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Prevalence of Chronic Kidney Disease in Relatives of Patients with Advanced Renal Disease in a Nigerian Tertiary Hospital

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Authors' contributions

This work was carried out in collaboration between all authors. Author MOO designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors EIA and VNS managed the analyses of the study. Author OOA managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Genetic predisposition plays a key role in many forms of Chronic Kidney Disease (CKD). Family members of patients with advanced renal disease have been reported to have an increased prevalence of CKD. We sought to investigate the prevalence of CKD among first and second degree relatives of patients with CKD.

Methods: This was a hospital based descriptive cross sectional study. One hundred relatives of patients with advanced CKD as well as one hundred age and sex matched controls were recruited for the study. Glomerular filtration rate was estimated using the CKD-EPI formula. CKD was defined as eGFR < 60 mls/min/1.73m^2.

Results: A significantly higher prevalence of CKD was detected among relatives of patients with CKD (11%) compared with controls (6%). P-value <0.05. There were higher rates of hypertension,

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diabetes, use of herbal medications and non-steroidal anti inflammatory drugs as well as alcohol use in relatives of patients with CKD compared with controls.
Conclusion: This study has shown that relatives of patients with advanced CKD are at increased risk of developing CKD.

Keywords: Chronic kidney disease; relative; prevalence.

1. INTRODUCTION

Chronic kidney disease is common worldwide with the major risk factors being diabetes mellitus and hypertension [1]. Despite more aggressive treatment of diabetes and hypertension, the incidence and prevalence of end stage renal disease (ESRD) continue to increase worldwide [2]. One of the most important risk factors for developing CKD in an individual is the presence of a family history of CKD [2,3].

The likelihood of developing CKD in an individual is determined by interactions between genes and the environment. Family clustering of nephropathy has repeatedly been observed in all population groups studied and for multiple etiologies of kidney disease [3-5]. Individuals with a family history of CKD are at increased risk of ESRD. Several studies have demonstrated a consistent familial aggregation of ESRD in African Americans and Caucasians. For instance, Freedman et al. [3] reported a high prevalence of CKD (20%) in first and second degree relatives of incident dialysis patients in Georgia, North Carolina. Genetic Predisposition plays a key role in many forms of CKD [2,3]. In a cohort of 1742 people participating in targeted free community based CKD screenings (Kidney Education Outreach Program - KEOP) 24% of respondents reported a family history of Kidney disease and 902 respondents had CKD [6].

Family history of ESRD has been found to be more predictive for subsequent development of chronic kidney disease in a hypertensive or diabetic individual than is the level of blood pressure or glucose control [3,4]. This implies that individuals who are genetically susceptible to developing kidney disease need to pay even closer attention to modifiable risk factors.

Familial clustering of various causes of ESRD has been reported by several groups including families with members having nephropathy associated with types 1 and 2 diabetes mellitus, hypertension, chronic glomerulonephritis (CGN), systemic lupus erythematosis (SLE) and human immunodeficiency virus (HIV) infection [7,8,9,10].

In addition, a case control study by Lei et al. [11] concluded that familial clustering of renal disease occurred in excess of that which could be accounted for by the clustering of hypertension and diabetes mellitus within family. Additionally, family history of hypertension or diabetes was not significantly associated with ESRD, once adjustment was made for personal history of these conditions. Also a study conducted by Zaghloul G et al. [12] in Egypt the prevalence of microalbuminuria, a marker of renal damage among relatives of CKD patients was 10.6%.This suggests that additional factors beyond the presence of a permissive environment are necessary for nephropathy to develop.

We assessed the prevalence of CKD in relatives of individuals with advanced CKD (stages 4 and 5 CKD).

2. MATERIALS AND METHODS

This study was a hospital based descriptive cross sectional study conducted at the medicine department of Jos University Teaching Hospital, Jos, North Central, Nigeria. The participants for the study were relatives of patients with advanced CKD seen in the hospital.

One hundred relatives of patients with advanced CKD (estimated glomerular filtration rate less than 30 mls/min/1.73m^2) were recruited for the study. One hundred age and sex matched controls were also recruited.

First and second degree relatives of patients with CKD and controls who met the criteria were recruited purposively. Each participant was interviewed using a structured questionnaire and physically examined. Items recorded on the questionnaire were subjects' socio demographic data, history of hypertension, diabetes, dyslipidaemia, alcohol consumption, cigarette smoking, chronic ingestion of non-steroidal anti-inflammatory drugs (NSAIDS) and herbal medications. Subjects with heart failure, febrile illness, infections severe wasting diseases like infection with human immunodeficiency virus (HIV), cancer as well as pregnant women were excluded from the study.

Each participant had five mls of venous blood drawn from the antecubital vein under aseptic condition for serum creatinine determination by the kinetic method. Glomerular filtration rate was estimated using the CKD-EPI formular [13,14].

Definition of terms:

Dyslipidaemia was defined as:

Hypercholesterolaemia- total cholesterol ≥ 6.2 mmol/L.

Hypertriglyceridaemia- triglycerides ≥ 1.7 mmol/L.

High density lipoprotein (HDL) ≤ 1.03 in males and ≤ 1.29 in females or on treatment for dyslipidaemia [15].

Hypertension was defined as blood pressure ≥140/90 mmHg or on anti-hypertensives [16].

Diabetes was defined as fasting plasma glucose ≥ 7 mmol/L or use of anti diabetic agent [17].

CKD was defined as eGFR < 60 ml/min/ $1.73m^2$.

Subjects were classified by social class according to the Registrar General's social class classification as follows- Table 1 [18].

Ethical approval for this study was obtained from the Human Research Ethics Committee of the Jos University Teaching Hospital JUTH/DCS/ADM/127/XIX/4550). Informed consent was obtained from all participants. Data generated from the study was entered into Microsoft excel spread sheet and imported into EPI. Info 2002 statistical programme version 5:3:2 (CDC, Atlanta GA) for analysis. Statistical analysis included simple frequency table, chi-square, (Fisher's exact where cells had less than five observations). Statistical significance was set at $P < 0.05$.

3. RESULTS

Socio-demographic and clinical characteristics of relatives of patients with advanced CKD and matched controls are listed in Table 2.

The prevalence of CKD was significantly higher in relatives of patients with CKD (11%) compared with controls (6%), $p < 0.05$.

Regarding the associated renal risk factors, there were higher rates of hypertension, diabetes mellitus, use of herbal medications and NSAIDS as well as alcohol use in relatives of patients with CKD compared with controls.

Univariate analysis between subgroups of relatives of CKD patients with and without CKD is shown in Table 3. The proportions of hypertension, diabetes mellitus, alcohol use, chronic NSAIDS use as well as use of herbal medications were similar in both groups studied.

4. DISCUSSION

One of the most important risk factors for developing chronic kidney disease is the presence of a family history of ESRD.

The finding from this study revealed a significantly higher prevalence of CKD in relatives of patients with advanced CKD, 11% compared with 6% in matched controls ($p<0.05$). The result from this study is similar with those reported from previous studies suggesting a higher risk of developing CKD among relatives of CKD patients. For example several United States reports reveal a three to nine fold greater risk of developing ESRD in individuals with relatives with CKD [19,20].

Table 1. The registrar general's (Britain) social class classification

Social class	Description	Examples
1	Professionals	Lawyers, Doctors
	Businessmen/women	Large employers
2	Lesser professions	Teachers
	Trade	Shopkeepers
3N	Skilled non-manual	Clerical workers
3M	Skilled manual	Electricians
		Lorry drivers
4	Semi skilled-manual	Farm workers
		Machine operators
		Masons
5	Unskilled manual to unemployed	Farm workers
		Labourers

Table 2. Sociodemographic and clinical characteristics of relatives of patients with CKD and controls

Variable	Relatives	Controls	P-value
Males	58	61	0.688
Education			
None	4	21	
Primary	2	15	0.001
Secondary	35	22	
Tertiary	39	42	
Occupation			
Civil servant	46	39	
Farmer	6	3	0.24
Self employed	20	27	
Unemployed/pensioner	28	31	
Social class			
I	9	14	0.704
II	27	14	
III	6	11	
IV	9	10	
V	49	51	
Hypertension	14	6	0.08
Diabetes	6	1	0.08
Use of NSAIDS	41	22	0.038
Herbal medication	35	21	0.588
Alcohol ingestion	18	6	0.08
Chronic kidney disease	11	6	.01

Table 3. Comparison of associated risk factors between relatives of CKD patients with and without chronic kidney disease

Variables	CKD present n (%)	CKD absent n (%)	P-value
Hypertension	3(27.2)	11(12.4)	0.18
DM	0(0.00)	6(100)	0.48
Alcohol use	2(18.1)	16(17.9)	0.62
Chronic NSAID use	3(27.2)	38(42.7)	0.32
Use of herbal medication	2(18.1)	33(37.1)	0.18

Also, a case control study from North Carolina reported that African Americans with first degree relatives on dialysis had a nine-fold higher risk of developing ESRD than did age, sex and race-matched control subjects [19]. Additionally, Freedman BI et al. in their study stated that family history of ESRD is more predictive for subsequent development of CKD in hypertensive or diabetic individuals than is the level of blood pressure or glucose control [7]. This implies that individuals who are genetically predisposed to developing kidney disease need to pay particular attention to modifiable risk factors as development of kidney disease is often from a combination of genetic and environmental factors. From this study, relatives of CKD patients without CKD had higher prevalence of hypertension and diabetes mellitus (Table 3). This suggests that the cause of CKD among relatives was more genetically determined than environmental factors. Lei H et al. [11] in a large multicentre population based case control study reported the association of ESRD with familial aggregation of renal disease in excess of that predicted by clustering of diabetes and hypertension within families.

The results show that familial aggregation of renal disease cannot be completely explained by clustering of diabetes and hypertension within families implying that there may be a genetic susceptibility to ESRD independent of that induced by diabetes and hypertension. This position was however countered by Berger M et al. [21] in their study on Diabetic Nephropathy where they reported that enhanced susceptibility to CKD is caused by the interaction of genetic and environmental factors and that a permissive environment like diabetes mellitus or hypertension is required for expression of genetic susceptibility.

Considerable evidence supports family history of renal disease as one of the most important risk factors associated with development of nephropathy. The familial clustering of ESRD

supports a genetic contribution to the pathogenesis of CKD. Familial clustering of various causes of ESRD has been reported by several groups including families of individuals having nephropathy associated with type 1 and 2 diabetes mellitus, hypertension, chronic glomerulonephritis, systemic lupus erythematous and HIV infection indicating that there might be genetic susceptibility of CKD for relatives. For instance it is well known that familial focal segmental glomerulosclerosis (FSGS) is a significant and growing cause of CKD. Given the progress in understanding the biology and pathology of podocyte, mutation of associated genes, such as $ACTN_4$, $TRPC_6$ and NPHS.2 contribute to the damage of podocyte and podocyte dysfunction [22,23]. Podocyte dysfunction has been associated with the development of proteinuria and FSGS [24]. These genes were recognized to be the genetic basis of FSGS. More related genes or chromosomal regions were identified in diabetic (3q,18q,22.3-23), non-diabetic nephropathy (Chromosome 10), SLE and familial IGA Nephropathy (60, 22 - 23) [25-27].

This study had some limitations. The sample size studied was relatively small and could have impacted on the findings. Another limitation of the study is the definition of CKD utilised. We assumed that participants who had eGFR less than 60 ml/min/1.73m2 had CKD. We did not repeat GFR estimation after three months to confirm a persistent reduction in GFR.

5. CONCLUSION

Relatives of individuals with CKD are at risk for developing CKD. Targeted screening of family members of patients with CKD is a cost effective measure to prevent CKD as well as slow the progression of CKD in those with already established nephropathy.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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