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RESEARCH ARTICLE

The use of nephrotoxic drugs in patients with chronic kidney disease

Roland Nnaemeka Okoro[1] · **Victor Titus Farate**[1]

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Abstract

Background The use of nephrotoxic drugs has the potential to accelerate the loss of kidney function and increase the risk of end-stage renal disease. *Objectives* To determine the prevalence of nephrotoxic drugs use in patients with chronic kidney disease at two major hospitals in Maiduguri and to evaluate the predictors of exposure to the contraindicated ones. *Methods* This retrospective study used data from the patients' medical records. Patients aged ≥ 18 years that were diagnosed with chronic kidney disease from 2013 to 2017 with documented serum creatinine levels for the period under review were included in the study. Descriptive statistics were used to summarize the socio-demographics, clinical and biochemical characteristics of the study population. Predictors of nephrotoxic, and contraindicated nephrotoxic medication exposure were assessed using Chi square and logistic regression tests respectively. *Results* The results are based on data from 201 patients. Of these, 96.0% received at least one prescription of a nephrotoxic drug within the period under review. Multivariate logistic regression showed that the odds of receiving the seven contraindicated nephrotoxic drugs increased in those aged 60 years or older (OR 8.00, 95% CI 1.67–38.40), and those with mild/moderate chronic kidney disease (OR 3.51, 95% CI 1.14–10.77). Main Outcome Measure Prevalence of nephrotoxic drug exposure in patients with chronic kidney disease. *Conclusions* Large proportions of patients with chronic kidney disease received nephrotoxic drugs, mainly diuretics. However, patients aged 60 years or older, and those at chronic kidney disease stages 2–3 were significantly more likely to receive contraindicated nephrotoxic drugs compared to other age groups and chronic kidney disease stages.

Keywords Chronic kidney disease · Contra-indication · Nephrotoxic drugs · Nigeria

Impacts on Practice

- Collaboration between prescribers and clinical pharmacists is a good option that may reduce the danger of exposing at-risk patients with nephrotoxic medications.
- Clinical pharmacist should be included in the renal care team in Nigerian hospitals to increase awareness of nephrotoxic drugs and optimize drug treatment in patients with CKD.
- The clinical pharmacists' educational interventions to optimize drug-treatment in this high-risk group of patients with chronic kidney disease should be mostly targeted at patients aged 60 years or older, and those at the CKD-disease stages 2–3.

Introduction

It is estimated that the yearly incidence of kidney disease is 100 per 1,000,000 Nigerians and the number of incident kidney failure diagnosed yearly in the population of 170 million is 17,000 [1]. Progression of chronic kidney disease (CKD) often leads to end-stage renal disease (ESRD) which impacts negatively on the patient and relatives' quality of life due to increased morbidity and disability, coupled with increasing healthcare costs [2]. Inappropriate drug prescribing is common, also in developing nations including Nigeria, and often leads to adverse events, certainly in CKD patients. Hence,

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✉ Roland Nnaemeka Okoro
orolandn@gmail.com

[1] Department of Clinical Pharmacy and Pharmacy Administration, Faculty of Pharmacy, University of Maiduguri, Maiduguri, Nigeria

many nephrotoxic drugs should be avoided or used with caution in individuals with underlying CKD.

Studies from many parts of the world have shown the use of nephrotoxic drugs in patients with CKD. A community-based analysis of inappropriate prescribing of nephrotoxic drugs in Sweden found that 18% of patients with CKD received nephrotoxic drugs inappropriaately, mainly non-steriodal anti-inflammatory drugs (NSAIDs) [3]. In Norway, a prospective study on the use of renal-risk drugs in patients with renal impairment reported incorrect drug dose and inappropriate drug choice as the most common problems [4]. A retrospective study that evaluated contraindicated medications use in the in-patients with renal insufficiency in a Saudi Arabian Hospital that has a computerized clinical decision support system (CDSS) found that a total of 314 patients received at least one medication that was renally cleared and/or potentially nephrotoxic, and 14% of these medications were contraindicated and resulted in a system alert. Yet they were administered to these patients [5]. A retrospective population-based study on the burden of nephrotoxic drug prescriptions in patients with CKD in Southern Italy reported that 49.8% and 45.2% of patients received at least one prescription for a contraindicated nephrotoxic drug within 1 year prior to or after first CKD diagnosis respectively, while 56.3% had at least one NSAIDs prescription between CKD diagnosis and end of follow-up [6].

Furthermore, a US-based large case–control study revealed that the inappropriate prescription of nephrotoxic or renally cleared medications occurred at a rate of 70% in patients hospitalized with renal impairment [7]. Another US study found that nephrotoxic medication exposure occurred in 72% of the study population with CDK. Of these, 47.2% and 52.8% were prescribed one and at least two nephrotoxic medications [8]. A UK-based study that identified patients with CKD from general practice computer records reported that 346 patients with CKD were prescribed potentially nephrotoxic drugs and over 4000 prescriptions were issued for drugs recommended being used with caution in renal impairment [9].

Deterioration of kidney function is often linked to the use (especially chronic use of high dosage) of nephrotoxic drugs such as NSAIDs [10, 11]. Nephrotoxic medication exposure among patients with CKD, whether presenting with a reduced glomerular filtration rate (GFR) or with kidney damage but preserved function, are at risk of acute kidney injury (AKI), permanent kidney function loss and costly preventable adverse drug events. Moreover, adverse drug events in CKD have the potential to worsen kidney function and may increase the risk of ESRD beyond what is expected from the disease's natural history [12]. Therefore, physicians caring for these patients must be familiar with the drugs that commonly cause nephrotoxicity. This will facilitate appropriate preventive strategies, early identification, and directed disease management.

Patients with CKD are exposed to numerous medications, many of which have the nephrotoxic potential. Even though reducing drug-related problems are important for all patients receiving medical care, identifying the use of nephrotoxic drugs in patients with CKD is of particular importance because it has the capacity to reduce increasing levels of drug-related morbidity and mortality associated with nephrotoxic drug use and to prevent the high financial cost of adverse drug events in this patient group. This measure will also reduce the prevalence of kidney failure, which has been increasing at a fast rate over the last few decades. In view of these issues, it is crucial that physicians caring for these patients use the appropriate drugs in recognition of drugs with nephrotoxic potential.

Aims of the Study

This study aimed to determine the prevalence of nephrotoxic drugs use in patients with CKD at two major hospitals in Maiduguri and to evaluate the predictors of exposure to the contraindicated ones.

Ethics Approval

The study protocol was reviewed and ethical approval granted by the Research and Ethics Committees of the study hospitals.

Methods

This was a retrospective study of CKD patients who received treatment between January 2013 and December 2017 at the Nephrology units of the University of Maiduguri Teaching Hospital (UMTH) and State Specialist Hospital (SSH) in Maiduguri, Borno State capital. UMTH is located along Bama road, Maiduguri. It is the tertiary institution (a federal referral hospital) that has numerous Specialty units that serve patients mainly from the northeastern part of Nigeria. SSH is located along Shehu Laminu Way, Maiduguri. It is a public secondary healthcare facility owned by Borno State government, which serves as a referral point for primary healthcare centres in Maiduguri.

Patients (≥ 18 years) diagnosed with CKD between 2013 and 2017 with GFR estimated with the modification of diet in renal disease (MDRD) formula from 1 to 89 ml/min/1.73 m^2 [13] as no other parameters (proteinuria, histological and imaging abnormalities test results) were available, and using at least one drug were included. Patients < 18 years, those without documented creatinine values,

those diagnosed with CKD from 2013 to 2017 without regular follow-up visits and those diagnosed with AKI were excluded from the study. Patients were evaluated according to their stage of CKD using the definition of the National Kidney Foundation: Stage 1 (kidney damage with normal or increased GFR) GFR ≥ 90 ml/min/1.73 m^2, Stage 2 (Kidney damage with mild reduction in GFR) GFR 60–89, stage 3 (moderate reduction in GFR) GFR 30–59 ml/min/1.73 m^2, stage 4 (severe reduction in GFR) 15–29 ml/min/1.73 m^2 and stage 5 (kidney failure) GFR < 15 ml/min/1.73 m^2 [14].

Data Collection

Data were collected for a 5 year period (2013–2017) from the patients' medical records. Information extracted included patient socio-demographics data (age, gender, religion, marital status, occupation, and ethnicity), prescriptions for drugs, and clinical characteristics such as CKD comorbidities, year of CKD diagnosis, blood pressure (BP), serum creatinine, fasting blood glucose, and serum uric acid.

Nephrotoxic Drugs Assessment

Nephrotoxic drug assessment was based on two types of underlying mechanisms: acute interstitial nephritis and tubular cell toxicity. Overall, a list of nephrotoxic drugs (see Table S1) was compiled from published literature [15], while a list of contraindicated nephrotoxic drugs (see Table S2) was drafted from an earlier study [6]. The only drugs available in Nigeria were included in the lists.

Data Analysis

Initially, the study population was described with the means and standard deviations for continuous variables and proportions for categorical variables. Chi square tests were used to evaluate the factors associated with the likelihood of patients receiving a nephrotoxic drug, whereas multivariate logistic regression was employed to determine the patient characteristics associated with receiving contraindicated nephrotoxic medications. The multivariate logistic regression dependent variable was the exposure to a contraindicated nephrotoxic medication (yes/no). The independent variables included patients' gender, age, number of comorbidities (≥ 4 versus ≥ 3), and CKD stage (severe renal failure versus mild/moderate). The risk of receiving at least a contraindicated nephrotoxic drug throughout the 5 year period was reported as odds ratio (OR), along with the 95% confidence interval (95% CI). *P* values of less than 0.05 were considered statistically significant. Estimated GFR was calculated with Omnio® GFR calculator version 3.24.6 (Aptus Health, Inc USA) using MDRD formula. Other analyses were performed using the Statistical Package for Social Sciences (SPSS) for Windows® version 21.0 (SPSS Inc, Version 21.0, Chicago, USA).

Results

A total of 201 patients with CKD were included in this study. The mean age of the study population was 49.5 ± 14.5 years. Over two-thirds of the patients were females (66.2%) with about 77.0% being 40 years or older. Slightly above one-half of the patients accessed care in the tertiary hospital while nearly all the patients were married, Kanuri is the most dominant ethnic group. The detailed account of the socio-demographic information of the study population is given in Table 1.

The majority of the patients had CKD of 2 years (26.4%) and 3 years (19.9%) duration with hypertension alone (35.3%) as the most common CKD comorbidity. More than three-quarter of the study population (87.1%) were at CKD stages 4–5 as at the time of diagnosis. The detailed clinical characteristics of the study population are shown in Table 2.

A total of 193 (96.0%) patients with CKD (51.3% in the tertiary hospital vs. 48.7% in the secondary hospital) received at least one nephrotoxic medication during the study period. There was a huge decline in the proportions of patients that were exposed to nephrotoxic medications from 2013 to 2014 followed by a slight reduction until 2016, then a slight increase in 2017 as shown in Fig. 1.

Of the 384 nephrotoxic medications prescribed during the period under review, 143 (37.2%) were diuretics followed by 58 (15.1%) proton pump inhibitors (PPIs), and 56 (14.6%) xanthine oxidase inhibitor (XOI). The opposite trend was observed for anticonvulsant, and aminoglycosides, which were only 1 (0.3%) each compared to NSAIDs (Fig. 2).

On the evaluation of individual nephrotoxic drugs prescribed, furosemide 94 (24.5%) ranked first, followed by allopurinol 56 (14.6%). Only 1 (0.3%) neomycin, ketoprofen, cotrimoxazole, phenytoin, pantoprazole, naproxen, hydrochlorothiazide (Hctz)/amiloride, and ampicillin/cloxacillin (Amp/clox) each were prescribed. The other individual nephrotoxic drugs prescribed are shown in Fig. 3.

Table 3 presents the characteristics of all included patients and for sub-populations of patients that were unexposed and exposed to a nephrotoxic drug. Of the patients who received a nephrotoxic drug, 96.4% (n = 186) were patients with three or fewer comorbidities compared to 3.6% (n = 7) of those who had four or more comorbidities with no significant difference ($p = 0.583$). Significant majority 75.1% (n = 145) of the patients were exposed to nephrotoxic drugs for a duration less than 90 days compared to 24.9% (n = 48) who were exposed for a duration of 90 days or more ($p < 0.001$). A

Table 1 Socio-demographic data of the study population

Variable	n (%)
Study population	
Tertiary	101 (50.2)
Secondary	100 (49.8)
Sex	
Female	133 (66.2)
Male	68 (33.8)
Age group (years)	
18–39	47 (23.4)
40–59	98 (48.7)
≥60	56 (27.9)
Mean age ± SD	49.5 ± 14.5
Marital status	
Single	10 (5.0)
Married	189 (94.0)
Widowed	2 (1.0)
Tribe	
Kanuri	91 (45.3)
Hausa	30 (14.9)
Babur	15 (7.5)
Shuwa	12 (6.0)
Bura	10 (5.0)
Fulani	9 (4.5)
Marghi	5 (2.5)
Chibok	4 (2.0)
[a]Others	25 (12.3)
Occupation	
House wife	115 (57.2)
Civil servant	28 (13.9)
Business person	28 (13.9)
Farmer	12 (6.0)
Student	8 (4.0)
[b]Others	10 (5.0)

[a]Glada, Igbo, Mandara, Bade, Mafa, Yoruba, Kilba, Kibaku, Tangale, Igala, Ngoshe, Uvoko, Gabai, Chadian, Kare-kare

[b]Labourer, Driver, Islamic scholar, Clergy

high number (145) of patients who received nephrotoxic drugs and all (8) patients who were not exposed to a nephrotoxic drug had the change of eGFR/month between − 0 and − 39 ml/min/1.73 m^2.

On the evaluation of contraindicated nephrotoxic drug use, it was found that only 25 (12.4%) patients were exposed to contraindicated nephrotoxic medications. Of these, more than one-half (52.0%) received low dose aspirin, an equal proportion (16.0%) of patients received diclofenac and aceclofenac respectively as shown in Fig. 4.

Table 2 Clinical and biochemical characteristics of the study participants

Variable	n (%)
Duration of CKD from time of diagnosis (year)	
≤1	39 (19.4)
2	53 (26.4)
3	40 (19.9)
4	37 (18.4)
5	32 (15.9)
CKD co-morbidities	
None	11 (5.5)
Hypertension alone	76 (37.8)
Hypertension and gout	29 (14.0)
Hypertension and peptic ulcer disease (PUD)	16 (8.0)
Hypertension, PUD and gout	11 (5.5)
Congestive heart failure	7 (3.5)
PUD alone	5 (2.5)
Hypertension and diabetes mellitus	5 (2.5)
Hypertension, diabetes mellitus, PUD and gout	4 (2.0)
Hypertension, diabetes mellitus and PUD	2 (1.0)
Diabetes mellitus alone	1 (0.5)
[a]Others	34 (17.2)
CKD stage at Diagnosis	
2–3	26 (12.9)
4–5	175 (87.1)
Mean blood pressure ± SD (mmHg)	
Systolic	135.1 ± 29.3
Diastolic	85.6 ± 15.0
Mean blood glucose ± SD(mmol/L)	
Fasting blood sugar	6.3 ± 3.2
Mean serum uric acid ± SD (μmol/L)	546.6 ± 225.4

[a]Urinary tract infections, Uropathy, Chronic glomerulonephritis, Chronic liver disease, Asthma, Tuberculosis, Peripartum cardiomyopathy, Sickle cell disease, Osteoarthritis, Schizophrenia

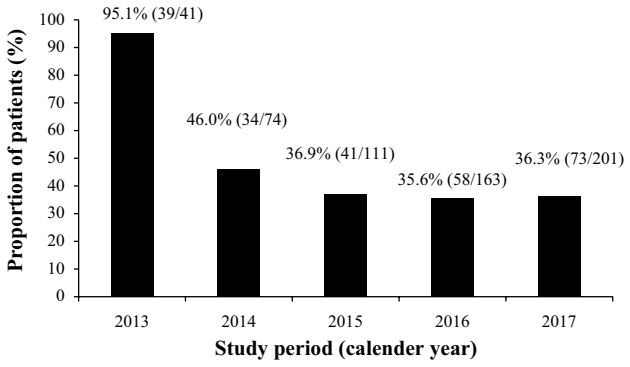

Fig. 1 Annual distribution of patients that were exposed to nephrotoxic drugs

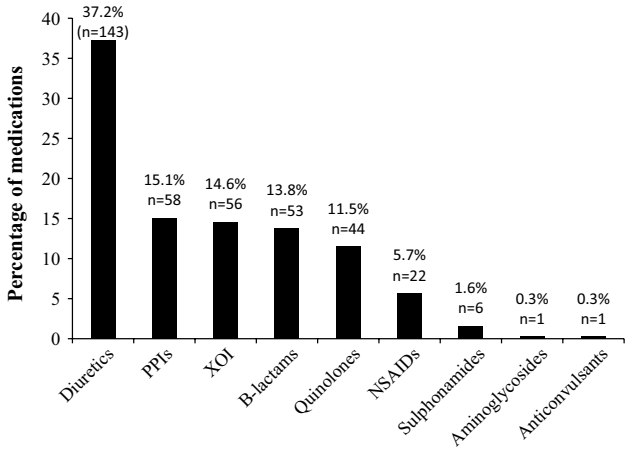

Fig. 2 Nephrotoxic drug exposure by drug classification

Table 4 demonstrates that the majority of patients that received low dose aspirin had reduced mean change in eGFR/month within the range of −0 to −39 ml/min/1.73 m^2.

Table 5 shows factors associated with the likelihood for contraindicated nephrotoxic drug exposure. After adjusting for all the confounding factors, patients aged 60 years or older were significantly more likely to receive one of the seven contraindicated nephrotoxic medications compared to patients aged 39 years or younger (OR 8.00, 95% CI 1.67–38.40). Similarly, patients at CKD stages 2–3 were significantly more likely to receive one of these seven contraindicated nephrotoxic medications compared to those at stages 2–3 (OR 3.51, 95% CI 1.14–10.77).

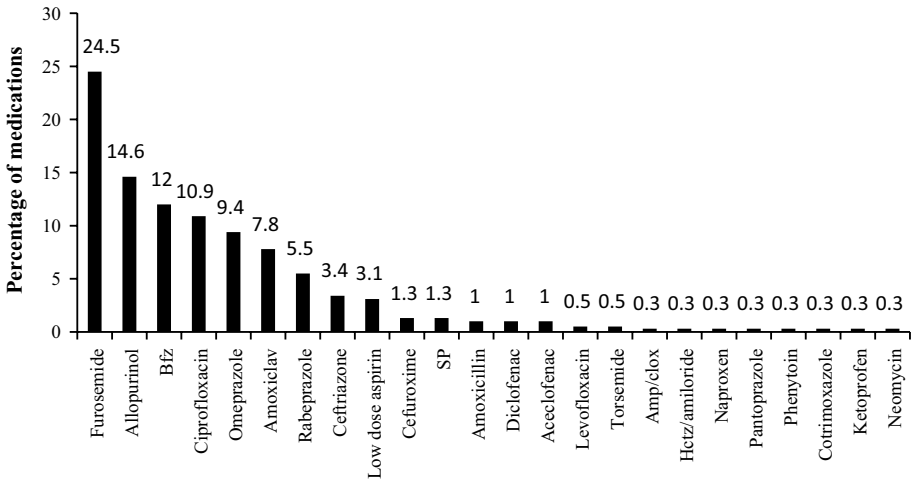

Fig. 3 Proportion of individual nephrotoxic drug prescribed for CKD patients. *Bfz* bendroflumethazide, *SP* sulphadoxine/pyrimethamine

Table 3 Characteristics of the patients' unexposed and exposed to a nephrotoxic drug

Variables	All patients N = 201 (%)	Patients unexposed to nephrotoxic drugs n = 8 (%)	Patients exposed to nephrotoxic drugs n = 193 (%)	*p* value
Gender				
Female	133(66.2)	6(75.0)	127(65.8)	0.590
Male	68(33.8)	2(25.0)	66(34.2)	
Age (years)				
18–39	47(23.4)	1(12.5)	46(23.8)	0.704
40–59	98(48.8)	4(50.0)	94(48.7)	
≥60	56(27.9)	3(37.5)	53(27.5)	
Number of co-morbidity				
≤3	194(96.5)	8(100.0)	186(96.4)	0.583
≥4	7(3.5)	–	7(3.6)	
CKD stage at diagnosis				
2–3	26(13.5)	0(0.0)	26(13.5)	0.266
4–5	175(87.1)	8(100.0)	167(86.5)	
Mean change in eGFR/month (ml/min/1.73 m^2)				
≥−40	3(1.5)	–	3(1.6)	
−0 to −39	153(76.1)	8(100.0)	145(75.1)	0.271
+0 to +39	45(22.4)	–	45(23.3)	

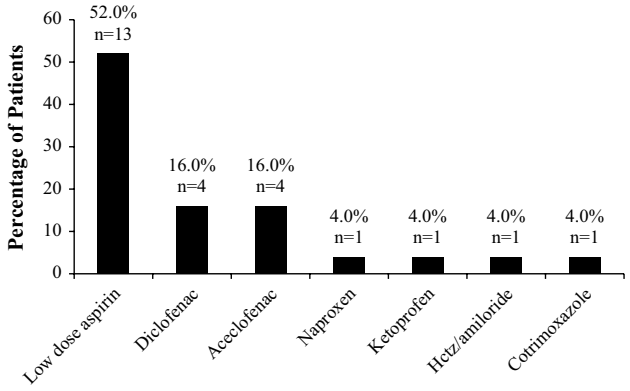

Fig. 4 Proportion of CKD patients who received one of the seven contraindicated nephrotoxic drugs

Table 5 Multivariate logistic regression for the factors associated with the increased likelihood of receiving one of the seven contraindicated nephrotoxic medications

Independent variable	Adjusted OR (95% CI)	*p* value
Gender		
Female	Reference	
Male	1.22(0.48–3.13)	0.674
Age (years)		
18–39	Reference	
40–59	2.06(0.42–10.19)	0.377
≥60	8.00(1.67–38.40)	0.009*
Number of co-morbidities		
≤3	Reference	
≥4	3.87(0.61–24.68)	0.152
CKD stage at diagnosis		
2–3	3.51(1.14–10.77)	
4–5	Reference	0.028*

*Indicates statistical significance (p value < 0.05)

Discussion

To our knowledge, this is the first hospital-based study exploring the use of nephrotoxic drugs in patients with CKD in the northeastern part of Nigeria. Overall, high proportions of the study population were exposed to nephrotoxic drugs, mostly diuretics (furosemide). Only a few patients received contraindicated nephrotoxic medications, mostly NSAIDs (low dose aspirin). Patients' age and CKD stage were the only significant determinants of contraindicated nephrotoxic drug exposure in the study population.

Individuals with CKD are at greater risk for disease progression and poor health outcomes when exposed to renal insults; therefore, preserving renal function is essential to avoiding ESRD. Preventing drug-induced nephrotoxicity requires close attention to choosing drugs, dosing, evaluating drug combinations, and patient outcomes when making unavoidable potentially nephrotoxic drug choices or where conflicting information about nephrotoxicity exists [16].

This study revealed a marked decline in nephrotoxic drug exposure in the study population from baseline (2013) to the year 2016 suggesting improvement in prescribing practice. The plausible reason for this result could be increased knowledge and awareness of drugs with nephrotoxic potentials among treating physicians since the study hospitals lacked clinical decision support systems that could aid them in reducing drug therapy problems. This increased knowledge and awareness of medication risks must have caused them to pay closer attention to choosing drugs and evaluating drug combinations for this population. On the other hand, the slight increase observed from 2016 to 2017 calls for continuous interventions among the treating physicians in order not to reverse the successes recorded in the previous years.

Our study shows that 96.0% of the study population were prescribed one or more medications associated with

Table 4 Prescribed contraindicated nephrotoxic medications according to the patient characteristics

Drugs	Total N (%)	Gender		Age (years)			Duration of therapy (days)		Change in eGFR/month (ml/min/1.73 m^2)		
		F	M	18–39	40–59	≥60	<90	≥90	≥−40	−0 to −39	+0 to +39
Low dose aspirin	13 (52.0)	9	4	–	6	7	5	8	–	12	1
Diclofenac	4 (16.0)	2	2	2	1	1	4	–	1	3	–
Aceclofenac	4 (16.0)	3	1	–	1	3	4	–	–	3	1
Naproxen	1 (4.0)	1	–	–	–	1	1	–	–	1	–
Ketoprofen	1 (4.0)	1	–	–	–	1	1	–	–	–	1
Hctz/amiloride	1 (4.0)	–	1	–	1	–	1	–	–	–	1
Cotrimoxazole	1 (4.0)	–	1	–	–	1	1	–	–	1	–

F female, *M* male

acute interstitial nephritis or tubular cell toxicity comparable to 72.0% reported by an earlier study conducted in the US [8]. This proportion is alarming with the call to prevent kidney disease progression in patients with pre-dialysis CKD and preserve residual renal function in post-dialysis CKD patients. Our finding underscores the need to develop workable strategies to prevent progression of kidney disease, especially in Nigeria where there is poor awareness and knowledge of the risk factors and high habitual use of analgesics and herbal medications as reported by previous studies [17–20]. In contrast, a study conducted in the region of Stockholm, Sweden reported very low (18.0%) exposure to nephrotoxic drugs [3]. This finding suggests that Swedish physicians were more knowledgeable about the drug nephrotoxicity and were more cautious prescribing them to this patient group than their Nigerian, and American counterparts.

The present study showed high use of diuretics, mainly furosemide in patients with CKD consistent with the findings of a similar study conducted in the southeastern part of the country [21]. In contrast, a Swedish CKD population-based study, and another study that analysed the use of nephrotoxic drugs in CKD patients in a general population of Southern Italy reported high use of NSAIDs [3, 6]. The result of our study may be due to poorly managed CKD, which leads to speedy development of complications such as fluid overload, which has been reported being a common problem in advanced CKD [22]. Therefore, fluid management in CKD still remains a primary issue for physicians: while, in general, despite furosemide considered to be the drug of choice in advance CKD, its nephrotoxic effects have to be given full attention. Moreover, the overuse of diuretics is particularly common due to their ability to treat a wide variety of medical conditions [23]. Aside fluid overload complication, patients with CKD have a higher occurrence of comorbidities (hypertension and heart failure) treated with diuretics and are therefore at high risk of being overprescribed, thus highlighting the importance of our results in CKD patients with such complication or comorbidities who are already using diuretics. Use of diuretics causes acute kidney injury. This fact has been substantiated by a Malaysian prospective observational study that assessed the association of diuretics use with severity of fluid overload and loss of renal function/decline in eGFR in CKD (stages 3–5 non dialysis) which found that the use of diuretics is linked with adverse kidney outcomes indicated by reduction in eGFR and increased risk of renal replacement therapy (RRT) initiation in CKD patients [24]. Therefore, prescribers should be cautious when prescribing diuretics to CKD patients by keeping in view benefit versus harm for each patient.

In addition, our study revealed also a substantial increase in the number of CKD patients exposed to XOIs, allopurinol (16.2%) to treat gout which CKD is an independent risk factor. Gout was found to be a common co-morbidity among the study participants, hence the high use of allopurinol. This study confirms the previous finding that allopurinol use in patients with CKD is quite high [25]. Although allopurinol is not contraindicated in CKD, it must be used with caution due to its ability to cause an intrinsic renal failure that could manifest 2 weeks after initiation of the drug [26]. Therefore, it is recommended that in CKD the starting dose of this drug should not be more than 100 mg/day in moderate to severe CKD, followed by gradual upward titration of maintenance dose, which can exceed 300 mg/day [27].

With regard to PPIs, in our study, there was substantial exposure of the study population to this drug class. The reason might be due to the high proportion of the study population with renal failure who might be experiencing gastrointestinal symptoms which is prevalent in them. Generally, PPIs are widely used in the clinical settings due to their perceived safety profile in the management of gastrointestinal tract acid-related disorders, but they are often used irrationally [28]. Studies have reported AKI as one of the severe adverse effects of PPIs [29–33]. Multiple studies had demonstrated that AKI is associated with the CKD progression to ESRD [33–36]. This reinforces the need for physicians exercise caution when prescribing PPIs for patients with CKD.

Our study revealed that only 12.4% of the study population received contraindicated nephrotoxic medications. This result is similar to the 14.0% reported by an earlier study done in Saudi Arabia [5]. It is lower compared to another previous study: 12.4% in our study versus 19.3% in a previous similar study [4]. In addition, an Italian population-based study also reported that contraindicated nephrotoxic drugs were highly prescribed in CKD patients [25]. Variation in the study settings, system and practice could explain the difference between the result of our study and this previous study. Use of contraindicated nephrotoxic drugs exposes patients with CKD to a high risk of worsening of kidney function. In our study, low-dose aspirin was the highest received contraindicated nephrotoxic drug by the study population and was associated with worsening renal functions. Although contraindicated in patients with severe CKD (GFR < 30 ml/min), it is widely prescribed for elderly patients with CKD for prevention of cardiovascular events [37], which is associated with high morbidity and mortality. As a result, the absolute benefits of low dose aspirin might be greater in CKD patients than the risk of worsening kidney function and increased risk of haemorrhage.

In the analysis of the determinants of contraindicated nephrotoxic drug exposure, our study found age as a significant determinant for the increased likelihood for contraindicated nephrotoxic drug exposure. Patients aged 60 years or older were more likely to receive one of the seven contraindicated nephrotoxic drugs compared to other age groups.

This result is comparable to 65 years or older reported by an earlier study [5]. The high number of elderly patients receiving low dose aspirin for the prevention of cardiovascular events and other NSAIDs for gouty arthritis could explain this observation. In addition, in our study, CKD stage was also a significant predictor for contraindicated nephrotoxic drug exposure. Patients at the CKD stages 2–3 were significantly more likely to receive one of the contraindicated nephrotoxic drugs compared to those at stages 4–5. This practice may increase the risk of preventable renal function deterioration; hence the need for increased awareness of contraindicated nephrotoxic drugs among patients with CKD and treating physicians as a strategy towards arresting the disease or slowing down the progression of this disease to stages 4 and 5. These findings highlight clinical and economic implications and reinforce the importance for calls for strategies to preserve renal these

Conclusion

Our study has demonstrated that large proportions of patients with CKD were exposed to nephrotoxic drugs (mostly diuretics). CKD patients aged 60 years or older, and those at CKD stages 2–3 were more likely to receive contraindicated nephrotoxic drugs compared to other age groups and CKD stages. It suggests that special attention should be focused on CKD patients that are 60 years old or older, and those at CKD stages 2–3 for contraindicated nephrotoxic medication exposure. Hence, our findings may provide valuable insights for CKD management and renal failure prevention. CKD requires vigilance in preventing negative patient outcomes that could add to the burden of the disease. Therefore, heightened awareness among medication prescribers is needed about the safety issues of using nephrotoxic drugs in CKD. Collaboration between those who prescribe drugs and clinical pharmacists is a good option that may reduce the danger of exposing at-risk patients with nephrotoxic medications.

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Conflicts of interest The authors declare no conflicts of interest.

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