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Original Article

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Knowledge and Practice of Sudanese Clinical Pharmacists Towards Drugs that Require Dosage Adjustment in Renally Impaired Patients: A Cross-Sectional Study

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Abstract

Objectives: Clinical pharmacist has a vital role in the multidisciplinary team; they hold a critical role in the process of dosage adjustment and improving quality of life. One of the aspects of clinical pharmacy is dosage adjustment, especially for patients with renal impairment, since a wide variety of drugs are excreted in the urine throughout the kidneys. The aim of the study was to evaluate the knowledge and practice of Sudanese clinical pharmacists towards drugs that require dosage adjustment in renally impaired patients. ***Design:*** A cross-sectional descriptive study. ***Methods:*** The study was conducted from March to November 2020 among Sudanese clinical pharmacists. A pretested online questionnaire filled by a total of 255 Sudanese clinical pharmacists to evaluate knowledge in drug-specific renal dosing strategies and patterns of clinical practice. Data were analysed by SPSS, and descriptive statistics and Chi-square tests were conducted at a significance level of $p < 0.05$. ***Results:*** Most of participants were females (87.4%), 53.4% were at the age between 29-33. Most participants had a master's degree (73.5%), and only 35% had undergone training on renal dose adjustment. Overall, 61.6% had demonstrated sufficient knowledge. Accurate identification of the need for renal dose adjustment was greatest for digoxin (84.6%), spironolactone (71.9%), lisinopril (70.8%), and enoxaparin (67.2%), and least for azithromycin (12.6%) and levofloxacin (12.3%). KDIGO guidelines were most frequently used for CKD (69.6%) and AKI (65.6%) classification, and creatinine clearance was the parameter most frequently used for monitoring CKD (36.8%) and AKI (25.3%). Prior training on renal dose adjustment ($p = 0.022$) and current clinical pharmacy practice ($p = 0.005$) were significant predictors of adequate knowledge. ***Conclusion:*** Most Sudanese clinical pharmacists demonstrated adequate knowledge about medications requiring dosage adjustments in patients with renal impairment. However, there remains a need to enhance interprofessional collaboration and address existing knowledge gaps.

Keywords: ***Clinical pharmacists, Dose adjustment, Knowledge assessment, Practice patterns, Renal impairment, Sudan.***

Introduction

Renal impairment has been described as the decreased capacity of kidneys to carry out fundamental excretory, regulatory, and endocrine functions, leading to the accumulation of metabolic waste products and imbalance of fluid, electrolyte, and acid–base balance [1]. Renal impairment can be broadly classified into three groups: acute kidney injury (AKI), drug-induced nephrotoxicity, and chronic kidney disease (CKD) [1,2]. AKI is characterized by an acute and usually reversible decline in renal function that occurs over a period of hours to days, whereas CKD is a slow, irreversible loss of kidney function that can progress to the need for renal replacement therapy, i.e., dialysis or transplantation, in the form of end-stage renal disease (ESRD) [3]. CKD is usually staged according to glomerular filtration rate (GFR) as follows: Stage 1: GFR ≥ 90 mL/min/1.73 m², Stage 2: 60–89 mL/min/1.73 m², Stage 3: 30–59 mL/min/1.73 m², Stage 4:

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15–29 mL/min/1.73 m² and Stage 5: <15 mL/min/1.73 m² (2). It also can be classified as: Grade 1: GFR ≥ 90, Grade 2: 60–89, Grade 3a: 45–59, Grade 3b: 30–44, Grade 4: 15–29 and Grade 5: <15 mL/min[2].

Precise determination of renal function is required for proper drug dosing, especially for drugs excreted through the kidneys [4]. Important parameters measured in renal function testing include serum creatinine (SCr), creatinine clearance (CrCl), GFR, and blood urea nitrogen (BUN) [5]. Renal impairment changes drug pharmacokinetics and pharmacodynamics by decreasing renal clearance, tubular secretion, filtration, and/or reabsorption [6,7]. It is estimated that an increase in serum creatinine of 0.6 mg/dL per day approximates a 25–30% decrease in renal function. Conditions like volume depletion (secondary to medications or dehydration) and hypoalbuminemia can affect renal function and drug binding, respectively [7].

Clinical pharmacists are part of multidisciplinary healthcare teams and help deliver safer, more economical, and evidence-based care [8]. Their presence on medical rounds–particularly in critical care units–decreases preventable adverse drug events. One of their most important interventions is the optimization of drug dosages, which involves interpretation of laboratory results and pharmacokinetic concepts [8,9]. In renal impairment, dosing adjustments are crucial to avoid toxicity, decrease hospitalization, and reduce healthcare expenses [10,11].

Several formulas are used for renal dosage adjustment, such as the Cockcroft-Gault, Modified Jelliffe, Salazar-Corcoran, and MDRD equations [12,13]. However, dosing errors still happen, often due to clinicians' lack of knowledge about renal dosage guidelines, oversight of renal impairment, or the unavailability of easily accessible evidence-based protocols [14]. Based on the renal dosing guidelines, some drugs like azithromycin and warfarin may not require dose adjustment; however, others like spironolactone, enoxaparin, lisinopril, digoxin, and levofloxacin need to be adjusted according to creatinine clearance (CrCl) [15]. For example, the guideline recommends a reduced maintenance dose (with the same frequency) for azathioprine, a reduced dose with a prolonged interval for meropenem, and no change for metronidazole [15].

In Malaysia, a study analyzing Malaysian pharmacists' self-perceived knowledge, attitudes, and practices with regards to dosage adjustments in patients with chronic kidney disease found that only 14.7% of the pharmacists practiced dose adjustment regularly. The main barriers reported were lack of access to renal function data and incomplete patient histories [16]. In Sudan, at Omdurman Military Hospital, a study looking into the knowledge and practices of physicians regarding acute kidney injury found that while 94% of them had managed AKI cases, only 5.7% had good practices, whereas over 56% had poor practices [17]. Despite the important role played by clinical pharmacists in the optimization of dosing in patients with renal impairment, little evidence exists on their impact and practice in Sudan and other African countries. The current research aims to bridge this gap by evaluating the knowledge, attitudes, and practice of clinical pharmacists in Sudan regarding dose adjustment for renal considerations and their impact on improving patient outcomes.

Methods

Study Design and Setting: A cross-sectional, descriptive study was conducted among Sudanese clinical pharmacists practicing in Khartoum State, Sudan. Due to restrictions during the COVID-19 pandemic and the lockdown, the study was applied using a web-based study. Data collection was undertaken from March to November 2020.

Study Population and Eligibility Criteria: The study population was Sudanese clinical pharmacists registered with the Sudan Medical Council (SMC). They were either practicing in Sudan or abroad at the time of data collection. According to SMC's statistics in June 2020, there were 687 registered clinical pharmacists. The inclusion criteria were having a valid clinical pharmacist license and being currently practicing clinical pharmacy or having experience in the clinical pharmacy practice. Pharmacists who were not active in clinical duties and those who did not complete the questionnaire were excluded in the study.

Sample Size Determination and Sampling Procedure: The sample size was calculated using the Raosoft® sample size calculator (Raosoft Inc., Seattle, WA, USA). The formula: n= N / 1+N(e)2 was applied, whereas, n is the sample size, N is the total population (687), and e is the margin of error (0.05). The estimated sample size was 253, the collected sample was 255 clinical pharmacists, achieving a response rate of (100%).

A convenient sampling technique was performed to collect the sample through invitations with the survey link that was shared via professional networks and on social media (WhatsApp, Facebook, and Telegram). The link was kept open until the target sample size was achieved.

Data Collection Instruments and Methods: Data were collected via a pretested and pre-structured online questionnaire. Pretesting of the questionnaire was carried out in a pilot study involving 10 clinical pharmacists, after which modifications were made to improve clarity and relevance. The final version consisted of three sections as follow: (1) Sociodemographic and professional characteristics (7 questions), (2) Knowledge section (10 questions) that addressing drug-specific dose modification approaches in patients with renal impairment. (3) Practice section (14 questions), which examining guideline utilization, renal function monitoring parameters, dosing equations used, weight adjustment in Cockcroft–Gault utilization, and satisfaction with physician collaboration.

Outcome Measures: The primary outcome of the study was the calculating the knowledge adequacy of the clinical pharmacists regarding the renal dose adjustment, which was measured based on the overall knowledge score, whereas as sufficient knowledge was above the median (≥5), and insufficient knowledge was equal or less than median (≤5). Secondary outcomes were clinical practice patterns, perceived pharmacist-physician collaboration, and the relationships between knowledge scores and sociodemographic or professional characteristics.

Statistical Analysis: Collected data were analysed using the Statistical Package for the Social Sciences (SPSS), Version 20 (IBM Corp., Armonk, NY, USA). Data were inspected for completeness and consistency before analysis. Descriptive statistics were reported as frequencies and percentages. Associations between knowledge adequacy and independent variables were examined using Chi-square (χ^2) tests, with a significance level of $p < 0.05$.

Ethical Considerations: The study was conducted in compliance with the 1975 Declaration of Helsinki and was approved by the Ethical Committee of the Faculty of Pharmacy at the University of Khartoum (FPEC-37-2020). Written informed consent was obtained from all participants, and confidentiality was maintained throughout the research process.

Results

Demographic characteristics of the clinical pharmacists: The study included 255 Sudanese clinical pharmacists. Most of them were females (78%), and the biggest age group was 29–33 years (53%), followed by 34–39 years (20%). Most of the participants were actively practicing clinical pharmacy (74%), with most working within Sudan (82%). The most frequent qualification was a master's degree (73.5%), while 19.8% had both MSc and Board of Pharmacy Specialties (BPS) certification. More than half of the pharmacists (55%) had 1–2 years of professional experience, while 18% had none, and just 5% had greater than four years of experience. Interestingly, only 35% had undergone training on dosage adjustment in renal impairment (**Table 1**).

Knowledge Assessment: Table 2. demonstrated variable accuracy in dose adjustment strategies. For metronidazole, 60.9% selected to keep the dosing interval and dose, whereas 36.8% used the "maintain interval/decrease dose" strategy for meropenem. For azathioprine, 47.4% selected to maintain the interval and reduce the dose. Most respondents accurately identified that spironolactone (71.9%), enoxaparin (67.2%), lisinopril (70.8%), and digoxin (84.6%) need dose adjustment in renal impairment. Fewer, however, identified the requirement for adjustment with warfarin (49.8%) or azithromycin (12.6%), whereas 73.5% incorrectly indicated that levofloxacin does not need adjustment. Overall, 157 (61.6%) of the clinical pharmacists achieved a sufficient knowledge score, while 98 (38.4%) had an insufficient knowledge score (**Figure 1**).

Practice Assessment: In relation to clinical practice (**Table 3**), the kidney disease: Improving Global Outcomes (KDIGO) guidelines were most used to classify patients with both chronic kidney disease (CKD) (69.6%) and acute kidney injury (AKI) (65.6%). Creatinine clearance (CrCl) was the most widely used parameter for monitoring CKD (36.8%) and AKI (25.3%). For dose adjustment in AKI, the Cockcroft–Gault equation was used by 64% of the respondents. When applying this equation, 36.4% adjusted according to the case, 26.9% based on actual body weight, and lower percentages on BMI, ideal body weight, or adjusted body weight. Consulting a nephrologist when adjusting doses was more practiced in CKD (68.4%) compared with AKI (64.8%). Most pharmacists considered that dose adjustment in AKI patients would "extremely" (43.5%) or "very" (36.8%) benefit patient outcomes. Satisfaction with collaboration between pharmacists and physicians was variable, with 31.6% very satisfied, 26.1% extremely satisfied, and 20.2% neutral. Pharmacists indicated seeing CKD cases more than AKI, with "sometimes" being the most frequent answer for both conditions.

Association between knowledge and score with clinical pharmacists' variables: As revealed in Table 4, adequacy of knowledge was found to be significantly related to having undergone training on dosage adjustment in renal impairment ($p = 0.022$) and current practice in clinical pharmacy ($p = 0.005$). There were no significant relationships with gender, age, or level of qualification.

Table 1: Sociodemographic Characteristics of Sudanese Clinical Pharmacists (N=255)

Variable	Frequency	Percentages (%)
Gender		
Male	56	22
Female	199	78
Age		
23-32	46	18
33-29	135	53
34-39	51	20
40-45	14	5.5
More than 45 years	7	2.5
Practicing participants		
Yes	186	74
No	69	27
Practicing place		
Inside Sudan	163	82
Outside Sudan	36	18
Qualifications		
Board of Pharmacy Specialties (BPS)	6	2.4
MSc	187	73.5
MSc, BPS	51	19.8
MSc, PhD	4	1.6
MSc, PhD, BPS	3	1.2
PhD	4	1.6
Experience		
No experience	46	18
Less than 1 year	38	15
1-2 years	140	55
3-4 years	18	7
More than 4 years	13	5
Training of Dosage Adjustment in Renal Impairment		
Yes	89	35
No	166	65

Table 2. Knowledge of Sudanese Clinical Pharmacists Towards Drugs that Require Dose Adjustment in Renally Impaired Patients (N=255)

Knowledge Question	Frequency	Percentages (%)
In case of using Metronidazole in a maintenance dose, what strategy do you use for dose adjustment?		
Maintain the interval/Maintain the dose	154	60.9
Maintain the interval/Decrease the dose	40	15.8
Increase the interval/Decrease the dose	34	13.4
Increase the interval/Maintain the dose	25	9.9
In case of using Meropenem in a maintenance dose, what strategy do you use for dose adjustment?		
Maintain the interval/Decrease the dose	93	36.8
Increase the interval/Maintain the dose	67	26.5
Increase the interval/Decrease the dose	58	22.9
Maintain the interval/Maintain the dose	35	13.8
In case of using Azathioprine in a maintenance dose, what strategy do you use for dose adjustment?		
Maintain the interval/Decrease the dose	120	47.4
Increase the interval/Decrease the dose	60	23.7
Increase the interval/Maintain the dose	37	14.6
Maintain the interval/Maintain the dose	36	14.2
According to your knowledge, does Warfarin require dosage adjustment in renally impaired patients?		
Yes	126	49.8
No	108	42.7
I don`t know	19	7.5
According to your knowledge, does Azithromycin require dosage adjustment in renally impaired patients?		
Yes	32	12.6
No	186	73.5
I don`t know	35	13.8
According to your knowledge, does Spironolactone require dosage adjustment in renally impaired patients?		
Yes	182	71.9
No	36	14.2
I don`t know	35	13.8
According to your knowledge, does Enoxaparin require dosage adjustment in renally impaired patients?		
Yes	170	67.2
No	51	20.2
I don`t know	32	12.6
According to your knowledge, does Lisinopril require dosage adjustment in renally impaired patients?		
Yes	179	70.8
No	44	17.4
I don`t know	30	11.9
According to your knowledge, does Digoxin require dosage adjustment in renally impaired patients?		
Yes	214	84.6
No	21	8.3
I don`t know	18	7.1
According to your knowledge, does Levofloxacin require dosage adjustment in renally impaired patients?		
Yes	31	12.3
No	36	14.2
I don`t know	186	73.5

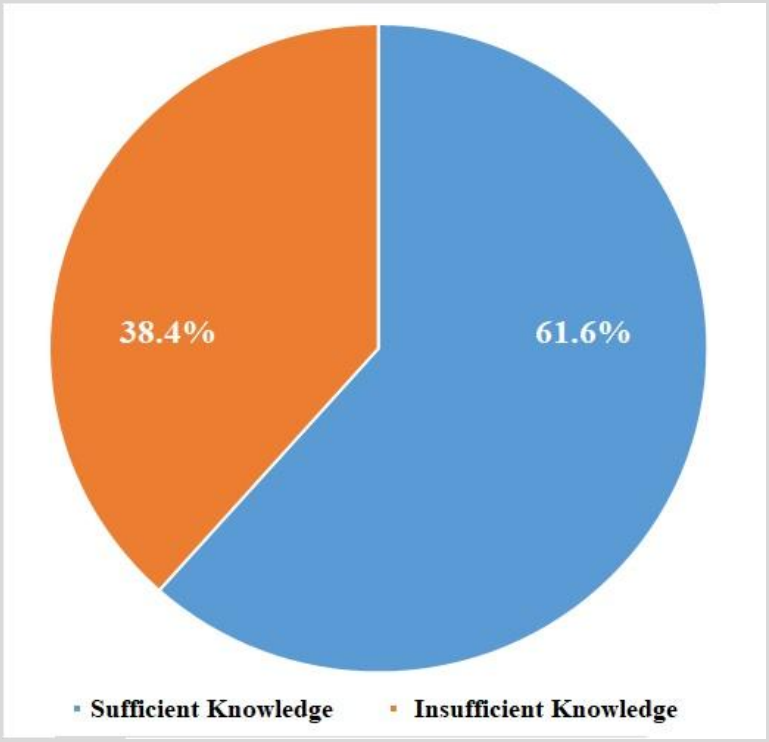

Figure 1: Overall knowledge score of the clinical pharmacists regarding drugs that require dose adjustment in renally impaired patients

Table 3: Practice of Sudanese Clinical Pharmacists Towards Drugs that Require Dosage Adjustment in Renally Impaired Patient (N=255)

Practice Question	Frequency	Percentages (%)
Which guideline do you use to categorize patients with CKD?		
KDIGO	176	69.6
KDOQI	77	30.4
Which guideline do you use to categorize patients with AKI?		
KDIGO	166	65.6
KDOQI	87	34.4
Which parameter(s) do you employ for monitoring patients with CKD?		
CrCl	93	36.8
BUN, CrCl	40	15.8
BUN, CrCl, SCr	31	12.3
CrCl, SCr	30	11.9
SCr	28	11.1
Which parameter(s) do you employ for monitoring patients with AKI?		
CrCl	64	25.3
SCr	55	21.7
BUN	42	16.6
CrCl, SCr	31	12.3
BUN, SCr	29	11.5
Which equation do you use for dose adjustment in AKI?		
Cockroft-Gault	162	64.0
Modified Jelliiffie	44	18.6
MDRD	47	17.4
In case of using Cockroft-Gault equation, do you employ:		
Depending on the case	92	36.4
Actual body weight	68	26.9
BMI	46	18.2
Ideal body weight	30	11.9
Adjusted body weight	17	6.7
When adjusting doses for patients with AKI, do you consult a nephrologist?		
Yes	164	64.8
No	89	35.2
When adjusting doses for patients with CKD, do you consult a nephrologist?		
Yes	173	68.4
No	80	31.6

How do you think adjusting doses in patients with AKI improves patient outcome?		
Extremely	110	43.5
Very	2	36.8
Slightly	10	15.0
Rarely	38	4.0
Never	93	0.8
How satisfied are you with the collaboration between the clinical pharmacist and the physician in determining the appropriate dose for patients with renal impairment?		
Very satisfied	80	31.6
Extremely satisfied	66	26.1
Neither satisfied nor dissatisfied	51	20.2
Not so satisfied	41	16.2
Not satisfied at all	15	5.9
How often do you encounter cases of AKI?		
Sometimes	87	34.4
Very often	51	20.2
Always	44	17.4
Occasionally	37	14.6
Rarely	23	9.1
Never	11	4.3
How often do you encounter cases of CKD?		
Sometimes	90	35.6
Very often	60	23.7
Always	47	18.6
Rarely	22	8.7
Occasionally	21	8.3
Never	13	5.1

Table 4: Association Between Sociodemographic Characteristics and Knowledge of Sudanese Clinical Pharmacists Towards Drugs that Require Dose Adjustment in Renally Impaired Patients

Variable		Knowledge Adequacy		P value
		Insufficient	Sufficient	
Gender	Female	38.4%	61.6%	.643
	Male	41.8%	58.2%	
Age category (Years)	23-28	45.7%	54.3%	.800
	29-33	39.3%	60.7%	
	34-39	33.3%	66.7%	
	40-45	35.7%	64.3%	
	> 45	42.9%	57.1%	
Qualifications	Board of Pharmacy Specialties (BPS)	50%	50%	.130
	MSc	40.9%	59.1%	
	MSc, BPS	26%	74%	
	MSc, PhD	75%	25%	
	MSc, PhD, BPS	33.3%	66.7%	
	PhD	75%	25%	
Training of Dosage Adjustment in Renal Impairment	No	44.5%	55.5%	**.022**
	Yes	29.2%	70.8%	
Are you currently practicing clinical pharmacy?	No	53.7%	46.3%	**.005**
	Yes	33.9%	66.1%	

Discussion

This study shows a comprehensive assessment of the knowledge and practice of drug dose adjustments by Sudanese clinical pharmacists in patients with renal impairment. The findings reveal considerable differences in both the theoretical understanding and actual practice, even though a large proportion of the clinical pharmacists have academic degrees and are actively engaged in clinical practice. Demographically, most of the respondents were female (78%), which indicates that pharmacy is a female-dominated profession in Sudan. Such findings were also observed in several previous studies in Sudan, that also show the same pattern of the gender demographic [18-20]. Furthermore, the relatively recent development of clinical pharmacy as a specialty, and the increased use of online media by younger pharmacists are likely the reasons for the clustering of respondents in the 29-33 age range (53.4%), and the low representation of participants over 45 (2.8%).

At the time of the study, most of the participants (74%) were actively practicing clinical pharmacy, signifying the integration of clinical pharmacists into Sudanese hospitals' system, and good collaboration with other healthcare providers [21,22]. Most respondents (82%) were employed domestically, which is in line with the research population's national orientation [23]. Participants' early professional stage and limited access to advanced credentials

like the Board of Pharmacy Specialties (BPS), which necessitates travel overseas for examination, are likely the reasons for the high prevalence of MSc-only qualifications [24]. Moreover, only 35% of respondents reported having attended workshops on renal dosage adjustment, which is a significant gap in institutional training programs given the study's findings showing a high association between training and knowledge sufficiency, which is consistent with previous research demonstrating a link between knowledge adequacy and exposure to targeted training [25,26].

In accordance with international nephrology practice, KDIGO recommendations were most frequently applied for the classification of CKD (69.6%) and AKI (65.6%) [27,28]. However, the accuracy of renal function estimation may be compromised by the widespread use of creatinine clearance (CrCl) alone, which is used by 25.3% for AKI and 36.8% for CKD monitoring. It is anticipated that a more comprehensive strategy that includes takes SCr and BUN into account will increase dosage accuracy; this claim has been supported by the literature on nephrology (5). Although doctors most frequently utilized the Cockcroft–Gault (CG) equation to adjust dosage (64% in AKI, 73.1% in CKD) [29,30], this method has been shown to have accuracy limits when applied to varying body weights and clinical contexts. There is a requirement for internal standardization, as evidenced by the fact that 36.4% of weight selection when utilizing CG varied by clinical circumstance, with others choosing real, ideal, or adjusted weights. Although there is conflicting evidence, it has been shown that adjusted body weight, specifically a correction factor of 0.4 provides more accurate estimations in obese patients [29,31]. Moreover, most of patients with AKI and CKD reported consulting a nephrologist, indicating a collaborative approach that has also been recommended in the literature to improve dosage [32-34]. There is room for improvement in interprofessional collaboration, though, as almost one-third of respondents expressed only moderate satisfaction with the partnership.

Knowledge evaluations for adjusted drugs like digoxin (84.6%), lisinopril (70.8%), enoxaparin (67.2%), and spironolactone (71.9%) shown strong agreement with published recommendations. On the other hand, there were clear knowledge gaps with azithromycin (73.5% appropriately indicated no adjustment required), warfarin (only 49.8% appropriately indicated no adjustment necessary), and especially levofloxacin (73.5% unclear). As has also been noted in other contexts, these inadequacies may be indicative of curricular deficiencies and inconsistent continuing education [35,36]. Variable compliance was shown when compared to the renal dosage guideline; metronidazole and azathioprine were approached accurately, but meropenem was not (most preserved interval rather than prolonging as advised).

Several limitations are observed in the current study. First, the cross-sectional design only assesses the knowledge and practice at one moment time, and thus does not able to determine the causality. Second, dependence on the self-reported practices is liable to recall bias, which can overestimate compliance with best practices. Third, even the study included a large sample of clinical pharmacists from various settings, the findings may not be entirely generalizable to all Sudanese clinical pharmacists, particularly those employed in rural or non-hospital settings. Fourth, although the knowledge questionnaire was extensive, it did not examine all drugs necessitating renal dose adjustment, which can underestimate knowledge deficits in the scenario of less frequently utilized drugs. Despite these limitations, the present study has several strengths. It is one of the limited studies in Sudan to assess both knowledge and actual practice regarding renal dose adjustments among clinical pharmacists in a systematic manner. Recruiting a large and representative sample from diverse practice settings enhances the generalizability of the results. In addition, the use of drug-specific questions allows the determination of specific knowledge gaps, thus guiding future training initiatives and policy formulation.

In conclusion, although Sudanese clinical pharmacists exhibited decent adherence to international guidelines, significant gaps remain in correct renal function estimation and drug-specific dose adjustment knowledge. Notably, focused training and active clinical involvement played a key role in enhancing knowledge sufficiency. To reduce risks linked to renal impairment pharmacotherapy, national efforts should prioritize the implementation of standardized dosing guidelines, reinforced pharmacist–physician collaboration, and continuing education programs. Such measures can close the observed gaps and ultimately enhance patient safety and outcomes in the setting of renal dysfunction.

Declarations

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Conflict of interest declaration

The authors declare that there is no conflict of interest

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Contributors

MSM, AME and SIH: Conceptualization, Methodology, Investigation, Data collection and curation, Writing original draft, MMAA, AAA, AMS: Methodology, Data collection and Formal analysis, Data curation, Visualization. SBA: Data analysis, Software, Writing – review and editing. SB and BAY: Supervision, Formal analysis, Data collection and curation, Writing – review and editing. All authors approved the final manuscript

Ethical Clearance

The study was conducted in compliance with the 1975 Declaration of Helsinki and was approved by the Ethical Committee of the Faculty of Pharmacy at the University of Khartoum (FPEC-37-2020). Written informed consent was obtained from all participants, and confidentiality was maintained throughout the research process.

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