 participants. The mean age was 66.53 years, with a standard deviation of 7.68 years. Gender distribution was balanced, with 48.8% males and 51.2% females. Regarding education, 51.2% had no formal education, while 48.8% had received formal education. Geographically, 37.2% resided in urban areas and 62.8% in rural settings, reflecting broad representation. Comorbidities were prevalent, with 74.4% reporting one or more medical conditions. Notably, 32.6% had diabetes mellitus, 58.1% had hypertension, 4.7% had chronic obstructive pulmonary disease (COPD), while 23.3% reported other comorbidities.

Frequency of patients with pDDIs

The prevalence of pDDIs among our patient population is shown in Table 2. With a total of 197 prescribed medications, the average number per patient was 4.58 (SD = 1.36), reflecting a moderately complex medication profile. Analysis of pDDIs using both Medscape Drug Checker and Drugs.com revealed similar but distinct interaction patterns. Medscape Drug Checker identified that 37.6% of patients had no reported interactions, while 44.2% experienced 1-3 interactions, with smaller percentages having 4-6 (4.7%) and 7-9 (13.9%) interactions. Concurrently, Drugs.com analysis indicated that 32.2% of patients had no interactions, 44.2% had 1-3 interactions, 18.6% had 4-6 interactions, and 4.6% had 7-9 interactions. These findings highlight the presence of pDDIs in a substantial proportion of our elderly patient population.

Types of pDDIs

Classifying pDDIs according to their severity provides a comprehensive evaluation of their potential impact on patient care. The different severity levels recorded are presented in Table 3. The severity levels were analyzed using data from both Medscape (n=80) and Drugs.com (n=92). According to Medscape, 18.75% of interactions were classified as *minor*, 66.25% were categorized under *monitor closely*, signifying the need for caution and vigilant observation. Furthermore, 15%

Table 2. Proportion of pDDIs

Number of pDDIs	Medscape (n, %)	Drugs.com (n , %)
Patients with no interactions	16 (37.6)	14 (32.2)
1-3 interactions	19 (44.2)	19 (44.2)
4-6 interactions	2 (4.7)	8 (18.6)
7-9 interactions	6 (13.9)	2 (4.6)
Total	**27 (62.7)**	**29 (67.8)**

pDDIs: potential drug-drug interactions

Table 3. Categorization of pDDIs according to severity

Parameters	Frequency	Percentage	Description
Interactions severity level **(Medscape, n=80)**			
Minor	15	18.75%	Minor/significance unknown
Monitor closely	53	66.25%	Use caution/monitor
Serious-use alternative	12	15%	Avoid or use alternate drug
Interaction severity level **(Drugs.com, n=92)**			
Minor	8	8.69%	Minimally clinically significant
Moderate	70	76.08%	Usually avoid combinations; use it only under special circumstances.
Major	14	15.21%	Avoid combinations; the risk of the interaction outweighs the benefit.

pDDIs: Potential drug-drug interactions

of interactions warranted consideration for alternative drugs or avoidance. In alignment with Drugs.com findings, 8.69% were deemed *minor*, 76.08% were categorized as *moderate*, suggesting combinations to be usually avoided and reserved for special circumstances, while 15.21% were labeled *major*, indicating high-risk scenarios where the interaction's potential harm outweighs any potential benefit.

Determinants of drug-drug interactions

To identify significant risk factors associated with pDDIs, multivariate logistic regression analysis was performed. The analysis identified that the number of medications is a significant predictor of pDDIs, as shown in Table 4. Patients using multiple medications were associated with a higher risk of DDIs (OR = 4.515, p = 0.033). This indicates that patients using more medications have a significantly higher risk of pDDIs compared to those using fewer medicines.

Registration of major/serious interactions: Drugs.com vs. Medscape

Table 5 lists various drug pairs with potential *major* interactions as identified by either Drugs.com or Medscape drug interaction websites. In comparing the databases, discrepancies were noted where one database (i.e., Drugs.com) categorized specific drug pairs as *major* interactions, while the other database did not. However, the latter still classified these interactions as *monitor closely*.

Discussion

The examination of pDDIs presented in our study provides essential insights into the complex landscape of medication management within elderly patient populations. Our findings underscore the critical importance of understanding and addressing these

Table 4. Logistic regression analysis of pDDIs determinants

Variable	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
Age	0.97	0.82 – 1.13	0.665
Sex (female vs. male)	1.11	0.07 – 5.59	0.687
COPD	Not estimable[#]	—	0.999
Diabetes mellitus	25.05	0.39 – 1602.34	0.129
Hypertension	1.90	0.01 – 552.87	0.825
Other diseases	27.81	0.09 – 8587.82	0.256
Comorbidities (number)	0.12	0.004 – 3.84	0.233
Number of medications prescribed	4.52	1.13 – 18.01	0.033*

Reference category for sex: Male. [#]Not estimable due to data limitations. *Statistically significant at $p < 0.05$

Table 5. Drugs with major/serious interactions

Drug 1	Drug 2	Registered by Drugs.com	Registered by Medscape	Potential adverse effects
Azithromycin	Lumefantrine	✓	✕	Irregular heart rhythm
Clarithromycin	Artemether/ lumefantrine	✓	✓	Increase QTc interval Affecting hepatic/intestinal enzyme CYP3A4 metabolism
Sodium bicarbonate	Moxifloxacin	✕	✓	Sodium bicarbonate decrease GI absorption of moxifloxacin stone formation
Omeprazole	Digoxin	✕	✓	Omeprazole increase the level or effect of digoxin by increasing gastric pH
Clopidogrel	Omeprazole	✓	✓	Omeprazole inhibit CYP2C19, so efficacy of clopedogrel is affected
Linezolid	Tramadol	✓	✓	CNS toxicity Linezolid and tramadol both increase serotonin levels
Nifedipine	Amlodipine	✕	✓	Nifedipine affect CYP3A4 and increase or affect the level of amlodipine
Clopidogrel	Rosuvastatin	✓	✕	Liver damage, rhabdomyolysis

✓, Captured by the website; ✕, Did not captured by the website

interactions. The severity categorization, analyzed through both Medscape and Drugs.com, further enriches our understanding and sheds light on the potential impact of these interactions on patient care.

The high prevalence of pDDIs observed in our patient group, with 62.79% identified by Medscape and 67.44% by Drugs.com, aligns with global trends reported in similar demographics, such as the 74.7% prevalence in CKD patients undergoing hemodialysis and 69.7% in a study conducted at Cerrahpasa Nephrology Unit [10,11]. However, some studies have reported even higher prevalence rates in kidney patients compared to our findings. For instance, one study reported a prevalence of 85.3%, while a Spanish study found prevalence rates as high as 91% [12,13]. The reason for this discrepancy could be that these studies primarily focused on patients with CKD, whereas our study included a broader population of patients in a renal ward, many of whom do not necessarily have CKD. This prevalence is concerning, given that polypharmacy is common practice among elderly patients, particularly those with chronic conditions like kidney disease, which necessitates the use of multiple medications.

Our regression analysis revealed a significant association between the number of prescribed medications and the risk of pDDIs (OR = 4.515, p =

0.033). Unsurprisingly, as the number of medications increases, the risk for pDDIs also increases. Several prior studies have investigated the association of polypharmacy with pDDIs in line with the current study [14,15]. However, the current study suggests that further multicenter studies are needed to investigate the association of polypharmacy and pDDIs in patients with CKD. Potential drug-drug interactions in kidney disease are influenced by various other risk factors as well. Studies have shown that older age (⩾60 years), longer hospital stays (⩾10 days), and polypharmacy (⩾10 drugs) significantly increase the likelihood of pDDIs in CKD patients [16,17]. Comorbidities such as hypertension, diabetes, and heart disease significantly increase the risk of pDDIs [12,18,19]. These findings are crucial as they emphasize the need for careful prescribing practices, especially in polypharmacy scenarios. Healthcare providers must be vigilant in reviewing and managing medication regimens to minimize the risk of pDDIs.

The 15% of interactions deemed high-risk by both Medscape and Drugs.com further highlight the potential severity of pDDIs in this population. High-risk interactions can lead to severe adverse drug events, which are particularly detrimental to elderly patients with kidney disease, given their compromised physiological state and reduced drug clearance capacity. Other studies have highlighted this issue, reporting that 16.41% and 16.8% of drug-drug interactions in CKD patients were classified as severe [20,21]. In kidney transplant patients, 29% experienced severe interactions contributing to adverse drug reactions (ADRs) [22]. Therefore, it is imperative to implement strategies that enhance the safety of pharmacotherapy in this population.

This study highlights the high prevalence of pDDIs among elderly patients with kidney disease in Pakistan, underscoring significant implications for patient safety and healthcare delivery. The utilization of free electronic tools, such as Medscape and Drugs.com, in our study demonstrates their effectiveness in identifying pDDIs, even in resource-limited settings, thereby providing accessible solutions for healthcare professionals to monitor and mitigate associated risks. Our findings advocate for the implementation of accurate prescribing practices, the adoption of electronic surveillance tools, and the integration of clinical pharmacists into healthcare teams to reduce pDDI-related risks. Future research should focus on developing and evaluating interventions aimed at reducing pDDIs and improving patient outcomes in this high-risk population.

This study was confined to a single institution, thereby restricting the generalizability of findings to broader populations. The retrospective nature of our study, coupled with the absence of an electronic Patient Data Management System, precluded the determination of a calculated sample size; nevertheless, every eligible patient was included in the analysis using consecutive sampling. Furthermore, due to limited data availability, we were unable to identify or document any tangible adverse effects or outcomes associated with the investigated parameters. These limitations underscore the need for cautious interpretation and acknowledgment of the study's scope within the confines of the constraints.

Conclusions

This study highlights a significant clinical concern: 62.79% of elderly patients exhibiting exposure to at least one pDDI, according to the Medscape drug checker. This high prevalence is compounded by universal kidney disease and a 74.4% comorbidity burden, substantially increasing vulnerability. Notably, 15% of these pDDIs were severe, necessitating consideration of alternative drug usage.

While interaction checker programs have limitations in identifying clinically significant DDIs and show inter-program variability, our findings underscore an imperative need: implementing robust electronic surveillance systems integrated with clinical pharmacist expertise. This proactive approach is crucial to mitigate preventable adverse outcomes, especially in this vulnerable population. Future research must determine the clinical consequences of these pDDIs within this high-risk group. Furthermore, large-scale, prospective, multicenter studies are essential to validate our findings and inform the development of evidence-based clinical guidelines.

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Conflict of interest

The authors declare no conflict of interests.

Author contributions

NA: conceptualization, methodology, data curation, formal analysis, writing original draft. SH: conceptualization, data analysis, review and editing. AYR: writing, review and editing and visualization. AM: writing, review and editing and visualization.

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