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Pharmacists' Knowledge of Nephrotoxicity and Renal Dose Adjustment: A Cross-Sectional Study in Najaf, Iraq

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ABSTRACT

Background: Changes in the structure and function of the kidney caused by a number of factors are the hallmarks of chronic kidney disease, a degenerative condition. Drug-induced nephrotoxicity, which is defined as kidney damage caused either directly or indirectly by medications, is one of the most common side effects of clinical drug therapy. DIN is the main cause of both acute renal damage and chronic kidney disease. Many different mechanisms can lead to drug-related nephrotoxicity, such as immunological and inflammatory mechanisms that cause interstitial nephritis or acute or chronic glomerulonephritis; altered intra-glomerular hemodynamics that cause acute kidney injury; tubular cell toxicity that increases the risk of acute tubular necrosis; crystal nephropathy; and rhabdomyolysis or thrombotic microangiopathy. This study aimed to assess the knowledge of clinical pharmacists employed in emergency department, dialysis ward and internal medicine and nephrology ward regarding Nephrotoxic Medications and Renal Dose Adjustment in Patients with Chronic Kidney Disease. A descriptive cross-sectional study was completed in October of 2024. The study employed a newly created questionnaire that has undergone validity testing by eight academic specialists.: two in clinical pharmacy, three in pharmacology, two in biostatistics and one nephrology subspecialist. The modified questionnaire was distributed to 20 pharmacists for a pilot research, yielding a Cronbach alpha score was 0.79. The questionnaire was delivered by hand to 100 pharmacists employed in emergency department, dialysis ward and internal medicine and nephrology ward at four healthcare institutions: Al-Hakeem General Hospital, Al-Sader Medical City, Al-Najaf Educational Hospital, and Al-Forat Al-Awsat Teaching Hospital, who were assured that participation was voluntary, confidentiality would be maintained, and the completion time would not exceed 15 minutes. They received instructions as well. Result: A total of 100 clinical pharmacists were enrolled. The mean age of pharmacists was 27.2 ± 2.7 (range: 24 – 45) years and 64% of the participating pharmacists were aged between 24-27 years. Female pharmacists were the dominant among the studied group; they accounted for 79%. The level of knowledge of pharmacists had been found that only 10% of the participating pharmacists had good knowledge about nephrotoxic medications and dosing adjustment for patients with chronic kidney disease, 41% had fair and 49% had poor knowledge. This study underscores the urgent need for continuous educational programs and workshops can help maintain and enhance knowledge of pharmacists after graduation.

Keywords: Chronic kidney disease, pharmacist, renal dose adjustment, nephrotoxic medications

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I. INTRODUCTION

Chronic renal disease is a progressive disorder characterized by changes in the structure and function of the kidneys resulting from multiple etiologies. Chronic kidney disease is usually marked by a drop in kidney function, which can be seen by an estimated glomerular filtration rate (eGFR) of less than 60 mL/min per 1.73 m², or by signs of kidney damage, such as albuminuria, haematuria, or problems found through lab tests or imaging, that last for at least three months. (1).

In the twenty-first century, CKD has emerged as a major global public health concern and a leading cause of morbidity and mortality. The global prevalence of CKD has increased substantially, with an estimated 843.6 million individuals affected worldwide in 2017. This rising burden is largely attributed to the increasing prevalence of major risk factors, including obesity and diabetes mellitus (2).

Patients are categorized using the CGA approach based on their cause, albuminuria (A1–A3), and GFR (G1–G5). The famous colorful CKD table makes use of the final two biological markers. The definition and classification of CKD are supported by epidemiological studies carried out by the CKD-prognosis consortium (CKD-PC) that show associations between adverse outcomes such as mortality or renal failure and estimated GFR (eGFR) < 60 mL/min/1.73 m2 and/or ACR (A2-A3) (3).

Drug-induced nephrotoxicity (DIN) represents a significant clinical problem and is a leading contributor to both acute kidney injury and the progression of chronic kidney disease (4, 5). The incidence of DIN has been reported in approximately 14–26% of adults and 16% of adolescents, with a higher risk observed among elderly patients due to multiple comorbidities and polypharmacy (6). Although drug-induced renal dysfunction is often reversible following timely drug discontinuation, delayed detection and management may result in irreversible structural damage involving various nephron segments, including the glomeruli and renal tubules (7).

Drug-related nephrotoxicity may occur through several mechanisms, including inflammatory and immune-mediated processes that lead to acute or chronic glomerulonephritis or interstitial nephritis; changes in intraglomerular hemodynamics that cause acute kidney injury; tubular cell toxicity that can lead to acute tubular necrosis; crystal nephropathy; and rhabdomyolysis or thrombotic microangiopathy (8) .

The removal of most drugs, including their active metabolites, depends on the rate at which the kidneys filter, excrete, and reabsorb them. In renal insufficiency, the elimination of renally excreted medications is altered, requiring dosage modifications for patients with renal impairment (9). As a result, some drugs and their active metabolites can cause nephrotoxicity or make kidney failure worse (10).

Failure to adjust doses of renally excreted medications has been associated with serious clinical consequences, including nephrotoxicity. In hospital settings, approximately 19% of medication-related acute kidney injury has been attributed to inappropriate drug dosing (11). Furthermore, previous studies have reported that 29–74% of prescriptions requiring renal dose adjustment were either incorrectly modified or not adjusted at all (12).

Pharmacists, integral to multidisciplinary healthcare teams, are pivotal in addressing drug-related concerns, given their clinical training. They excel in ensuring patient safety through activities, such as screening, dispensing, inspecting, counseling, and offering inpatient pharmaceutical services (13). Multiple studies highlight the positive influence of pharmacists in managing CKD and end-stage renal disease, thereby enhancing outcomes and refining patient care (14).

Health systems have set up guidelines for pharmaceutical dosing to make practices

more uniform and improve the quality of care for patients. An established example involves inpatient pharmacist-led renal dosage protocols. Pharmacists check how well a patient's kidneys are working and use pharmacy and therapeutics protocols that are specific to their institution to make sure that the right dose is given when a patient has acute or chronic kidney problems. This stops both over- and under-dosing when kidney clearance changes. Renal dosing services may reduce the toxicity of medications, make nurses' jobs easier, and lower the costs of healthcare related to medications (15).

II. MATERIALS and METHODS

Study Design:

A descriptive cross-sectional study was conducted in October 2024 to evaluate pharmacists' knowledge regarding nephrotoxic medications and drug dose adjustment in Al-Najaf city, Iraq. The study carried out at four healthcare institutions: Al-Hakeem General Hospital, Al-Sader Medical City, Al-Najaf Educational Hospital, and Al-Forat Al-Awsat Teaching Hospital. The study employed a newly created questionnaire specifically for this research, based on a comprehensive review of the scientific literature and previously published studies on drug-induced nephrotoxicity and pharmacist interventions in chronic kidney disease that has undergone validity testing by eight academic specialists.: two in clinical pharmacy, three in pharmacology, two in biostatistics and one nephrology subspecialist . The modified questionnaire was distributed to 20 pharmacists for a pilot research, yielding a Cronbach alpha score. According to the Cronbach's alpha analysis for the questionnaire, the 50 items were entered ,We got the following:

Reliability Statistics		
Cronbach's Alpha	Cronbach's Alpha Based on Standardized Items	N of Items
0.730	0.79	50

Interpretation:

Cronbach's Alpha (0.730):

This value indicates that questionnaire has a reasonable level of internal consistency. Generally, values above 0.7 are considered acceptable, and it means that the questionnaire in all items Pass the reliability test and it is valid.

Cronbach's Alpha Based on Standardized Items (0.79):

This value is similar to the original alpha and suggests that standardizing the items (i.e., adjusting for differences in variance) does not significantly affect the reliability. This is a good sign, indicating that the scale's performance is consistent regardless of item variance. Which also indicates the good consistency, reliability and Validity of the questionnaire Cronbach's Alpha.

Survey Design:

The questionnaire consisted of three main sections. The first gathered demographic data such as workplace, department, age, gender, academic qualifications, clinical experience, and prior training in nephrotoxicity or dose adjustment. The second section assessed pharmacists' knowledge across five domains: CKD definition and classification, mechanisms of drug-induced nephrotoxicity, risk factors, identification of nephrotoxic drugs, and appropriate dose adjustment strategies. The third section explored pharmacists' opinions about the causes of dosing errors and non-adherence to renal dosing guidelines, including barriers like lack of training, delayed lab results, and conflicting guidelines.

For scoring of responses of participating pharmacists, each correct response was scored one while incorrect response scored zero. The mean score for each of the 50 items and the mean score for each section were calculated. The overall mean score for the total 50 items ranged between 0 and 50, with a rate between 0% to 100%. Knowledge was

classified into three classes according to Bloom's taxonomy for categorizing educational goals. Knowledge was classified as good when the correct response between 80%-100% (40-50 out of the 50 item), Fair (moderate) knowledge when the rate of correct response and score between 60%-79% and poor (low) when the correct response and mean score less than 60%. According to these cut-off values, the participating pharmacist assigned to have good knowledge if he/she had correct responses for 40- 50 out of the 50 items, Fair (moderate) when they have a total of 30-39 correct responses and poor when they have less than 30 correct responses toward the 50 items (16, 17).

Participants

The four institutions comprised 110 clinical pharmacists employed in emergency department, dialysis ward and internal medicine and nephrology ward. The Raosoft online calculator was utilized to determine the necessary sample size (18). With a 95% confidence interval, a 5% margin of error, and a 50% response distribution, the minimum effective sample size required is 83. The questionnaire was delivered by hand to 100 pharmacists, who were assured that participation was voluntary, confidentiality would be maintained, and the completion time would not exceed 15 minutes. They received instructions as well.

A census of all eligible pharmacists (n = 110) across four major hospitals in Al-Najaf province was conducted. Out of these, 100 pharmacists agreed to participate and completed the questionnaire, yielding a response rate of 91%. No sampling method was applied, as all eligible pharmacists were invited to take part in the study.

Inclusion and exclusion criteria

The study included all pharmacists employed in the clinical wards of the four selected healthcare institutions. The exclusion criteria include pharmacists employed at the mentioned institutions but not inside the emergency department, dialysis ward and internal medicine and nephrology ward , as well as those working in other healthcare institutions.

Data Analysis

Data of the participating pharmacists were entered managed and analyzed using the statistical package for social sciences version 28 (SPSS28). The scale (continuous) variables including the age and the produced total scores were examined for normal statistical distribution and expressed as mean ± standard deviation and median accordingly. The categorical variables including the correct responses towards the items of questionnaire were presented as frequencies and percentages. The scale variables were compared using the student's t test and ANOVA test when the variable followed the normal statistical distribution while Mann-Whitney test and Kruskal-Wallis H test used to compare the scale variables which were not normally distributed. All statical tests and processing were performed at a two-tailed level of significance of <0.05.

III. RESULT

In this study a total of 100 pharmacists were enrolled from four main hospitals in Al-Najaf province, they were 35 from Al-Hakeem Hospital, 27 Al-Sader Teaching Hospital, 24 Al-Najaf Teaching Hospital and 14 pharmacists from Al-Forat Teaching Hospital. The mean age of the participating pharmacists was 27.2 ± 2.7 (range: 24 – 45) years and 64% of the participating pharmacists were aged between 24-27 years. Female pharmacists were the dominant among the studied group; they accounted for 79%. Most the participating pharmacists, (93%), had bachelor of pharmacy degree, 31% had a duration in practice of ≤ one year, 55% between 2-5 years and 14% had a duration in practice of > 5 years. Only 3 participating pharmacists had participated in a training course on nephrotoxicity or dosing adjustment, (Table 1).

Table 1. Baseline characteristics of 100 participating pharmacists in Najaf

Variable		No. of pharmacists	%
Hospital/ work place	Al-Hakeem Hospital	35	35.0
	Al-Sader Teaching Hospital	27	27.0
	Al-Najaf Teaching Hospital	24	24.0
	Al-Forat Teaching Hospital	14	14.0
Department/ Ward:	Internal Medicine	47	47.0
	Emergency department	29	29.0
	Dialysis ward	24	24.0
Age (year)	24 - 25	30	30.0
	26 - 27	34	34.0
	28 - 29	24	24.0
	≥ 30	12	12.0
Gender	Male	21	21.0
	Female	79	79.0
Degree/ graduation	Bachelor of pharmacy	93	93.0
	Diploma/ Master	7	7.0
Duration in clinical practice	≤ one year	31	31.0
	2 - 3 years	37	37.0
	4 - 5 years	18	18.0
	> 5 years	14	14.0
Having a previous training course*	Yes	3	3.0
	No	97	97.0

*Previously participated in a course on nephrotoxicity or Dosing Adjustment

General information of participating pharmacists about CKD (section 2-A) (5 items): the overall mean score for this section was 0.65 ± 0.20 which is within the fair level of knowledge, (Table 2).

Table 2. Responses of participating pharmacists about the general information about CKD (5 items).

Item	No.	%	No.	%	Mean score (SD)
Definition of CKD	95	95.0	5	5.0	0.95 (0.22)
Checking CrCL before dispensing medications	92	92.0	8	8.0	0.92 (0.27)
The KDIGO staging of CKD criteria	46	46.0	54	54.0	0.46 (0.50)
GFR in Stage III a CKD	41	41.0	59	59.0	0.41 (0.49)
Albumin/creatinine ratio in A2 stage CKD	54	54.0	46	46.0	0.54 (0.50)
Overall knowledge score for this section and evaluation					0.65 (0.20) Fair

SD: standard deviation

Knowledge about Mechanism of nephrotoxicity (section 2-B) (10 items): Regarding this section, the overall mean score for the total 10 items was 0.54 ± 0.19 providing an overall poor knowledge level about this section, (Table 3).

Table 3. Knowledge about Mechanism of nephrotoxicity (10 items)

Item	Correct		Incorrect		Mean score (SD)
	No.	%	No.	%	
Nephrotoxic medications safety at lower doses	66	66.0	34	34.0	0.66 (0.30)
All nephrotoxic medications act through the same mechanism	86	86.0	14	14.0	0.86 (0.32)
Certain nephrotoxic medications act through their effect by renal vasodilation and increasing blood flow to the kidney	43	43.0	57	57.0	0.43 (0.19)
Radiocontrast media nephrotoxicity occur due to High osmolarity, medullary vasoconstriction, ↑ active transport in thick ascending loop of Henle leading to ↑ O2 demand	44	44.0	56	56.0	0.44 (0.25)
Captopril can cause nephrotoxicity through Impair angiotensin II–mediated afferent arteriole dilation during kidney hypoperfusion	41	41.0	59	59.0	0.41 (0.18)
The aminoglycosides nephrotoxicity occur through direct tubular toxicity	69	69.0	31	31.0	0.69 (0.29)
Ibuprofen can cause nephrotoxicity through hemodynamically induced AKI caused by vasoconstriction via reduced prostaglandin production	78	78.0	22	22.0	0.78 (0.28)
Sulfonamides nephrotoxicity occurs due to acute interstitial nephritis and crystal nephropathy	48	48.0	52	52.0	0.48 (0.31)
The Amphotericin nephrotoxicity occur through afferent vasodilation and direct action to reduce GFR	33	33.0	67	67.0	0.33 (0.18)
Omeprazole may cause nephrotoxicity due to metabolic alkalosis	41	41.0	59	59.0	0.41 (0.21)
Overall knowledge score for this section					0.54 (0.19) Poor

SD: standard deviation

Knowledge about risk factor of nephrotoxicity, (Section 2-C): (10 items): In total, the overall mean score for this section was 0.69 ± 0.16 giving a fair knowledge level, (Table 4).

Identifying Nephrotoxic drug, (Section 2-D), (10 items): the overall mean score for this section was 0.64 ± 0.22 which is a fair level of knowledge in this section, (Table 5)

Knowledge about dose adjustment and optimization, (Section 2-E), (15 items): Table 6 summarizes the responses of participating pharmacists towards the knowledge about dose adjustment and optimization where they asked about 15 drugs. The rate of correct responses was generally low to medium (31%-64%) except for meropenem (79%), which resulted in an overall mean score for this section of 0.49 ± 0.22 which is a poor knowledge level.

Overall knowledge score for all sections and evaluation (50 items): As shown in (Table 7) which summarizes the overall mean knowledge score for each section and the overall total score for all sections (50 items), it had been found that the overall mean score was 0.59 ± 0.14 and it was within the poor level of knowledge. Furthermore, according to the level of knowledge obtained for the total 50 items and the evaluation of each participating pharmacist's score, it had been found that only 10% of the participating pharmacists had good knowledge about nephrotoxic medications and dosing adjustment for patients with chronic kidney disease, 41% had fair and 49% had poor knowledge, (Figure 1).

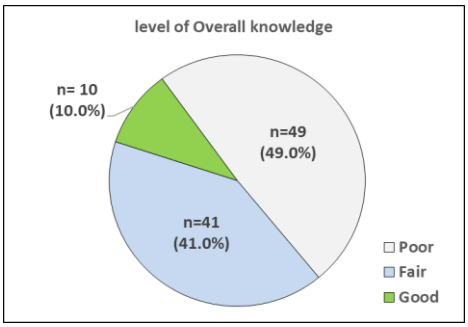

Figure 1. Pie-chart showing the distribution of the participating pharmacists according to the level of overall knowledge for the total 50 items. The pie slices clarify that only minority, (10%), of the pharmacist had good knowledge, a large proportion (49%) had poor and (41%) had fair level of overall knowledge.

Table 4. Knowledge about risk factor of nephrotoxicity (10 items)

	Correct		Incorrect		Mean score (SD)
Item	No.	%	No.	%	
Patient older than 60 years	89	89.0	11	11.0	0.89 (0.30)
Baseline GFR of 60 ml/min/1.73 m^2	54	54.0	46	46.0	0.55 (0.21)
Volume depletion or dehydration	78	78.0	22	22.0	0.79 (0.17)
Combination the nephrotoxic drugs	84	84.0	16	16.0	0.84 (0.14)
Presence of comorbidities ex hypertension ,diabetes mellitus and heart failure	87	87.0	13	13.0	0.87 (0.30)
Recent surgery	44	44.0	56	56.0	0.44 (0.27)
Genetic factor	67	67.0	33	33.0	0.67 (0.27)
Use of acetaminophen	67	67.0	33	33.0	0.67 (0.29)
Using of cisplatin	59	59.0	41	41.0	0.59 (0.29)
contrast media exposure	62	62.0	38	38.0	0.62 (0.31)
Overall knowledge score for this section and evaluation					0.69 (0.16) Fair

SD: standard deviation

Table 5. Identifying Nephrotoxic drugs (10 items)

	Correct		Incorrect		Mean score (SD)
	No.	%	No.	%	
Amphotericin	72	72.0	28	28.0	0.72 (0.30)
Metronidazole	68	68.0	32	32.0	0.69 (0.22)
Vancomycin	75	75.0	25	25.0	0.75 (0.31)
Captopril	53	53.0	47	47.0	0.53 (0.31)

Cisplatin	59	59.0	41	41.0	0.59 (0.31)
Ceftriaxone	72	72.0	28	28.0	0.72 (0.29)
Amikacin	79	79.0	21	21.0	0.79 (0.26)
Acyclovir	45	45.0	55	55.0	0.45 (0.31)
Sitagliptin	41	41.0	59	59.0	0.41 (0.30)
Ibuprofen	79	79.0	21	21.0	0.79 (0.31)
Overall knowledge score for this section					0.64 (0.22) Fair

SD: standard deviation

Table 6. Knowledge about dose adjustment and optimization (15 items)

	Correct		Incorrect		Mean score (SD)
	No.	%	No.	%	
Amikacin	54	54.0	46	46.0	0.54 (0.25)
Co-trimoxazole	37	37.0	63	63.0	0.37 (0.23)
Piperacillin	56	56.0	44	44.0	0.56 (0.33)
Vancomycin	64	64.0	36	36.0	0.64 (0.41)
Meropenem	79	79.0	21	21.0	0.79 (0.40)
Heparin	48	48.0	52	52.0	0.48 (0.30)
Tramadol	31	31.0	69	69.0	0.31 (0.18)
Spironolactone	49	49.0	51	51.0	0.49 (0.22)
Atorvastatin	58	58.0	42	42.0	0.58 (0.33)
Empagliflozin	37	37.0	63	63.0	0.37 (0.16)
Enoxaparin	48	48.0	52	52.0	0.48 (0.21)
Ceftazidime	58	58.0	42	42.0	0.58 (0.32)
Amlodipine	49	49.0	51	51.0	0.49 (0.27)
Omeprazole	50	50.0	50	50.0	0.50 (0.29)
Allopurinol	37	37.0	63	63.0	0.37 (0.11)
Overall knowledge score for this section					0.49 (0.22) Poor

SD: standard deviation

Table 7. Mean knowledge scores for the five sections and the overall knowledge score of all sections

Section	Mean	SD	Evaluation
General information about CKD (5 items)	0.65	0.20	Fair
Mechanism of nephrotoxicity (10 items)	0.54	0.19	Poor
Risk factor of nephrotoxicity (10 items)	0.69	0.16	Fair
Identifying Nephrotoxic drug (10 items)	0.64	0.22	Fair
Dose adjustment and optimization (15 items)	0.49	0.22	Poor
Overall knowledge score for all sections and evaluation (50 items)	0.59	0.14	Poor

SD: standard deviation

Reasons of common errors in dosing adjustment: The participating pharmacists attributed the errors in dosing adjustment to several reasons and these were displayed in (Table 8), however, most participating pharmacists mentioned more than one reason.

Table 8. Reasons for common errors in dosing adjustment

Reasons	No.	%
Lack of awareness of guidelines	84	84.0
Inadequate staff training: Healthcare providers may not be well-trained in dosing adjustments.	76	76.0
Guidelines are difficult or inconvenient to use	57	57.0
Lack of therapeutic drug monitoring (TDM) so Failure to measure drug levels in medications requiring monitoring.	61	61.0
Not involving pharmacists in prescribing of drug	55	55.0
Need for new resources or facilities that are not available in our hospitals	53	53.0
Disagreement between guidelines is confusing	44	44.0
Delayed lab results so Dose adjustments may not be made promptly if renal function changes before lab results are reviewed	54	54.0
Poor documentation so Missing or unclear records can lead to incorrect dosing	67	67.0
Others (please mention)	62	62.0

Correlation between knowledge scores and other variables

The correlation analysis performed between the knowledge scores for the 5 sections as dependent variables against the participating pharmacists (independent) variables, age and duration in practice using Spearman's bivariate correlation analysis, this test used because both, the dependent and independent variables did not follow the normal statistical distribution, however, no significant correlation was found between age and duration in practice from one side against all the knowledge scores for the five sections, in all comparisons, (P. value>0.05), (Table 9). Further analysis was performed by comparing the median value of the total score for each of the five sections across the independent categorical variables using non-parametric tests ((Kruskal Wallis Test and Mann-Whitney U., no significant differences had been found in median values across all these categorical variables except only one significant correlation between gender and total score of section 2-E where male pharmacists had significantly higher median total knowledge score at section 2-E , (P. value = 0.001), the detailed median values and interquartile range (IQR) are summarized in (Table 10).

Table 9. Results of Spearman's bivariate analysis for the correlation of knowledge scores and pharmacists' age and duration in clinical practice / professional experience

Variable	Statistics	Total score section 2-A	Total score section 2- B	Total score section 2- C	Total score section 2- D	Total score section 2- E
Age (year)	Cor. Coeff	0.041	0.091	0.048	0.088	0.112
	P. value	0.688	0.367	0.635	0.386	0.265
Duration in clinical practice / professional experience	Cor. Coeff	0.002	0.124	0.049	0.11	0.087
	P. value	0.984	0.219	0.629	0.278	0.387

Cor. Coeff: Correlation coefficient, *Significant

Table 10. Comparison of median scores across different categorical variables

Variable	Section 2-A	Section 2-B	Section 2-C	Section 2-D	Section 2-E
Hospital/ work place:	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)
Al-Hakeem Hospital	3 (3-4)	5 (4-6)	7 (7-8)	6 (6-8)	6 (6-9)
Al-Sader Teaching Hospital	3 (3-4)	5 (5-7)	7 (7-8)	7 (6-8)	8 (7-9)
Al-Najaf Teaching Hospital	3 (3-4)	5.5 (5-7)	7 (7-9)	8 (8-9)	7.5 (6-9)
Al-Forat Teaching Hospital	3 (3-4)	6 (6-10)	7 (7-9)	6 (6-7)	9 (9-11)
P. value (Kruskal Wallis Test)	0.579	0.342	0.733	0.132	0.171
Department/ Ward:					
Internal Medicine	3 (3-4)	6 (6-8)	7 (7-8)	7 (6-8)	8 (7-9)
Emergency department	3 (3-4)	5 (5-6)	7 (7-8)	6 (6-8)	8 (7-11)
Dialysis ward	3 (3-4)	5.5 (4-7)	7 (7-8)	6.5 (6-8)	7 (6-10)
P. value (Kruskal Wallis Test)	0.955	0.719	0.863	0.395	0.781
Gender					
Male	3 (3-4)	6 (6-8)	7 (7-8)	8 (8-9)	10 (9-11)
Female	3 (3-4)	5 (5-6)	7 (7-8)	6 (6-7)	7 (6-9)
P. value (Mann-Whitney U)	0.573	0.055	0.377	0.142	**0.001***
Degree					
Bachelor of pharmacy	3 (3-4)	5 (5-6)	7 (7-8)	7 (7-8)	8 (7-9)
Diploma/ Master	4 (4-5)	5 (4-8)	7 (7-9)	7 (6-9)	9 (6-12)
P. value (Mann-Whitney U)	0.676	0.88	0.885	0.832	0.385
Participated in a training course					
Yes	3 (0-0)	5 (4-6)	9 (9-9)	9 (9-9)	12 (5-14)
No	3 (3-4)	5 (5-6)	7 (7-8)	7 (7-8)	8 (7-9)
P. value (Mann-Whitney U)	0.611	0.609	0.404	0.17	0.197
***Significant**					

Moreover, the correlation between the overall mean knowledge score for the whole 5 sections (total of 50 items) assessed against other variables by comparing the mean overall total score values across the categories of each independent variable, as the mean overall total score showed normal statistical distribution, it compared across the across all categorical variables with parametric tests (student's t test and Analysis of variances (ANOVA). Results of comparisons of mean scores are summarized in (Tables 11 and 12), the mean score was not significantly different ($P>0.05$) across all categorical variables except the gender where males showed a significantly higher overall total knowledge score compared to female pharmacists, the mean score was 32.95 ± 4.99 and 28.68 ± 7.10 out of 50, respectively, (p. value=0.011). For more clarification of the correlation between male gender and higher knowledge score, boxplot was conducted and supported this finding where the median score value was higher in male than female pharmacists, (P. value = 0.027), (Figure 2).

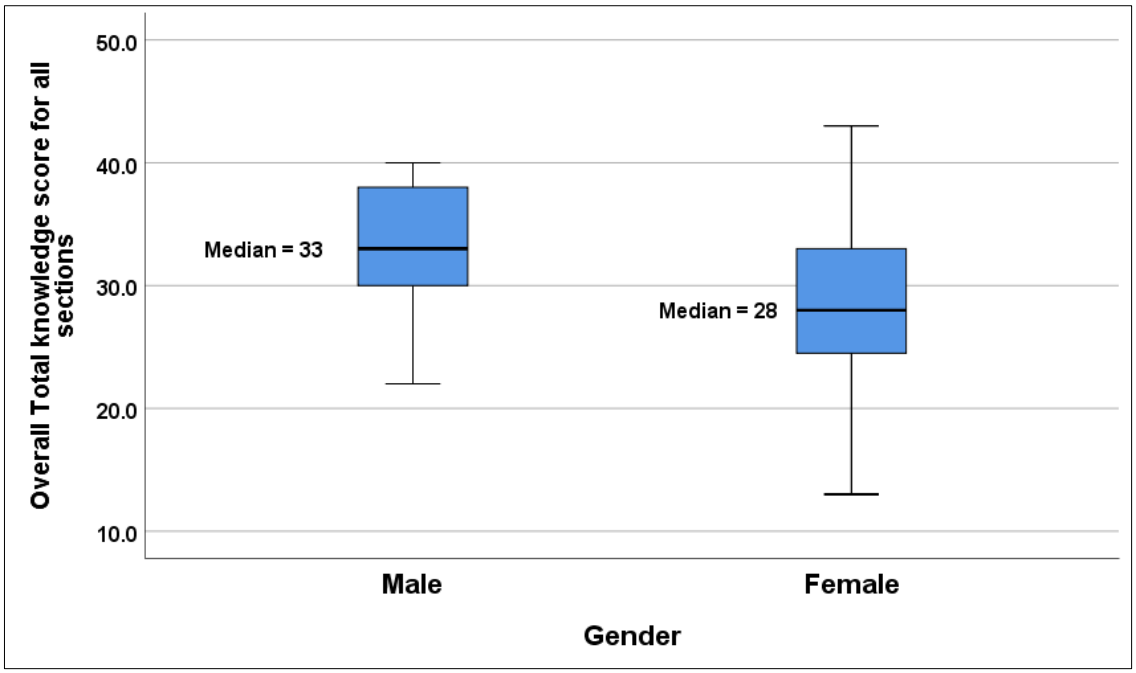

Figure 2. Boxplot showing the distribution of the overall knowledge scores across gender, the median knowledge score was significantly higher among male pharmacists (median =33) compared to females (median =28), (Mann-Whitney U test, P. value = 0.027). The box represents the interquartile range (IQR), the horizontal line within the box represents the median and the whiskers represent the minimum andmaximum score which reflect the spread of the scores and highlight the variability among both genders.

Table 11. Comparison of mean total score of participating pharmacists according to workplace

		Mean	SD	P. value
Hospital	Al-Hakeem Hospital	28.14	7.06	0.294*
	Al-Sader Teaching Hospital	29.15	7.25	
	Al-Najaf Teaching Hospital	31.29	6.93	
	Al-Forat Teaching Hospital	31.07	5.48	
Department/ Ward	Internal Medicine	30.02	7.24	0.802*
	Emergency department	28.93	7.16	
	Dialysis ward	29.50	6.15	

* Analysis of variances (ANOVA) test used in comparison

Table 12. Comparison of mean total score of participating pharmacists according to demographic characteristics of participating pharmacists

Variable		Mean	SD	
Age (year)	24 - 25	29.23	7.06	0.995*
	26 - 27	29.50	8.12	
	28 - 29	29.63	5.87	
	≥ 30	30.58	5.30	
Gender	Male	32.95	4.99	**0.011*sig**
	Female	28.68	7.10	
Degree	**Bachelor of pharmacy**	**29.52**	**7.03**	**0.738****
	Diploma/ Master	30.43	5.56	
Duration in clinical practice / professional experience	≤ one year	28.65	7.29	0.412*
	2 - 3 year	30.84	7.87	
	4 - 5 year	28.00	5.11	
	> 5 years	30.36	5.05	
Have a previous training course	**Yes**	**34.67**	**9.29**	**0.198****
	No	29.42	6.84	

*ANOVA test used in comparison, ** student's t test (two independent groups) used in comparison, sig: Significant

IV. DISCUSSION:

Several published studies have identified substantial difficulties in dose modification and medication errors among patients with chronic kidney disease (19).A lack of understanding of the importance and optimization of pharmaceutical dosages often leads to mistakes in prescribing for patients with renal impairment (20). Additionally, the length of hospital stays, the costs associated with them, and the death rate all rise with each negative medication event. A considerable percentage of drug-related hospital admissions are preventable and contingent upon dosage.The Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice guideline recommends the avoidance or dosage reduction of nephrotoxic drugs for individuals with chronic kidney disease (CKD) Stage ≥ G3 [estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m²] (22). In the present study, 100 pharmacists from four major hospitals in Al-Najaf province were enrolled, with the majority being young and predominantly female , since most of the workers in hospitals clinical wards are females, while males tend to occupy managerial positions, working in the dispensary or taking night shifts. This study shows a comprehensive assessment of the knowledge nephrotoxic medications and drug dose adjustments by Iraqi clinical pharmacists in patients with renal impairment. The findings reveal

General knowledge about CKD :

Participants demonstrated a fair level of knowledge in the section assessing general CKD concepts, achieving a mean score of 65% . Although this section did not represent the highest performance in the survey, participants still showed strong understanding of some essential CKD principles. For example, 95% correctly identified the definition of chronic kidney disease, and 92% recognized the need to evaluate creatinine clearance when assessing renal function. These findings indicate that pharmacists possess an acceptable baseline awareness of core renal concepts due the general concepts of CKD—such as its basic definition, diagnostic time frame, and the importance of evaluating creatinine clearance—are commonly emphasized in undergraduate pharmacy curricula and these principles are frequently encountered in daily

pharmacy practice, as renal function assessment is an essential part of dispensing many commonly used medications, including antibiotics, anticoagulants, and antidiabetics.This aligns with previous study conducted in palestine , to evaluate Pharmacists' Knowledge about Chronic Kidney Disease and its Management. 48% of the participant pharmacists reported poor chronic kidney disease knowledge and 60% reported poor knowledge about CKD management (23) and another study conducted in pakistan , to evaluate Pharmacists' Knowledge regarding Chronic Kidney Disease and mean knowledge was found to be 54.76% (24).

Knowledge about nephrotoxic medications:
Participants demonstrated a poor level of knowledge about mechanisms of nephrotoxicity concepts, achieving a mean score of 54%. Pharmacists particularly struggled with items linked to complex renal injury pathways, such as glomerular and tubular mechanisms due to emphasizing the limited exposure to practical pharmacology and clinical toxicology in routine practice To the best of our knowledge, pharmacists' knowledge of the mechanisms of drug-induced nephrotoxicity has not been extensively studied, particularly in developing countries.

Level of Knowledge concerning risk factors for nephrotoxicity was fair, with a score of 69% representing the highest performance among all assessed domains. This relatively elevated score may be explained by the fact that many of the commonly recognized risk factors—such as advanced age, pre-existing CKD, dehydration, heart failure, diabetes, and hypertension—are routinely encountered in daily clinical practice. Pharmacists frequently monitor these conditions when reviewing medication profiles, which increases their familiarity with patient-related determinants of renal vulnerability.

The pharmacists' ability to correctly identify nephrotoxic drugs showed a fair level of performance 64%. While drugs such as amikacin and ibuprofen were well recognized, others (e.g., sitagliptin, aceclovir) had lower recognition rates. can be explained by, pharmacists tend to demonstrate stronger recognition of nephrotoxicity among drug classes that are frequently encountered in daily practice—such as aminoglycosides, vancomycin, amphotericin B, and NSAIDs. These medications are commonly highlighted during pharmacy education, frequently monitored in hospital settings, and widely discussed in antimicrobial stewardship programs. This repeated exposure increases the likelihood that pharmacists correctly identify their nephrotoxic potential. Numan A. et.al.2018, show Respondents showed different levels of knowledge about the 25 risk factors for acute kidney injury (AKI) and the 15 nephrotoxic agents. For example, 96% of them knew about nephrotoxic medications, but only 20% knew that being female was a risk factor for AKI. Moreover, 92% identified aminoglycosides, while 47% identified ciprofloxacin as nephrotoxic agents. A significantly larger percentage of physicians acknowledged specific AKI risk factors in comparison to pharmacists; conversely, a substantially higher proportion of pharmacists recognized individual AKI-inducing medications than physicians (25). Farid S. et al. (2022) examined 424 responses, consisting of 40.1% males, 39.2% physicians, 34.0% senior medical students or resident physicians, 16.3% nurses, and 10.6% pharmacists. The most well-known risks and weaknesses for AKI were sepsis/septic shock (95.0%) and diabetes mellitus (91.3%). The less well-known risks and weaknesses were exposure to gadolinium-based contrast (23.3%) and chronic liver disease (55.7%). The most commonly recognized nephrotoxic drugs were vancomycin (82.3%) and diclofenac (80.4%), whereas the least recognized were acyclovir (34.0%) and cotrimoxazole (30.4%) (26).

Knowledge about dose adjustment and optimization:
The poorest performance across all domains was related to renal dose adjustment and optimization, with a mean score of 49% , classified as poor. This is a critical clinical area, as inappropriate dose adjustment in CKD patients is a major cause of preventable adverse drug events. The low scores may indicate insufficient pharmacokinetic training, lack of practical exposure, or limited access to standardized dosing guidelines. earlier study conducted in Saudi Arabia reported the knowledge score of pharmacists concerning renal dose adjustment was 79% (27) .another study conducted in Sudan , to evaluate Knowledge and

Practice of Sudanese Clinical Pharmacists Towards Drugs that Require Dosage Adjustment in Renally Impaired Patients reported 157 (61.6%) of the clinical pharmacists achieved a sufficient knowledge score, while 98 (38.4%) had an insufficient knowledge score (28) .also in Pakistan, to assess The knowledge, attitudes, and opinions of pharmacists addressing renal dosage modification in chronic kidney disease patients indicated a knowledge score of 88% (29). Additionally, in Malaysia, a study assessed pharmacists' attitudes, self-reported knowledge, and practices regarding dosage adjustment for chronic kidney disease patients, revealing a knowledge score of 60% addressing renal dose adjustment(30).

Our study found no significant differences in knowledge based on age, work place, institution, degree, years of experience,or participated in a training course or No except Gender , where males showed a significantly higher knowledge score compared to female pharmacists. Study from Pakistan similarly revealed that there was a positive association between the perception score of pharmacists with gender; males have higher score as compared to females (31). One possible explanation is that male pharmacists may have greater flexibility or institutional support to participate in workshops, clinical rounds, and specialized training programs related to pharmacotherapy and renal dose adjustment. Enhanced access to such professional development activities can significantly improve clinical competence and may therefore contribute to the observed gender-based difference in knowledge scores.

The Strengths of the study :

To the best of our knowledge,This is first study in Iraq that comprehensively evaluates pharmacists' knowledge about nephrotoxic medications and renal dose adjustment using a structured, validated questionnaire. Inclusion of multiple hospitals and diverse clinical wards enhances the representativeness of the findings.

The limitations of study :

The sample size, although adequate for statistical analysis, may not fully represent pharmacists in other Iraqi provinces. As a recommendation, we advise Develop targeted continuing education programs focusing on nephrotoxic medications, CKD management, and renal dose adjustment. Hospitals should provide pharmacists with up-to-date, easily accessible renal dosing guidelines (e.g., KDIGO, Medscape, UpToDate). Encourage interdisciplinary collaboration between pharmacists, nephrologists, and intensivists .Additionally, advanced clinical pharmacy training programs and certification in renal pharmacotherapy should be promoted.

For Future Research, we recommend assessing the impact of these implemented educational programs on pharmacists' performance and patient outcomes.

II. CONCLUSION :

The results of this study indicate that the general overall knowledge of clinical pharmacists in Al-Najaf hospitals regarding nephrotoxic medications and drug dose adjustments in patients with CKD was 59% it was within the poor level of knowledge. only 10% of the participating pharmacists had good knowledge, 41% had fair and 49% had poor knowledge. Indeed, similar level of knowledge was found between participants with different characteristics except for gender, where males showed a significantly higher knowledge score compared to female pharmacists. As a recommendation, This study highlights significant gaps in Iraqi clinical pharmacists' knowledge, particularly in the areas of nephrotoxicity mechanisms and renal dose adjustment. Despite fair understanding of general CKD concepts and risk factors, insufficient knowledge in these critical clinical domains may contribute to preventable medication-related kidney injury. Therefore, there is an urgent need for targeted, continuous educational programs and practical training initiatives aimed at improving pharmacists' competence in nephrotoxic drug identification and dose optimization, which can enhance patient safety and clinical outcomes in hospital settings.

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