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Original Research Article

Assessment of drug utilization pattern and prescribing quality indicators among chronic kidney disease patients in a tertiary hospital in Northern Ghana

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ABSTRACT

Background: Drug utilization research in chronic kidney disease (CKD) patients can help identify drug utilization pattern, and evaluate quality of drug use by comparing to standard prescribing indicators or clinical guidelines. There is dearth of drug utilization study among CKD patients in Ghana, therefore this study aims to assess drug utilization pattern and quality prescribing indicators in CKD patients in Ghana.
Methods: Retrospective study was conducted among CKD patients in the Tamale Teaching Hospital in northern region of Ghana.
Results: Cardiovascular drugs were the commonly utilized across all stages of CKD (n=790,31.7%). Potential appropriate prescribing of antihypertensive agents (93.5%), and renin-angiotensin system (RAS) inhibitors alone (66.1%) were higher compared to combined RAS inhibitor with a diuretic (55.4%), phosphate binders (50.0%) and statins (35.6%). Patients with advance CKD stages received lower RAS inhibitors but higher statins compared to CKD stag-3 patients. There was optimal compliance with inappropriate prescription of dual RAS inhibitors, erythropoietin stimulating agent (ESA) and digoxin. Contraindication of metformin (57.9%) was higher than nonsteroidal anti-inflammatory drugs (NSAIDs) and NSAIDs + RAS inhibitor + diuretic; (1.2%) and (1.1%) respectively.
Conclusions: This study is the first to assess prescribing quality indicators among CKD patients in Ghana and hence will serve as a baseline data for future drug utilization studies in the country. Priority areas for optimal prescribing include RAS inhibitors alone or combined with a diuretic, phosphate binders and statins when indicated. However, there is urgent need to mitigate contraindication prescription of metformin in the CKD patients.

Keywords: Chronic kidney disease, Drug utilization pattern, Prescribing quality indicators

INTRODUCTION

The increasing prevalence of CKD presents a significant public heath challenge, with patients facing heightened risks of kidney failure, complications and mortality.[1] Given that appropriate pharmacotherapy can mitigate these risks, ensuring quality of medication treatment is critical for improving the CKD patients' outcomes. In this context, drug utilization research in CKD patients is important because it helps identifies gaps in pharmacotherapy and ensures rational drug use, ultimately improving patient outcomes.[2] Drug utilization research provides insights into drug prescribing including pattern, and quality of drug use.[2] Assessing drug utilization pattern and applying prescribing quality indicators are essential tools to measure, monitor and ultimately improve

appropriateness of drug therapy in CKD patients.[3;4] By regularly analyzing prescribing patterns and using prescribing quality indicators, it can help identify deviations from clinical guidelines, minimize nephrotoxic drug use, and reduce polypharmacy, thereby improving patient outcomes and safety.[3-5] The study of drug utilization pattern is important because it helps identify gaps in pharmacotherapy and promote rational use of drugs.[2] It is very difficult to improve prescribing activities in a particular patient population without knowing about the pattern of drug use in those patients.[6]

Generally, drug treatment pattern vicissitudes with disease conditions, duration of the chronicity and environment.[7] Likewise, drug utilization pattern in patients with CKD changes with time period, comorbidities, and clinicians, which makes it essential to study drug utilization among CKD patients over different time periods.[8] Undertaking study of drug utilization pattern in CKD patients is important to know about the current prescribing trends, understand common co-morbidities associated with CKD and study the therapeutic basis of the drug therapy.[6] Furthermore, study of drug utilization pattern among CKD patients in a specific setting helps in detecting setting specific prescribing trends, and analyze rational use of drugs.[9]

Quality of drug use indicator such as the World Health Organization (WHO) core drug use indicators assess rational drug utilization practices in the general patient population, and hence it is limited in identifying key aspects of drug utilization in specific patient population like CKD patients. Consequently, drug use indicators specific to CKD patients are imperative to evaluate drug utilization in this special patient population. Drug utilization indicators such as prescribing quality indicators specific to CKD patients are important to ensure the rational drug use in CKD management.

The prescribing indicators specific to CKD patients are typically developed based on evidence-based clinical guidelines and expert consensus.[4] As a result, these indicators serve as tools to guide clinical practice and assess the quality of care provided to patients with CKD. Prescribing quality indicators related to patients with CKD describes different characteristics of prescribing including appropriateness of prescribing guidelines recommended therapies for specific CKD comorbidities such as hypertension, diabetes mellitus, anemia and mineral bone disorder in patients with CKD as well as insights into potential medications or combination of medications unsafe for CKD patients.[10;11]

Despite, the relevance of drug utilization study in CKD patients, our search of literature shows lack of published literature in Ghana. Hence, this study aims to contribute literature to this knowledge gap by assessing drug utilization pattern and prescribing quality indicators among CKD patients admitted at a tertiary hospital in northern Ghana.

METHODS

Study site

The medical ward of Tamale Teaching Hospital in the northern region of Ghana was the study site. The medical ward is part of the internal medicine department and has a bed capacity of 216. At time of the study, 5 physician specialists, 6 medical officers, 2 Specialist pharmacists, and 6 pharmacists comprised the clinical team of the medical ward.

Study design

A hospital-based retrospective study was carried out from January 2021 to December 2021.

Study population

This study included patients diagnosed with CKD on admission at the medical ward of Tamale Teaching Hospital between January 2021 to December 2021.

Inclusion criteria

We included patients with CKD using the functional definition criteria by KDIGO: (a) Glomerular filtration rate < 60 ml/min/1.73m^2 for ≥ 3 months with or without structural abnormalities.[12] The estimated glomerular filtration rate (eGFR) of the patients was calculated using the 2021 CKD-EPI creatinine equation online calculator.[13]

Exclusion criteria

Patients whose renal function tests were either not undertaken or missing or with incomplete medical records were excluded from the study.

Sampling

A purposive sampling was used where all patients who met the inclusion criteria comprised the study population. Overall, 212 patients with CKD were included in the study.

Data collection

Data was retrieved from the hospital's electronic medical record system i.e. Light Wave Hospital Information Management System (LHIMS). The electronic medical records of all patients with kidney diseases admitted during the study period was obtained from the data management records section of the medical department. Data collected from the electronic medical record of the eligible patients included age, sex, laboratory tests (renal function, urine protein, phosphate levels, calcium levels, and hemoglobin), blood pressure measurements, etiologies, complications and drug prescription data (generic name of drug and dose).

Data analysis

The completeness of the data was checked, coded and entered into Statistical Package for Social Sciences (SPSS) Version 29 (IBM, Illinois, USA) for analysis. We classified patients clinical stages of CKD according to estimated glomerular filtration criteria by KDIGO.[12] Patients' etiologies and complications diagnosis were analyzed according to definitions. Drugs were classified using the first level of the WHO Anatomical Therapeutic Chemical (ATC) classification system which classifies drugs based on the main anatomical organ or system on which the drug acts.[14] We analyzed the distribution of the main anatomical drug classes across the stages of CKD. PQIs specific to CKD patients based on clinical guidelines by Smit et al was adopted for this study.[4] The initial sixteen (16) PQIs were modified to twelve (12) PQIs that were appropriate for our study population based on the available data (Table 2). Four PQIs were excluded because there were no eligible patients and these comprised two appropriate prescribing of angiotensin converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) or combination of an ACEI or ARB and a diuretic in CKD patients with micro-albuminuria and diabetes, one appropriate prescribing of non-calcium-containing phosphate binder in CKD patients with elevated calcium level and one inappropriate prescribing of active vitamin D in CKD patients with elevated calcium level. Descriptive statistics were conducted, and data were summarized into mean and standard deviation for numerical data and frequencies and percentages for categorical data. Data was presented with tables and figures.

RESULTS

Characteristics of the CKD patients

A total of 212 patients with CKD comprised the study participants. More than half of the patients were males (n = 122, 57.5%), and the mean age was 45 years (44.90 years±17.738). The average eGFR was (14.14±20.193) with majority of the patients presented with CKD stage-5 (n= 152, 71.7%). The common etiology was hypertension 144/212 (67.9%) and anemia was the prevalent complication 170/212 (80.2%) among the patients (Table 1).

Drug utilization pattern

A total of 2494 drug prescriptions was prescribed to all the CKD patients. The top-5 main anatomical drug classes included cardiovascular system (n=790, 31.7%), alimentary tract and metabolism (n=521, 20.9%), blood and blood forming organs (n=403, 16.2%), anti-infectives for systemic use (n=390, 15.6%), and nervous system (n= 201, 8.1%) shown in (Figure 1). Distribution of the top-5 main anatomical drug classes (n=2305) according to CKD stage indicated that patients with CKD stage-5 received the highest number of drugs 1660/2305 (72.0%). Among all stages of CKD, group C drugs were the highest and group N were the lowest prescribed to CKD stage-3 (n=113/335, 33.7% vs n=30/335, 9.0%), CKD stage-4 (n=103/310, 33.2% vs n=28/103, 9.0%), and CKD stage-5 (n= 574/1660, 34.6% vs n=143/1660, 8.6%) in (Figure 2).

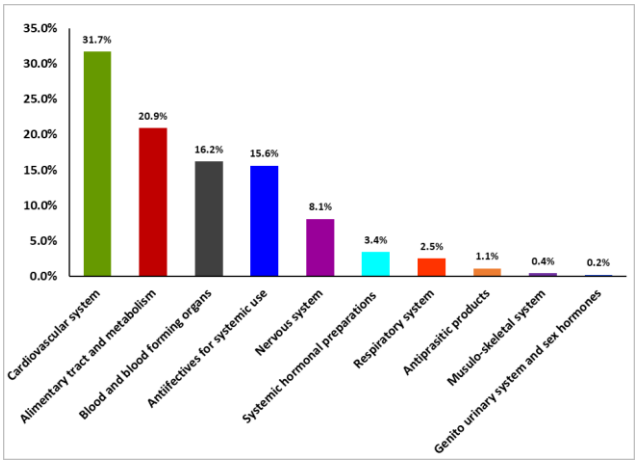

Figure 1: Top-10 therapeutic classes of drugs utilized among the CKD patients.

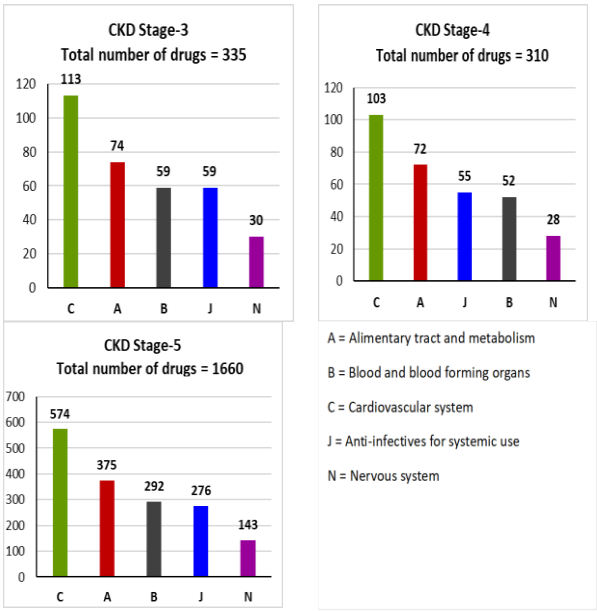

Figure 2: Top-5 main anatomical drug classes pattern by number of drugs utilized.

Prescribing quality indicators

Potentially appropriate prescribing indicators showed that; 116/124 (93.5%) patients with hypertension received antihypertensive agents. More than fifty percent of CKD patients with proteinuria were prescribed ACEI or ARB 37/56 (66.1%) and ACEI or ARB in combination with diuretic 31/56 (55.4%). About one-third (35.6%) of patients that needed statin therapy were appropriately prescribed. Phosphate binders were utilized in 5/10 (50.0%) of patients with elevated phosphate levels and all

patients with elevated phosphate levels and low calcium levels received calcium-containing phosphate binders (Figure 3). Assessment of potentially inappropriate prescribing indicators, revealed that about one percent; (1.2%) of patients with eGFR<30 ml/min/1.73m^2 received prescription of NSAID and (1.1%) patients with CKD stages 3-5 was prescribed a combination of NSAID, RAAS inhibitor and diuretic. Contraindication of metformin was observed in 57.9% (11/19) of patients with eGFR<30 ml/min/1.73 m^2 (Figure 3).

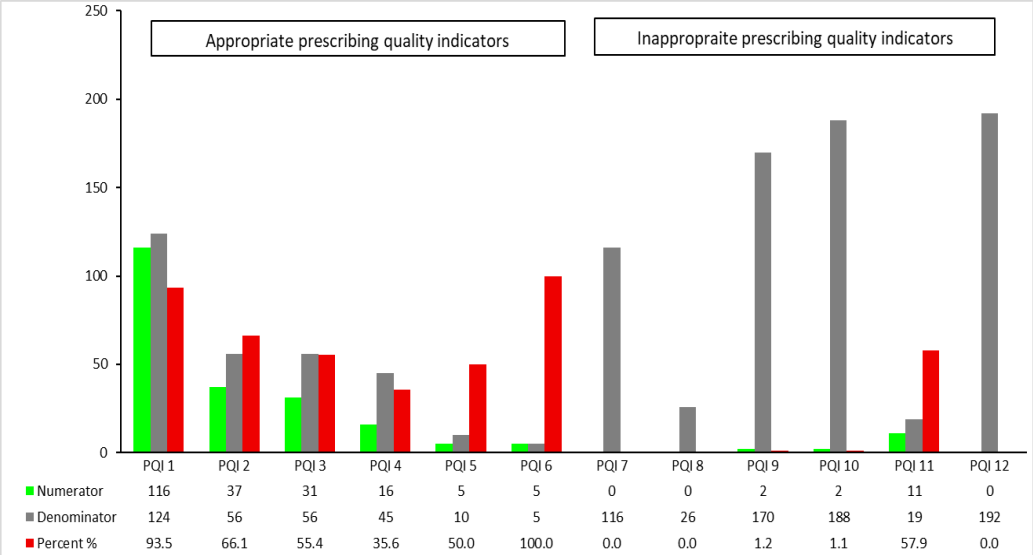

Figure 3: Overall prescribing quality indicators among the CKD patients.

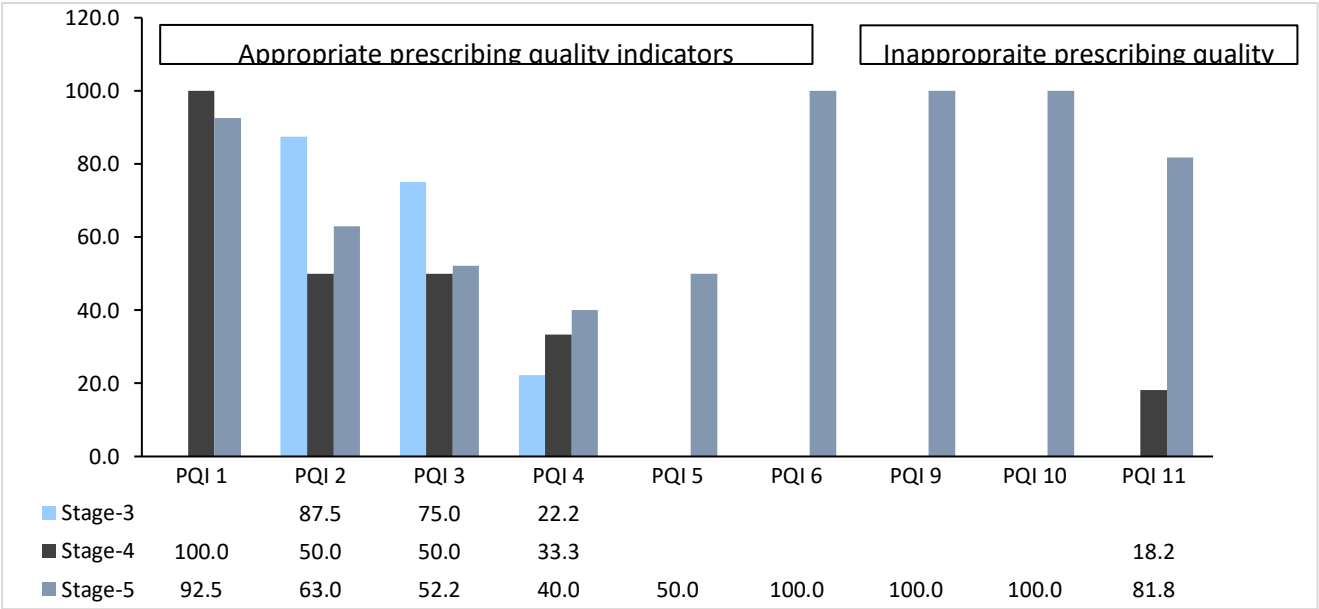

Figure 4: Overall prescribing quality indicators among the CKD patients.

There was no inappropriate prescription of; combination of ACEI and ARB (RAS inhibitors), erythropoietin stimulating agent (ESA) for patients with normal hemoglobin level (≥7.5 mmol/l), and digoxin dose of more than 0.125mg daily for patients eGFR< 50 ml/min/1.73m^2 (Figure 3). Potential appropriate prescription of antihypertensive agents was higher in patients with CKD stage-4 (n=17/17, 100.0%) relative to CKD stage-5 (n= 99/107, 92.5). Among the stages of CKD, patients with stage-3 were the highest to have received RAAS inhibitors (n=7/8, 87.5%), and combination of RAAS inhibitors and diuretics (n=6/8, 87.5%) in (Figure 4). Statin therapy was potentially appropriately prescribed most to patients with CKD stage-5 (n=11/30, 36.7%), compared to patients with CKD stage-4 (n=2/6, 33.3%) or stage-5 (n=3/9, 33.3%). Potential inappropriate prescription of metformin was predominant among patients with CKD satge-5 (n=9/11, 81.8%) in comparison to CKD stage-4 (n=2/11, 18.2%) in (Figure 4).

Table 1: Characteristics of the CKD patients (n=212).

Parameter	Number of patients (%)	Mean ± SD
Sex		
Male	122 (57.5)	
Female	90 (42.5)	
Age (years)	212 (100)	44.9 ± 17.738
EGFR (ml/min/1.73m^2)	212 (100)	14.14 ± 20.193
CKD stage		
< 60–30 ml/min/1.73m^2 (stage–3)	32 (15.1)	48.81 ± 13.376
< 30–15 ml/min/1.73m^2 (stage-4)	28 (13.2)	20.43 ± 5.301
< 15ml/min/1.73m^2 (stage-5)	152 (71.7)	5.38 ± 3.124
Blood pressure (BP)		
Systolic BP (mmhg)	212 (100)	
High systolic BP > 140 mmhg	105 (49.5)	154.5 ± 10.248
Diastolic BP (mmhg)	212 (100)	
Low diastolic BP < 70 mmhg	5 (2.4)	65.7 ± 2.345
Urine protein test	65 (30.7)	2.02 ± 1.097
Proteinuria; urine protein (≥ 1)	59 (27.0)	2.02 ± 1.097
Phosphate (mmol/l)	13 (6.1)	2.11 ± 0.789
High phosphate level (> 1.49 mmol/l)	10 (4.7)	2.39 ± 0.649
Calcium (mmol/l)	14 (6.6)	2.01 ± 0.156
Low calcium level (< 2.10 mmol/l)	14 (6.6)	2.01 ± 0.156
Hemoglobin (mmol/l)	188 (88.7)	4.82 ± 1.51
Normal hemoglobin level (≥ 7 mmol/l)	12 (5.7)	7.91 ± 0.735
Etiologies		
Hypertension	144	67.9
Diabetes mellitus	25	11.8
Glomerulonephritis	16	7.5
Obstructive uropathy	7	3.3
Idiopathic	32	15.1
Top-10 complications		
Anemia	170	80.2
Fluid overload	135	63.7
Leukocytosis	72	34.0
Heart failure	61	28.8
Uremic gastritis	61	28.8
Proteinuria	59	27.8
Hypoalbuminemia	54	25.5
Hyperkalemia	52	24.5
Urinary tract infection	45	21.2
Emesis	35	16.5

Table 2: Prescribing quality indicators utilized among the CKD patients (n=212).

#	Potential appropriate prescribing quality indicators
1	Percentage of patients between 18 and 80 years with CKD stages 4–5 and hypertension that is prescribed antihypertensives unless undesirable because of low diastolic blood pressure (< 70 mmhg)
2	Percentage of patients between 18 and 80 years with CKD stages 3–5 and proteinuria that is prescribed an ACE-I or ARB
3	Percentage of patients between 18 and 80 years with CKD stages 3–5 and proteinuria treated with multiple antihypertensives that is prescribed a combination of an ACE-I or ARB and a diuretic
4	Percentage of patients between 50 and 65 years with CKD stages 3–5 that is prescribed a statin
5	Percentage of patients between 18 and 80 years with CKD stages 3–5 and an elevated phosphate level (>1.49 mmol/l) that is prescribed a phosphate binder
6	Percentage of patients between 18 and 80 years with CKD stages 3–5 treated with phosphate binders and with low calcium level (< 2.10 mmol/l) that is prescribed a calcium-containing phosphate binder
#	Potential inappropriate prescribing quality indicators
7	Percentage of patients ≥ 18 years with CKD stages 3–5 treated with RAS inhibitors that is prescribed at least two RAS inhibitors (ACEI and ARB) simultaneously
8	Percentage of patients ≥ 18 years with CKD stages 3–5 and a normal hemoglobin level (≥7.5 mmol/l) that is prescribed an ESA
9	Patients ≥ 18 years with EGFR < 30 ml/min/1.73m^2 that is prescribed an NSAID
10	Patients ≥ 18 years with CKD stages 3–5 that is prescribed a combination of NSAIDS, RAS inhibitors and diuretics
11	Patients ≥ 18 years with EGFR < 30 ml/min/1.73m^2 and diabetes that is prescribed metformin
12	Patients ≥ 18 years with EGFR < 50 ml/min/1.73m^2 who are prescribed digoxin > 0.125 mg/day

DISCUSSION

Characteristics of the CKD patients

Majority of the patients were males (57.5%) and the observation is comparable to other publications in Ghana, and elsewhere in Nigeria.[15,16] The mean age of the CKD patients in this study was about 45 years which was similar to the 43.9 years identified in another study in Ghana.[17] There was predominance of CKD stage-5 which is consistent other studies in developing countries including Gambia, and Libya.[18,19] The predominant patient presentation at end stage of renal disease in developing countries could be due to lack of screening of patients with high risk factors for CKD. Hypertension was the prevalent etiology among the CKD patients which corresponds to the findings in other studies in Ghana.[15-20] Nevertheless, the finding is contrary to the global prevalent etiology which is diabetes mellitus.[21] Anemia was the most common complication among the CKD patients which is parallel to finding in an earlier study in Ghana.[17] This observation is akin to literature finding that anemia is the most common complication of CKD.[22]

Drug utilization pattern

It was realized in this study that, the following ATC main anatomical classes of drugs: cardiovascular system (group C), alimentary tract and metabolism (group A), blood and blood forming organs (group B), anti-infectives for systemic use (group J) and nervous system (group N) were the commonly utilized drugs. Earlier studies among CKD patients had comparable findings, although variations exist in the sequence of the drug classes.[3-6]

Drug classes acting on the cardiovascular system were the highest utilized among the CKD patients. Parallel findings to the current observation were recognized from previous studies in Asia.[7-9] A study assessing international prescribing pattern in Europe similarly reported drug classes acting on the cardiovascular system to be most frequently prescribed among CKD patients in Poland, Germany, Netherlands, Italy and United Kingdom.[23] This, implies generally cardiovascular comorbidities may be prevalent among CKD patients as observed in the present study. The second commonly prescribed drug class was the alimentary tract and metabolism drugs which comprised 20.9% of the total prescriptions. Earlier in United Kingdom, Alruqayb et al, reported that alimentary tract and metabolism drugs were rather the highest prescribed drugs among CKD patients, nevertheless the rate recorded 22.0% was similar to our finding.[3] On the hand, the present proportion is much lower than the documented 44.86% in India, implying a variation in the geographical prescriptions.[24]

Blood and blood forming organs were the third highest utilized among the CKD patients which accounted for 16.2% of the total drugs prescribed. The rate was lower than 21.38% noticed in an earlier publication, however, higher than 14.1% reported in similar setting of tertiary care hospital.[24,25]

Anti-infectives for systemic use represented 15.6% of the overall drugs utilized. From literature, a range of 1.04%–10.11% of anti-infectives for systemic use prescription in CKD patients have been published.[24-26] Hence, the prescription of anti-infectives for systemic use in our setting is higher than the literature reference. Drugs acting on the nervous system consisted 8.1% of the total prescriptions. A higher proportion of drugs acting on the nervous system compared to present result was recorded in a former study in Europe; 13.5%.[3] On the other hand, extremely lower percentages of drugs acting on the nervous system were reported in earlier publications in Asia; 1.46%–3.7%.[6-25]

Distribution of drug utilization according to CKD stage indicated that patients with CKD stage-5 received the highest drugs which was akin to an earlier report elsewhere in the United Kingdom.[3] Majority of CKD complications occur at advance stages of CKD especially in end stage renal disease, which usually require multiple drugs for treatment and thus may explain the highest drug utilization among patients advanced stages of CKD.[27]

Drugs acting on the cardiovascular system were the most frequently utilized across all stages of CKD. Common cardiovascular risk factors including hypertension, diabetes mellitus and hypercholesterolemia are more frequent in CKD patients.[28] The relationship between cardiovascular disease and CKD is bidirectional, CKD can worsen cardiovascular disease, and cardiovascular diseases can further damage the kidneys.[29] The risk of cardiovascular diseases is a much higher in CKD patients particularly in end-stage renal disease compared to the general population.[30] CKD is one of the most potent risk factors for cardiovascular disease, and patients with advanced CKD have up to 10–20-fold greater risk of cardiac death.[29] Therefore, this makes management of cardiovascular diseases crucial for individuals with CKD and this may explain the prevalent utilization of drugs acting on the cardiovascular system across all stages of CKD.

Prescribing quality indicators

The present data shows a high rate (93.5%) of prescribing antihypertensive agents to patients who would benefit from them. The adherence rate compares positively to some other studies, higher than the 79.9% reported in Australia, though slightly lower than the 96.0% in Poland.[23-31] The near optimal prescription of potential appropriate antihypertensive agents among the CKD patients is satisfactory as it aligns with the consensus in clinical guidelines that emphasize the importance of adequate hypertension treatment in advanced CKD patients to mitigate cardiovascular risk and slow renal disease progression.[32] Comparison among stages of CKD, we observed an optimal prescription of antihypertensive

agents in patients with stage-4 however, near optimal prescription in stage-5. Antihypertensive agents may not have been prescribed to some patients with CKD stage-5 probably due to factors such as risks of severe intradialytic hypotension, ineffectiveness and contraindication of antihypertensive agents. Antihypertensive agents can cause severe blood pressure reduction during dialysis, beta and alpha-beta blockers are associated with higher risk of intradialytic hypotension due to interference with normal cardiovascular reflexes during rapid volume removal and RAAS inhibitors (i.e. ACEIs and ARBs) increase the risk of hypotension by reducing vascular resistance.[33] Additionally, hypertension in patients with end stage renal disease is often caused by volume overload rather than sympathetic activity, making aggressive dialysis with ultrafiltration and dietary sodium restriction the principal strategy to manage hypertension in end stage renal disease rather than antihypertensive agents.[34]

The use of ACEIs or ARBs (RAS inhibitors) are the mainstay therapy for CKD patients with proteinuria helping to decrease albuminuria and slow CKD progression. The present study shows that 66.1% of CKD patients with proteinuria who would likely benefit from RAS inhibitors received this therapy. The proportion was comparatively higher than a report in the Netherlands where 56.5% of CKD stage 3–5 patients with proteinuria received RAS inhibitor.[35] Although, majority of the present study population were being prescribed RAS inhibitor therapy, a considerable therapeutic gap of 33.9% nonetheless exists among eligible patients. The existence of this substantial gap in optimal nephroprotective prescribing often signals the presence of clinical inertia and apprehension. RAS inhibitors is often stopped or withheld in patients with advanced CKD due to concerns over potential adverse effects, primarily hyperkalemia and acute kidney injury, although increasing evidence suggest maintaining RAS inhibitors particularly in the presence of proteinuria which often provides benefits that outweigh the risks.[36] Consistent with the aforementioned observation, the current study identified higher prescription of RAAS inhibitors in patients with CKD stage-3 than in advanced CKD stages (i.e. stage-4 and stage-5).

The indicator for combination therapy of ACEI or ARB and a diuretic in patients with proteinuria taking multiple antihypertensives was achieved in 55.4% of the patients which is suboptimal. Compared to a previous published literature, lower rate of this indicator was recognized in 20.4% of similar CKD patients.[31] This suggests that optimizing combination therapy which is often necessary to achieve blood pressure goals and maximize antiproteinuric effects is widespread challenge in CKD management including our setting. Prescription of combination therapy of ACEI or ARB and a diuretic was more frequent in CKD stage-3 compared to advanced CKD stages which was consistent to an erstwhile study in the Netherlands.[35] Except loop diuretics, thiazide and potassium-sparing diuretics are not recommended in advance CKD stages because thiazide diuretics become ineffective when eGFR falls below 30 ml/min/1.73m^2 and potassium-sparing diuretics increase risk of severe hyperkalemia[37], which may explain the above observation.

In our study, there was under prescribing of statin therapy for CKD patients for whom it is indicated. Among patients between 50 and 65 years with CKD stage 3–5, 35.6% were prescribed statin therapy. Earlier publication in a developed country observed higher statin prescription; 74.3% among CKD patients with the same characteristics.[4] In a primary care study in Singapore, the use of statins among CKD patients with dyslipidemia increased from 81.0% to 87.1%.[38] This implies that additional identification of cardiovascular disease or risk such as dyslipidemia contributes to increased prescription of statin therapy in CKD patients. Therefore, unknown or absence of cardiovascular disease or risk in the present CKD patients may have accounted for the lower prescription of statins. The prescription of statin therapy increased with higher stages of CKD which is comparable to an earlier report among CKD stage 3–5 patients.[35] Statin therapy was highest in patients with CKD stage-5, likely because this group have very high risk of cardiovascular death, myocardial infraction, and stroke often due accelerated atherosclerosis and vascular calcification and statin therapy is the primary pharmacological agent used to mitigate this risk.[39]

Among patients with CKD and elevated phosphate levels, 50% were prescribed phosphate binders. The proportion of CKD patients with indication for phosphate binders that were prescribed one were higher than prior documentation in Germany; 37.5%, but also lower than the 75.4% in the Netherlands.[23] The present finding indicates half of the patients experiencing the highest metabolic risk factors are not receiving the required baseline treatment suggesting a significant failure to initiate phosphate binder therapy in combination with dietary restriction which is recommended by clinical guidelines because dietary restriction alone is known to be insufficient and unreliable to keep phosphate levels within normal range.[36]

In the current study, there was excellent adherence in avoiding three major safety risks; dual RAS blockade (ACEI and ARB), ESA for patients with normal hemoglobin and high-dose of digoxin prescribing. The current observation of dual RAS blockade is consistent to what was documented in Poland.[23] Nevertheless, dual therapy of RAS inhibitors was prescribed to seven (4.9%) and 8 (2.0%) CKD patients in Germany and Italy respectively.[23] A combination of ACEI with ARB is known to be associated with an increased risk of hyperkalemia, kidney damage, and hypotension.[40] Therefore, dual therapy with RAS inhibitors is inappropriate in patients with CKD.[40]

The audit found out that only 1.2% patients with severe renal impairment were prescribed NSAIDs. This low rate is encouraging, as NSAIDs are known to pose a significant risk of acute kidney injury and accelerated CKD

progression especially when the eGFR is less than 30ml/min/1.73m^2. The present finding is similar to the reported 1.4% prescription of NSAIDs in Germany.[23] However, extremely higher proportion than current indicator rate was recorded in Australia;14.3%.[31] The combination of NSAID, RAS inhibitor, and diuretic known as the "Triple Whammy" was observed only 1.1% patients which is comparable to 1.4% and 1.0% recognized in Germany and United Kingdom respectively.[23] The observation is favorable because "Triple Whammy" combination is associated with increased risk of acute kidney injury. However, it was worrisome that the inappropriate prescription of NSAIDs and "Triple Whammy" solely occurred in patients with CKD stage-5 which are the most vulnerable group to experience the severe consequences of this drug-related problem.

Almost about half; 47.4% of the patients with eGFR<30 ml/min/1.73m^2 were inappropriately prescribed metformin. From literature a reference range of 14.1%–21.0% prescription of metformin for patients with eGFR < 30 ml/min/1.73 m^2 has been documented.[4-31] Thus, the finding in the current study is more than twice higher than the literature range of contraindicated prescription of metformin in CKD patients. This finding constitutes a critical failure in patient safety protocol in the setting which requires urgent attention. Metformin is not recommended in patients with eGFR less than with eGFR<30 ml/min/1.73 m^2 due to risk of accumulation leading to lactic acidosis, hence it is worrisome that patients with CKD stage-5 which are riskier of this phenomenon were the predominant group to have received this inappropriate prescription.

CONCLUSION

The current study is the first to assess drug utilization pattern and prescribing indicators among CKD patients in Ghana and hence will serve as a background data for future drug utilization studies among CKD patients across hospitals in Ghana. CKD specific PQIs demonstrated optimal compliance with some safety related indicators such avoidance of dual RAS blockade, inappropriate ESA, and digoxin prescription. There was near optimal adherence to appropriate prescription of antihypertensive agents, and avoidance of inappropriate use of NSAIDs and Tripple Whammy. However, there were notable gaps in the appropriate use of mainstay CKD therapy (ACEIs or ARBs and statins) and high contraindication prescription of metformin in advanced CKD which underscores the need for targeted interventions to mitigate these challenges.

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