Texila International Journal of Public Health
ISSN: 2520-3134
DOI: 10.21522/TIJPH.2013.10.03.Art014

A Systematic Review of Drug Therapy Problems Commonly Faced by Renal Patients with Chronic Kidney Disease in Nigeria

Oluwafemi Olumide Egbeyemi
Radio diagnostic Department, City Gate Health Diagnostic Services, Ogun state Nigeria

Abstract

Victims of Chronic kidney disease (CKD) are usually present with multi-morbid conditions and are later prescribed poly-pharmacy to contest these conditions leading to drug-drug interactions (DDI). This systematic review determines CKD prevalence, evaluates the relationships of CKD with drug therapy problems (DTPs), and provides possible interventions in Nigeria. PubMed, African Journal Online, BMC, and Google search between June 2005 and December 2019 for studies on the prevalence of CKD and pattern of DDIs in Nigeria. Sixty-three were evaluated, 40 were excluded, and only 23 were included in the final data analysis after realistic selection for quality assessment. Ten studies showed the prevalence of CKD, 13 DTPs, and DDIs. Two articles identified 24.4 % and 26 % prevalence of CKD, four studies had 12.3 %, 14.2 %, 2.5 % and 13.4. One study revealed a prevalence of CKD (11.4 %), two separate studies had a prevalence of CKD (of 7.8 %), and another two in Southwestern Nigeria had different CKD prevalences of 7.5 % and 27.6 %. Seven showed higher percentages of CKD in women than men. Obesity, diabetes mellitus, smoking, old age, elevated blood pressure, family history of renal disease, low-income occupations, abdominal obesity, and habitual intake of analgesics and herbs were the most common risk factors in CKD. Studies categorized furosemide, lisinopril, and amlodipine as commonly prescribed drugs, and ferrous sulfate and calcium carbonate were identified as DDIs. Clinical pharmacists and other prescribers should develop ways to administer drugs in co-morbidity for a special population like CKD to prevent DDIs peril.

Keywords*: Chronic Kidney Disease prevalence, Co-morbidity, Drug-Drug Interactions, Drug therapy problems.*

Introduction

Globally, chronic kidney disease (CKD) is on the increase due to its incidence, prevalence, and associated economic burden [1-3]. Chronic kidney disease is defined as abnormalities of the kidney structure or function that is present for > 3 months, with implications for health regardless of the underlying etiology [4].

The prevalence of CKD is estimated to be 11 % -13 % globally, and there is variation in this prevalence in Nigeria, varying between 6 % and 12 % from both community and hospital-based studies [3]. A wide margin was observed in a rural community-based study in Nigeria, with the prevalence of CKD up to 27.6 % [5]. Three separate studies with two in semi urban communities (Lagos State and South East Nigeria) had 7.5 % and 7.8 % prevalence of CKD respectively while another study in Bayelsa State maintains 7.8 % prevalence [6-8]. Prevention and control of CKD is dependent on the awareness, early detection of the disease and its risk factors as observed by studies [6, 9] as it is believed that with a better understanding of its risk factors, development of the disease and progression to end stage renal disease (ESRD) can be prevented [7, 9] Besides hypertension and diabetes mellitus, other CKD

Received: 24.06.2022 ***Accepted: 12.08.2022*** ***Published on: 30.09.2022***
Corresponding Author: femijoseph3@yahoo.co.uk

risk factors identified includes old age, obesity, family history of hypertension, proteinuria, glycouria, family history of renal disease, low-income occupation, use of traditional medications and abdominal obesity. Chronic Kidney disease with co-morbidity tends to endanger patients' life and involves the use of several medications such that poly-pharmacy is practiced [3.9]. Medications intended for the treatment, prophylaxis, or diagnosis of medical conditions may have negative effects on patients if not used appropriately [1]. With this background in mind, this systematic review is aimed to appraise the prevalence of CKD and identifies common risk factors as well as co-morbidities that necessitate the appropriate intervention of clinical pharmacists to prevent the possibility of DDIs among renal patients with CKD in Nigeria.

Materials and Methods

Search Strategy and Selection Criteria

The preferred Reporting Items for Systematic Review and Meta-Analyses guidelines was followed [10]. Systematic literature searched was performed in the PubMed, African Journal Online, Google, and BMC databases to identify articles reporting on the prevalence of CKD, drug therapy problems, and patterns of DDIs in Nigeria. Additional references through bibliographies from identified articles were carefully selected. These searches were restricted to articles published from June 2005 to December 2019. Documents without study design that have information based on controlled reports were also located and screened. References from relevant studies were considered complementary articles. Definitions of drug therapy problems among renal disease patients, including toxicity and interaction between drugs, are included. Articles that studied preventable measures to combat or minimize frequencies are as well included. Excluded literature are cohorts' studies with single causes and case reports. No attention was given to Meta-analysis. All the articles that meet inclusion criteria and are accessible as either full texts or abstracts were reviewed conscientiously.

Quality Assessment and Data Extraction

Studies were classified into major, middle, and minor to assess the quality of the study. This was done to have a focus and direction for the study and based on the sample from the population. The prevalence of CKD in Nigeria was categorized under major search followed by risk factors and drug therapy problems to include DDIs among renal patients with CKD in Nigeria as middle and minor categories. The prevalence of CKD was further grouped according to similarities in prevalence. Each of the search populations was at least 10 articles with Google search to complement insufficient data. The search for each population was based on literature from 2005 till date (at least June 2005 to December 2019). Search engines were as much as possible limited to PubMed, Google, BMC, and Ajol to ensure key studies. Included data were articles conducted in Nigeria alone which was performed for each of the population. The inclusion criteria were CKD in relation to DTPs and DDIs, other renal diseases were excluded. Drug therapy problems and DDIs that deviate from the targeted population were also excluded from the study. The data needed from each selected literature was clearly documented in the book. All effort was made to ensure no data was extracted twice and articulate concentration is made consistently on the documented evidence. To ensure accuracy and prevent mismanagement of data, data from individual article studies were extracted into Microsoft excel database for proper analysis. An observer was around most times to assist in the check and ensuring that all needed information is well noted. Any cancellation made within the data sheet is always been revisited to avoid error. Some of the tables, data including ages, sex, socioeconomic status, disease condition, nature

and risk factors identified in each study from the original studies were well documented to enable guide in the review and complement data analysis and results. The only criterion adopted was to ensure that the eligibility criteria were fully demonstrated. Studies that analyze the involvement of pharmacists were noted as well. All studies included in this study were all published work, no test statistics were done prior to this review. The studies that reported funding of research was documented and vice visa for analysis.

Data Analysis

The prevalence of CKD for each selected article, DTPs appreciated among renal patients of the selected population, and different DDIs noted within selected articles were all documented with frequencies captured in tabular forms. Common risk factors specified in each study were carefully selected to prevent vagueness in the review, and frequencies were tabulated. The prevalence of CKD was determined, and relationships between DDIs were observed and documented.

Results

The initial literature search retrieved 105 articles of which 63 were selected after the title and abstract for full-text review. Ten scholarly articles were screened for the major emphasis area (Prevalence of CKD), and 13 studies for the DTPs and DDIs (5 and 8 studies) were the middle and minor areas, respectively as shown in figure1. The combined 23 scholarly articles were assessed for eligibility and included in the review. Forty studies were previously excluded from the review because they do not meet the inclusion criteria. Among the middle and minor article selected for review, only four were finally included in the systematic review due to excessive duplication. Three of the studied articles on the prevalence of CKD were done in Western Nigeria, 4 in Southern Nigeria. Southeastern Nigeria carried out 2 studies, while 1 study was conducted in North-central. Drug choice, drug interaction, dosing problems, and drug use were the common DTPs identified in four articles but emphasized by only two pieces of literature. Seven of the studied article advised the acceptance of pharmacist intervention for the promotion of appropriate medication to CKD among the renal population. Eighteen of all the approved studied articles documented that there is no conflict of interest. Three declared funding of the research, the remaining were silent about the information.

Sex and Age Distribution in Prevalence of CKD

The sex and age distribution of the studied articles on the prevalence of CKD in Nigeria was showed in table 1. Six of the articles specified ≥ 18 years while 2 identified ≥ 50 years age distribution. Another two literatures specified 34.5 ± 9.5 and 38.84 ± 10.65 age ranges for their studied subjects. Five studies revealed that more women participated in the studies than men. A study showed that the participation of males was 95 participants (53.1 %) while that of the females was 84 (46.9 %) out of a total number of 179 participants. Two of the studies only gave the total number of participants (170 and 456 subjects) without showing in details specific number of female and males that were involved the studies. The age ranges were however mentioned to be 68.1 ± 7.7 and 48.9 ± 15.7 respectively.

Table 1. Sex and Age Distribution in Prevalence of CKD

Article No	Age (years)	Age range (years)	F	M	Total
1	≥ 18	45.8 ± 1.90	45.4 %	36.32 %	157
2.	≥ 18	43.70 ±14.12	57 %	43 %	1350
3.	Unspecified	35.4 ± 9.5	62.2 %	37.80 %	1317

4.	≥ 50	45.2 ± 10.76	84 (46.9 %)	95 (53.1 %)	179
5.	≥ 18	48.09 ± 15.7	-	-	456
6.	≥ 18	-	21 (70 %)	9 (30 %)	30
7.	Unspecified	38.84 ± 10.6	-	-	-
8.	≥ 18	54.8 ± 12.8	-	-	-
9.	≥ 18	-	1.9	1	2520
10.	≥ 50	68.1 ± 7.7	-	-	170

Prevalence of CKD According to Classification

Table 2 shows the grouping of prevalence of CKD in the studied articles as group 1 were studies conducted in semi and urban areas (7.8 %, 7.8 % and 7.5 %). Studies conducted in joint communities (rural and urban settings) were noted as group 2 (18.8 %, 15.8 % and 13.4 %), Third and fourth groups were complete rural populations and retirees from service (27.6 %, 27.2 % and 22.9 %) and (49.1 %) respectively.

Table 2. Frequency Distribution of Prevalence of CKD According to Article Studied

Numbers of Article	Prevalence of CKD (%)	Classification
3	7.8	Group 1
	7.8	
	7.5	
3	18.8	Group 2
	13.4	
	15.8	
3	27.2	Group 3
	22.9	
	27.6	
1	49.1	Group 4

Distribution of Common Risk Factors of CKD in the Studied Articles

Seven of the article identified hypertension, diabetes mellitus, and obesity as risk factors of CKD. Hypertension was consistently noted as having the highest frequencies in five of the articles and highest with old age in one of the articles (36.9 % and 36.3 %), respectively. The estimated glorumerula filtration rate (eGFR) was second highest to hypertension in a study, though disparity was still very obvious 45.7 % hypertension as against 26.6 % eGFR. Herbal concoctions had 75 % in a study leaving hypertension to be 30 %. Habitual analgesic, alcohol, and smoking habit were observed at 20 %, 19 %, and 7 %, respectively in a study. Protenuria (13.5 %, 16.3 %), glycosuria (5 %), haematuria (3.1 %), Hyperuricemia (0.001 %) and fasting plasma glucose (4.8 %) were scantily reported in all the studies. Diabetes mellitus is represented in 7 of the article but with irregular lower percentages (3.7 %, 8.8 %, 6.7 %, 7.9 %, 2.4 %, 2.1 % and 4.2 %).

Distribution of Commonly used Drugs among CKD Patients with Possible DDIs

Table 3 shows the most frequently prescribed medications according to usage and purpose as identified by studies. Furosemide and lisinopril were the most commonly used drug among CKD patients (11.48 %; 11.68 %) and (8.85 %; 9.01 %), respectively in two studies. Furosemide was 71.6 % as against lisinopril (52.9 %) in a study. Another study identified the usage of furoside and lisinopril to be equal (7.7 %). The use of ferrous sulphate ($FeSO_4$) was noted by 3 studies (1.56 %, 1.56

%, and 5.1 %). Amoldipine and calcium Carbonate ($CaCO_3$) were the most frequently used drugs after furosimide and lisinopril. Two studies noted the use of Amoldipine to be higher than $CaCO_3$, 7.3 %; 7.43 %, and 6.42 %; 6.53 %, respectively. Okoro and Farate. rated the use of $CaCO_3$ to be 51.2 %, and Olumuyiwa et al. studied the lowest rate to be 2.6 %. Highest DDIs was reported by one article between $CaCO_3$ and $FeSO_4$ (45.8 %), $CaCO_3$ decreases the absorption of FeSO4. Two articles reported the DDIs between Lisinopril plus Furosimide and Lisinopril plus $CaCO_3$ (9.06 % and 8.08 %; 6.11 % and 5.13 %), respectively, no adverse effect was specified. Furosemide plus Lisinopril was reported by two separate articles 7.7 % and 2.65 % Olumuyiwa et al. specified acute hypotension and renal insufficient, while the other article studied severe postural hypotension as the possible adverse effect. Three articles studied furosemide plus $CaCO_3$, and only one of the articles stated that furosemide increases renal clearance of $CaCO_3$. Two of the articles identified frequencies at 7.22 % and 6.28 %. The DDIs with Amoldipine was identified by three studies by Adibe et al. and Onyedikachi et al. specifying interaction with CaCO3 (4.31 % and 3.85 %), respectively. Only one study (0.4 %) commented that interaction with erythromycin increases the risk of hypotension, shock, acute kidney failure, and sudden death.

Table 3. Distribution of Commonly Used Drugs among CKD Patients and Possible DDIs

	Articles with frequency of use			
Common drugs	Adibe et al., 2017	Adanne et al., 2017	Olumuyiwa et al., 2017	Okoro and Farate, 2019
Ferous Sulphate ($FeSO_4$)	16 (1.56)	16 (1.56)	14 (5.1)	-
Lisinopril	91 (8.85)	91 (9.01)	21 (7.7)	65 (52.9)
Calcium Carbonate ($CaCO_3$)	66 (6.42)	66 (6.53)	7 (2.6)	63 (51.2)
Furosemide	118 (11.48)	118 (11.68)	21 (7.7)	88 (71.6)
Amoldipine	75 (7.30)	75 (7.43)		
Most common DDIs among renal patients with CKD and some adverse effects				
$CaCO_3$ + $FeSO_4$	-	12 (1.54)	-	125 (45.8) $CaCO_3$ ↓ absorption of iron
Lisinopril + $CaCO_3$	44 (6.11) Unspecified adverse effect	40 (5.13) Unspecified adverse effect	-	-
Furosemide + Lisinopril	71 (9.06) Unspecified adverse effect	63 (8.08) Unspecified adverse effect	21 (7.7) *Acute hypotension and renal insufficient*	49 (2.65) *Severe Postural hypotension*
Furosemide + $CaCO_3$	52 (7.22) Unspecified adverse effect	49 (6.28) Unspecified adverse effect	*Furosemide ↓ Renal clearance of $CaCO_3$*	-
CaCO3+ Amoldipine	31 (4.31)	30 (3.85)	-	-
Amoldipine + Erythromycin	-	-	-	↓ *Risk of*

				hypotension, shock, acute kidney failure and sudden death. 1(0.4)

Discussion

This systematic review focuses on DTPs commonly faced by renal patients with CKD in Nigeria only. It analyses the prevalence of CKD from 10 selected articles that are part of those that met the inclusion criteria. The prevalence of CKD discovered from different specific populations were 7.8 %, 7.8 %, 7.5 %, 18.8 %, 13.4 %, 15.8 %, 27.2 %, 22.9 %, 27.6 % and 49.1 %. The set of the reduced prevalence of CKD noted within this review were studies conducted in semi-urban and purely urban communities. Increased prevalence of CKD was those carried out in rural communities, and those of mid values were mixed communities studies of rural and urban settings. A very high prevalence of CKD noted within the review should have been attributed to old age, as reported by [8]. The rural communities studies have been influenced by the socio-economic status and possibly lack of awareness and exposure [9] Already been noted that level of awareness is a major factor in the prevalence of CKD [9]. Risk factors of CKD allow its prevalence, and co-morbidities have been noted in this review to champion the cause. Hypertension, diabetes mellitus, obesity, eGFR < 60ml/ min have been noted in this review to be consistent and studied as risk factors of prevalence of CKD in most regions in Nigeria [3, 4, 6,12].Drug-drug interactions were captured in most of the studies as one major reason for mortality [1, 6, 7, 11] an attempt to administer nephrotoxic medications to the patient in this population who are having co-morbid conditions like hypertension, diabetes mellitus, or any other risk factors of CKD that needed attention may lead to co-treatment or poly-pharmacy [1,11,12]. Studies were not available from the core north of Nigeria on the prevalence of CKD, not all risk factors were maximally explored. Though the ratio of female that participated in most studies was more than that of the male counterpart, but total numbers for most of the studies were not adequate enough. Not all nephrotoxic drugs were researched in all the studies. Major DDIs like furosemide, Lisinopril and amoldipine were not sufficient studies with most drugs, but only drugs like FeSO4, CaCO3, and Erythromycin were tested in a few studies.

Conclusion

There is varying values of the prevalence of CKD in Nigeria due to population differences studied. The presence of risk factors that most likely will not allow one-off management to compliment dialysis or other local treatment provided by the physician will need adequate man-power development. It is essential that pharmacists and possibly stake others in the pharmaceutical companies are allowed to ensure control of the risk factors, especially in the areas of hypertension, diabetes, and obesity, to consistently prevent mortality. Necessary clinical investigations should be made routine in CKD patients prior to drug administration.

Acknowledgement

The contributions of Dr. K Gopal is well noted from the selection of the topic to the completion of the article.

Conflict of Interest

No conflict of interest.

References

[1] Adibe MO, Igboeli NU, Ukwe CV. Evaluation of Drug Therapy Problems among Renal Patients Receiving Care in Some Tertiary Hospitals in *Nigeria. Tropical Journal of Pharmaceutical Research*. 2017; 16(3):697-704.

[2] Okoro RN, Farate VT. Evaluation of Potential Drug-Drug Interactions among Patients with CKD in Nigeria. *African Journal of Nephrology*. 2019; 22 (1): 77-81.

[3] Olumuyiwa JF, Akinwunmi AA, Ademola OA, Oluwole BA, Ibiene EO. Prevalence and Pattern of Potential Drug-Drug Interactions among Chronic Kidney Disease Patients in South Western Nigeria. Nigeria *Postgraduate Medical Journal*. 2017; 24:88-92.

[4] Oluyombo R, Ayodele OE, Akinwusi PO, Okunola OO, Gbadegesin BA, Soje MO, Akinsola A. Awareness, Knowledge, and Perception of Chronic Kidney Disease in a Rural community of South- West Nigeria. *Nigeria Journal of Clinical Practice*. 2016; 19(2):161-169.

[5] Oyebisi OO, Okunola OO, Jaiyesimi AE, Arogudade FA, Adelaja MA, Erohibe CE, Sanusi AA, Akinsola A. Prevalence and Pattern of Chronic Kidney Disease and its Associated Risk Factors in a Rural Community in South-Western Nigeria. *West African Journal of Medicine*. 2018; 35(2):109-116.

[6] Chukwuonye II, Ohagwu KA, Adelowo OO, Chuku A, Obi EC, Onwuchekwa U, Anyabolu EN, Oviasu E. Prevalence and Predictor of Chronic Kidney Disease in a Semi-urban Community in Lagos. *International Journal of Nephrology*. 2019:1-4.

[7] Egbi OG, Okafor UH, Wiebodei KE, Kasia BE, Kunle-Olowu OE, Unuigbe EI. Prevalence and Correlates of Chronic Kidney Disease among Civil Servants in Bayelsa State Nigeria. *Nigerian Journal of Clinical Practice*. 2014; 17(5): 602-607.

[8] Okwuonu CG, Chukwuonye II, Adejumo OA, Agba EI, Ojogwu LI. Prevalence of Chronic Kidney Disease and its Risk Factors among Adults in a Semi-Urban Community of South-East Nigeria. *Nigerian Postgraduate Medical Journal*. 2017; 24: 81-87.

[9] Ayokunle DS, Olugbenga AJ, Oladimeji AA, Olatayo AA, Adekunle AE, Joseph FO. Awareness of Chronic Kidney Disease: A Community Survey in Ado Ekiti, Southwestern Nigeria. *Tropical Journal of Nephrology*. 2015; 10 (1): 19-25.

[10] Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA, PRISMA- P Group. Preferred Report Items for Systematic Review and Meta-Analysis Protocol (PRISMA- P). BMC. 2015; 4(1): 3-9.

[11] Adanne OE, Maxwell OA Kosisochi CE. Evaluation of Drug –Drug Interaction among Chronic Kidney Disease patients of Nephrology Unit in the University Unit in the University of Nigeria Teaching Hospital, Ituku-Ozalla, Enugu State. *Journal of Basic clinical Pharmacy*. 2017; 8(1): 49-53.

[12] Olanrewaju T, Aderibigbe A, Blankestinju P, Grobbee D, Klipsterime-Grobusch K. Estimated Prevalence of Chronic Kidney Disease, and its risk factors in North- Central Nigeria: Analysis of Agreegates Data from eight communities. Nephrology Dialysis Transplantation. 2018; 33(1):142.