PREVALENCE AND RISK FACTORS OF CHRONIC KIDNEY DISEASE AMONG FIRST DEGREE RELATIVES OF PATIENTS WITH CHRONIC KIDNEY DISEASE AT AMINU KANO TEACHING HOSPITAL, KANO.

A DISSERTATION SUBMITTED TO THE NATIONAL POSTGRADUATEMEDICAL COLLEGE OF NIGERIA IN PART FULFILLMENT OF THE REQUIREMENTS FOR THE AWARD OF THE FELLOWSHIP OF THE COLLEGE IN INTERNAL MEDICINE (NEPHROLOGY)

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DEDICATION

This work is dedicated to my father, Alhaji Sa'ad Bello who succumbed after prolong battle with chronic kidney disease, may paradise be his final abode.

Also, to the many patients with chronic kidney disease, their families and friends as well as their care givers.

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ABBAS SA'AD BELLO

DECLARATION

It is declared that this work is original unless otherwise acknowledged. This work has not been presented to any other college for fellowship and has not been submitted elsewhere for publication.

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ABBAS SA'AD BELLO

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LIST OF ABBREVIATIONS

ACE gene	-	Angiotensin Converting Enzyme gene
ACE-I	-	Angiotensin Converting Enzyme Inhibitors
AD	-	Autosomal Dorminant
ADPKD	-	Autosomal Dominant Polycystic Kidney Disease
AKTH	-	Aminu Kano Teaching Hospital
APOL1	-	Apo-Lipoprotein1
AR	-	Autosomal Recessive
ARBs	-	Angiotensin Receptor Blockers
BMI	-	Body Mass Index
BP	-	Blood pressure
BUN	-	Blood Urea Nitrogen
CGN	-	Chronic glomerulonephritis
CKD	-	Chronic Kidney Disease
CRF	-	Chronic Renal Failure
CrCl	-	Creatinine Clearance
CS	-	Current Smoker
CVD	-	Cardiovascular Disease
DBP	-	Diastolic Blood Pressure
DL	-	Dyslipidaemia
DM	-	Diabetes Mellitus

ESRD	-	End-Stage Renal Disease
FBS	-	Fasting Blood Sugar
FDRs	-	First Degree Relatives
FHDM	-	Family History of Diabetes Mellitus
FHTN	-	Family History of Hypertension
FSGS	-	Focal Segmental Glomerulosclerosis
GBM	-	Glomerular Basement Membrane
GFR	-	Glomerular Filtration Rate
HAEM	-	Haematuria
HD	-	Haemodialysis
HDL	-	High Density Lipoprotein
HF	-	Heart Failure
HIV	-	Human Immunodeficiency Virus
HPF	-	High Power Field
HTN	-	Hypertension
ISN-COMGAN-		International Society of Nephrology Commission for the Global Advancement of Nephrology
KEAPS	-	Kidney Evaluation and Awareness Program in Sheffield
KEEP	-	Kidney Early Evaluation Program
KDIGO	-	Kidney Disease Improving Global Outcomes
K/DOQI	-	Kidney/Dialysis Outcomes Quality Initiative

LDL	-	Low Density Lipoprotein
MA	-	Microalbuminuria
MALD	-	Mapping by Admixture Linkage Disequilibrium
MMP20	-	Matrix Metalloprotein 20
MYH9	-	Myosin IIA heavy chain genes
NANCONF	-	Nigeria Association of Nephrology annual Conference
NHANES III	-	National Health and Nutrition Examination Survey III
NKF	-	National Kidney Foundation
NSAIDs	-	Non Steroidal Anti-inflammatory Drugs
NTS	-	Nephrotoxic Substances
PROT	-	Proteinuria
PSR	-	Previous Skin Rash
RAS	-	Renin Angiotensin System
RBCs	-	Red Blood Cells
RRT	-	Renal Replacement Therapy
RST	-	Recurrent Sore Throat
SADTR	-	South Africa Dialysis and Transplant Register
SBP	-	Systolic Blood Pressure
SCr	-	Serum Creatinine
SD	-	Standard Deviation
SPSS	-	Statistical Package for Social Sciences

SSA	-	Sub-Saharan African
T2DM	-	Type 2 Diabetes Mellitus
TB	-	Tuberculosis
TC	-	Total Cholesterol
TG	-	Triglycerides
TOR	-	Type of Relation
UMOD	-	Uromodulin
USRDS	-	United State Renal Data System
WHO	-	World Health Organization

SUMMARY

Chronic kidney disease (CKD) is a global public health problem, with a high burden and prohibitive cost of care particularly in developing countries rendering preventive measures the best option in managing the rising tide, however, universal screening of the general population would be time-consuming and expensive and has been shown to be not cost effective unless selectively directed toward the high risk groups. Most previous studies showing familial clustering of CKD were based abroad hence the need for this present study in Nigeria. This study determined the prevalence of CKD and its risk factors among first degree relatives (FDRs) of patients with CKD.

Methods: A cross-sectional study of first-degree relatives of CKD patients was conducted in Aminu Kano Teaching Hospital, Kano Nigeria. A total of 341 first-degree relatives were reviewed and screened for proteinuria, microalbuminuria, haematuria, fasting plasma glucose, fasting serum lipid and serum creatinine for determination of estimated glomerular filtration rate (eGFR). Microalbuminuria, proteinuria, haematuria and eGFR were repeated after 3months for FDRs with initial abnormal results.

CKD risk factors including hypertension, diabetes mellitus, obesity, dyslipidaemia, were also investigated.

CKD was diagnosed according to the criteria of the National Kidney Foundation-Kidney Dialysis Outcomes Quality Initiative.

Results: Of the 341 FDRs screened, mean age was 33.04±10.88 years and 68.6% were males. The prevalence of CKD among first-degree relatives of CKD patients was 28.4% of which screening identified majority (40.2%) at stage 1 of CKD, hypertension was seen in 25.8% of

which 24% were newly diagnosed, diabetes mellitus was seen in 14.4% of which 12% were newly diagnosed, dyslipidaemia (6.5%), obesity (16.4%), proteinuria (24.9%), haematuria (13.2%), 37.8% had microalbuminuria. On multivariate logistic regression analysis older age, female gender, hypertension, diabetes mellitus, obesity and proteinuria were independent risk factors of CKD.

Conclusion: The prevalence of CKD and its risk factors appears to be quite common among the first-degree relatives of CKD patients in Aminu Kano Teaching Hospital, Kano. Suggesting that first degree relatives of patients with CKD also have a risk of developing CKD, and the group should be targeted for CKD screening and prevention program.

Key Words: Chronic Kidney Disease, First-degree relatives, Prevalence, Risk Factors.

CHAPTER ONE

1.0 Introduction

Chronic kidney disease (CKD) is defined as either kidney damage or a glomerular filtration rate (GFR) less than 60ml/min/1.73m^2 body surface area that has been present for 3 months or more,[1,2] manifesting by either pathologic abnormalities or markers of kidney damage, including abnormalities in the composition of the blood or urine, or abnormalities in imaging tests.

It also represents a progressive and persistent deterioration in kidney structure and function, ultimately resulting in accumulation of nitrogenous waste, disruption of acid base homeostasis and derangements of the kidney's metabolic and endocrine functions, rendering the patient to be permanently on renal replacement therapy (RRT) which could be dialysis or renal transplant for better quality of life.[2]

CKD is increasingly recognized as a public health problem and is linked to the risk of development of cardiovascular disease (CVD) and end-stage renal disease (ESRD) with increasing incidence, prevalence, high morbidity, mortality, and increased health care cost.[2]

The increasing number of people with ESRD is a reflection of the worldwide rise in the number of patients with CKD. There are over 2 million people worldwide currently receiving treatment with dialysis or a kidney transplant to stay alive, yet this number may only represent 10% of people who actually need treatment to live.[3] In the United Kingdom (UK), the annual incidence of ESRD has doubled over the past decade to reach about 100 new patients per million population,[3,4] and this trend is expected to continue to rise at an annual rate of 5-8 per cent largely due to aging of the population and global epidemic of type 2 diabetes mellitus (T2DM). In the United States of America (USA), an estimated 485,000 persons are on treatment for end-

stage renal disease (ESRD), with an overall annual incidence of 336 new patients per million populations.[4]

Prevalence of early stages of CKD in the general population is approximately 11% of adults.[4] In the United States of America, 16.8% of the population aged > 20years had CKD,[4,5] approximately 15 to 20% of persons 40 years of age or older have a reduced eGFR. It was reported that about 2-3% of medical admissions in tropical countries is due to renal related disease, in South Africa, CKD constituted 10% of all medical admissions.[5] In Nigeria, CKD constituted 6-8% of medical admissions with an estimated prevalence of 2.5%,[6] the incidence is much higher in Africans especially in the underdeveloped and developing nations where poverty is the most challenging socio-economic problem, it was reported that 70% of ESRD patients cannot afford long term dialysis at the University College Hospital (UCH) in Ibadan.[7]

However, the prevalence of impaired kidney function was estimated to range between 10% and 20% of the adult population in most countries worldwide.[4] In developing countries like Nigeria, the prevalence of preventable renal diseases is not known. Akinsola *et al*. reported that renal failure constituted 8% of hospital admissions.[8] However, Abioye-Kuteyi *et al*. reported a prevalence of 19.9% of undetected renal diseases in a rural populace in Nigeria[9] while Nalado *et al*. found overall prevalence of renal impairment in adult population in Kano to be 26.0%.[10]

In sub-Saharan Africa (SSA), and indeed also in Nigeria, hypertension (HTN), chronic glomerulonephritis (CGN) and diabetes mellitus (DM) are the major causes of CKD compared to the developed world where the main causes are diabetic nephropathy and hypertention.[8] The major risk factors for CKD include older age, family history of CKD, diabetes mellitus,

hypertension, cardiovascular disease, obesity, smoking, excessive alcohol consumption and recreational drug use.[3-5]

The global rise in the number of patients with CKD who would ultimately require RRT is increasing at an alarming rate. A change in global approach to CKD from treatment of ESRD to much more aggressive primary and secondary prevention is therefore imperative.[3,4]

There are a number of susceptibility, initiation, and progression factors known to affect or modulate the onset of CKD and this concept has a significant application in devising preventive strategies to curb the menace of CKD. It helps in the identification of individuals at high risk for development and progression of CKD. In-addition, risk factor identification aids in further development of intervention strategies to retard and or prevent progression of CKD[4].

It has been suggested that development of strategies for the early detection and prevention of non-communicable diseases (NCD), including CKD is the only realistic strategy to avert an imminent global health and economic crisis and enhance equity in health care worldwide.[11,12] Targeted screening for high-risk populations has been proposed as a comprehensive public health strategy to ensure the cost-effectiveness of CKD prevention and management also to achieve improved patient outcomes.[13]

Family members of patients with ESRD have been found to have a higher risk of CKD.[14] Familial clustering of CKD and ESRD may be explained by the dual effects of genetic susceptibility and environmental exposures. Family members of ESRD patients are considered as a high risk population for ESRD or CKD.[14,15]

In 1997, Freedman *et al*.[16] found that 20% of dialysis patients treated in Georgia, North Carolina, and South Carolina reported having first- or second-degree relatives with ESRD. Subsequently,

several other studies were conducted to investigate the prevalence of CKD in relatives of ESRD patients.[17,18,19,] Jurkovitz *et al*. reported that 49.3% of family members of ESRD patients have undetected kidney disease and 13.9% had creatinine clearance (CrCl) less than 60 ml/min.[15] Also, Tsai *et al*. found that the prevalence of CKD in relatives of haemodialysis (HD) patients was 15.8%.[17] A more recent study carried out by Wei *et al.* found that the prevalence of CKD in FDRs of CKD patients in southern China was 29.7% , and identified that they are at high risk of developing CKD.[19]

1.1 Definition of the Research Problem

Patients with CKD are at increased risk of progression to ESRD and cardiovascular disease if they are not identified and properly managed.[3,4] Studies have shown that early identification and institution of appropriate treatment strategies is associated with slowing of progression to ESRD and other adverse outcomes.[2,3,7] it is estimated that by 2030, 70% of patients with ESRD will be in developing countries where the burden of ESRD management will put further demands on the overstretched budgetary capabilities of health care systems,[4,18] where majority of the patients have no access to RRT due to economic reasons.[7] This has reawaken interest in global CKD prevention through early detection and intervention.[12-14] However there are few guidelines for early detection of CKD in sub-Saharan African countries.[7]

Screening efforts directed at group of population at high risk of CKD such as first-degree relatives of CKD patients, hypertensives, diabetics and elderly have been found to be more cost effective, minimizing the huge financial and logistic burden associated with general population screening while making the preventive option more realistic, practicable and achievable.[15-19] Data exists in other parts of the world on high prevalence of CKD and its risk factors among

relatives of CKD patients,[14-19] as such policies with national guidelines developed targeting this group among others for preventive control of CKD. Accordingly, it is desirable to determine the prevalence of CKD, and its risk factors through a targeted screening of first-degree relatives of CKD patients in our environment. This will be of clinical and scientific value towards informing a rational screening policy that will improve the burden of CKD and ESRD in our environment.

1.2 Justification for the Study

Health screening exercises are generally very important as they enable early detection of diseases with subsequent early intervention that is beneficial to individual subjects. Also, screening enables data collection for the purpose of estimating disease burden in the population which are useful in health policy making to the overall community.

The worldwide rise in number of patients with CKD and consequent ESRD requiring RRT and associated cardiovascular disease (CVD) is tending toward epidemic proportions in the next few decades.[20,21]

Attention being paid globally to CKD is attributable to the rapid increase in its prevalence, the enormous cost of treatment, its major role in increasing the risk of CVD, and the discovery of effective measures to prevent its progression. These factors render CKD an important focus of health care planning even in the developed world, but the burden of CKD in the developing world are far more challenging because many lack government policies on surveillance and mass screening and for the fact that some researchers have challenged the cost effectiveness of general population screening of CKD when compared to targeted CKD screening.[18]

Several similar studies reported from Kaohsiung in Taiwan,[17] Damanhour in Egypt[18] and Guangzhou in China[19] in which mass screening targeting high risk population such as relatives of

CKD patients has been shown to be more cost effective than general population screening in CKD prevention and management as early detection and intervention for these high risk population prevent or delay progression of CKD and achieve improved patient outcome. It is hoped the data generated from this study, would help draw the attention of the physicians and other health care professionals on the need for screening and surveillance of CKD and its risk factors in high risk population to reduce the rising tide. It will also stimulate the call for action against CKD in terms of intensive advocacy, promotion of awareness, and public health policies by the government. Similarly, it will help obviate extrapolating from researches conducted in other geographically and ethnically distinct populations. Furthermore, the risk factors and clinical characteristics associated with CKD in this group of population need to be identified.

1.3 Aims and Objectives

Aim

The aim of this study is to determine the prevalence and risk factors of CKD among first-degree relatives (FDRs) of patients with CKD at Aminu Kano Teaching Hospital.

Objectives

1. To determine the prevalence of CKD among FDRs of CKD patients.
2. To identify the risk factors for CKD among FDRs of CKD patients.
3. To make recommendation on targeted health screening for prevention of CKD.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 An Overview of Chronic Kidney Disease Burden

Chronic kidney disease is a worldwide public health problem with an increasing incidence and prevalence, poor outcomes and high cost of management.[3,4] Outcome of CKD includes not only kidney failure but also complications associated with decreased kidney function as well as cardiovascular disease. It is the clinical syndrome of the metabolic and systemic consequences of a gradual, substantial and irreversible reduction in the excretory and homeostatic functions of the kidney, ultimately leading to ESRD which represent a clinical state or condition in which there has been irreversible loss of endogenous renal function of a degree to render the patient permanently on Renal Replacement Therapy (RRT) - Dialysis or Transplantation for survival.[3] Despite the magnitude of the resources committed to the treatment of ESRD and the substantial improvements in the quality of dialysis therapy, these patients continue to experience significant mortality differences in disease burden among renal groups, under-recognition of earlier stages of CKD and of risk factors for CKD may to some extent explain this growth[3,4].

The modified Kidney Disease Improving Global Outcomes (KDIGO) [2] stages of CKD are as shown in the table below.

Table 1: KDIGO Stages of CKD.

Stage 1:	Patients with normal glomerular filtration rate (GFR), but some evidence of kidney disease as manifested by microalbuminuria/proteinuria, haematuria or histological changes on kidney biopsy.
Stage 2:	Mild CKD characterized by GFR of 89-60ml/min/1.73m^2 with some evidence of kidney disease as manifested by microalbuminuria/proteinuria, haematuria or histological changes.
Stage 3:	Moderate CKD with GFR 59-30m1/min/1.73m^2 3a: moderate CKD with GFR 45-59ml/min/1.73m^2 3b: moderate CKD with GFR 30-44ml/min/1.73m^2
Stage 4:	severe CKD with GFR 29-15m1/min/1.73m^2
Stage 5:	CKD with GFR <15m1/min/1.73m^2, where patient survival depends on provision of RRT in the form of dialysis or transplant.[1,2,5]

2.2 Epidemiology

Regional differences exist in the epidemiology of CKD. The annual growth rate of CKD worldwide is estimated at 8%, and the prevalence of early stages of CKD in the general population is approximately 11% in adults.[20,21] More than two million patients are on RRT worldwide and it is expected to rise to about 300 million by the year 2025.[22,23] Diabetes mellitus and hypertension are major risk factors for CKD. Globally, the number of people with diabetes mellitus is expected to rise from 194 million in 2003 to 333 million in 2025,[24] and most of this epidemic is projected to be in developing countries, likewise hypertension affects 20% of the

adult population, and an estimated 691 million people worldwide.[25] The prevalence of CKD is about 1500 per million population in the United States.[21] and about 800 per million population in the European Union.[26] In developing countries figures vary from 100 per million population in SSA and India, to about 400 per million population in Latin America.[27] The prevalence of CKD is even higher when those at risk, including relatives of patients with the disease are screened.[17,18,19]

In SSA, an estimated 2-3% of medical admissions in tropical countries are reported to be for renal related symptoms, and majority being cases of glomerulonephritis.[5] Another study from two West African countries (Benin and Togo) found 3.3% of all admitted patients have renal disease.[28] In Nigeria, CRF constituted 6-8% of medical admissions.[6] However data are still emerging.

2.3 Aetiology and Risk Factors

Worldwide the common causes of CKD include hypertension, diabetes mellitus, chronic glomerulonephritis, analgesic nephropathy, obstructive uropathy, polycystic kidney diseases and others. In the United States of America, most common causes of CKD are diabetic nephropathy and hypertension, while most common causes of CKD in developing countries are chronic glomerulonephritis, systemic hypertension, diabetes mellitus and obstructive uropathy.[3,4,5]

It was reported from the South African Dialysis and Transplant Registry (SADTR),[29] that glomerulonephritis was the cause of ESRD in 52.1% of patients, and hypertension in 45.6%. In North Africa, the incidence of CKD is much higher than in West Africa and principal causes are interstitial nephritis (14 to 32%), glomerulonephritis (11 to 24%), diabetes (5 to 20%), and hypertensive nephroscelorosis (5 to 21%).[29] It was reported from Nigeria that hypertension was

the leading cause of CKD accounting for 54.9% and chronic glomerulonephritis accounted for 29.5%, while some other studies showed chronic glomerulonephritis as the leading cause of CKD.[8,30]

Risk factors associated with CKD can be categorized into two classes: Modifiable and non-modifiable factors. Non-modifiable factors include, older age, male gender, genetics, race/ethnicity Blacks more than Whites. Modifiable factors include, systemic hypertension, diabetes mellitus, proteinuria, dyslipidaemia, smoking, obesity, excessive alcohol consumption, low socio-economic status, infections/ infestations, drugs herbs/analgesic abuse and obstructive uropathy/stones.[31] In Lagos, prevalence of CKD risk factors were screened and hypertension was found in 36.3% of the 1,416 respondents, 2.6% had diabetes and 23.9% had overt protenuria.[32] A prevalence of 19.9% of undetected renal disease was reported in a rural population in Western Nigeria.[9] In a screening done in Nigeria (Abuja), during the world kidney day, proteinuria was found in 19% of the screened group.[11]

Jurkovitz *et al.*[15] reported that among the 769 screened adults 29.2% have family history of ESRD and CKD was present in 13.9%, Freedman *et al.*[16] reported 23% positive family history of ESRD and far more are likely to have relatives with clinically silent proteinuria or CKD. Wei *et al.*[19] found that the prevalence of CKD in FDRs of CKD patients in southern China was 29.7%.

2.4 Genetics and Chronic Kidney Disease

The inter-individual variability in the development of CKD and rate of progression to ESRD has an important heritable component. Genes that may be involved in inherited renal diseases and markers of kidney function are inherited in 27-33% of cases (serum creatinine, GFR, albumin, proteinuria, BUN),[33] and as such may play a role in aggregation of CKD in particular group of

population. Most extensively studied has been an insertion/deletion polymorphism of the angiotensin-converting enzyme (ACE) gene and the homozygous deletion (D/D) variant is associated with greater risk of CKD progression.[33] Recently Kottgen *et al.*[34] identified several susceptibility variants for renal function and CKD at Uromodulin (UMOD), Shroom protein 3 (SHROOM3) and Stanniocalcin 1 (STC1) loci.

Genes that are associated with CKD[(34-40)] include the following;

- APOL1; Apolipoprotein L1: It is a protein that in humans is encoded by the APOL1gene, an apoprotein component of HDL which is synthesized in the liver and also in many other tissues, including pancreas, kidney, and brain. APOL1 is found in vascular endothelium, liver, heart, lung, placenta, podocytes, proximal tubules. The protein has a secreted form that allows it to circulate in the blood. It is a member of a family of apolipoproteins which consists of 6 other proteins and it is a member of bcl2 genes which are involved in autophagic cell death. APOL1 may play a role in the inflammatory response.[39,40]

  APOL1 has a role in innate immunity by protecting against Trypanosoma brucei infection, which is a parasite transmitted by the tsetse fly. Trypanosomes endocytose the secreted form of APOL1 which forms pores on the lysosomal membranes of the trypanosomes which causes in influx of chloride, swelling of the lysosome and lysis of the trypanosome.[39]

  Recently, two coding sequence variants in APOL1 have been shown to associate with kidney disease in a recessive fashion while at the same time conferring resistance against Trypanosoma brucei rhodesiense. People who have at least one copy of either the G1 or

G2 variant are resistant to infection by trypanosomes, but people who have two copies of either variant are at an increased risk of developing a non-diabetic kidney disease.[40]

The distribution of the variants most associated with kidney disease risk was analyzed in African populations and found to be more prevalent in western compared to northeastern African populations and absent in Ethiopia. In the Yoruba people of Nigeria (West Africa) the prevalence of G1 and G2 risk alleles are 40% and 8% respectively.[39,40] The existence of these variants are only found on African chromosomes and exist in people with recent African ancestry (<10,000 years).

Many African Americans are descendants of people of West African nations and consequently, also have a high prevalence of APOL1 risk alleles as well as APOL1 associated kidney diseases. The frequency of the risk alleles in African Americans is more than 30%.[39,40] The existence of these alleles has been shown to increase the risk of developing diseases such as Focal Segmental Glomerulosclerosis (FSGS), Hypertension Attributed-ESRD, and HIV-Associated Nephropathy (HIVAN). The prevalence of the risk alleles in African Americans with these kidney diseases shown in recent studies are 67% in HIVAN, 66% in FSGS, and 47% in hypertension-attributed ESRD. Hispanic populations such as Dominicans and Puerto Ricans demonstrate a mixture of genetic influences that include African ancestry resulting in a prevalence of the APOL1 variants as well.[40]

Although possession of the APOL1 risk variants increases susceptibility to non-diabetic kidney disease, not all people who possess these variants develop kidney disease, which indicates another factor may initiate progression of kidney disease. Similarly, in HIV positive patients, although the majority of African-American patients with HIVAN have

two APOL1 risk alleles other as yet unknown factors in the host, including genetic risk variants and environmental or viral factors, may influence the development of this disorder in those with zero or one APOL1 risk allele.[39,40]

People with these allelic variants who develop ESRD begin dialysis at an earlier age than ESRD patients without the risk alleles. On average, those with two risk alleles begin dialysis approximately 10 years earlier than ESRD patients without the risk variants.

FSGS is a kidney disease that affects younger individuals. In a recent study, the mean ages of onset of FSGS for African Americans with 2, 1, and 0 APOL1 risk alleles was 32yrs, 36yrs and 39yrs, respectively.[40] APOL1 variants also have a tendency to manifest FSGS at relatively young ages; FSGS begins between the ages of 15 to 39 in 70% of individuals with two APOL1 risk alleles and 42% of individuals with of 0 or 1 risk alleles.[40]

Kidneys from donors containing two APOL1 variants experience allograft failure more rapidly than donors with 0 or 1 variants. Kidney recipients who have copies of the APOL1 risk variants, but do not receive kidneys from donors with the risk variants do not have decreased survival rates of the donated kidneys. These observations together suggest that the genotype of the donor only affects allograft survival.[39,40]

- UMOD; Uromodulin: encodes urodoulin protein which is involved immunologically, transcribed exclusively in renal tubular cells of thick ascending limb of loop of Henle.
- MMP20; Encodes a member of the matrix metalloproteinase family which is involved in the breakdown of extracellular matrix in normal physiology and is implicated in kidney disease associated with ageing.

- MYH9; Myosin IIA, heavy chain gene, is expressed in podocytes and implicated in several inherited syndromes with glomerular involvement.
- rs 4293393-T; Associate with autosomal dominant forms of kidney disease, medulary cystic kidney disease type 2 and familiar juvenile hyperuricemic nephropathy.

Genetic risk does not translate into clinical risk due to several complex interaction with environmental factors. Some notable hereditary causes of CKD[39,40] include;

- Autosomal dorminant polycystic kidney disease (ADPKD), constitute 10-12% of CKD receiving haemodialysis in U.S.A, ranked 6th major cause of CKD in Nigeria, commonest hereditary cause of CKD. Many patients may be missed as they succumb to cerebrovascular or cardiovascular death early in life.[39]
- Alport syndrome is predominantly an X-linked disease, a disease of glomerular basement membrane (GBM) likely to be caused by a mutation in type IV collagen with associated sensorineural deafness, lenticonus and retinal abnormalities.[39,40]
- Congenital nephrotic syndrome of the finnish type inherited as autosomal recessive, confined to the Finnish population.[39]
- Familial juvenile nephronopthisis among many others is a disease of unknown aetiology, inherited as autosomal recessive, characterized by its occurrence in siblings and other FDRs also progression to ESRD before puberty.[39,40]

2.5 Hypertension and Chronic Kidney Disease

Hypertension is a well-established cause, a common complication and an important risk factor for progressive renal disease. Hypertension affects about 20% of adult population and an

estimated 691 million people worldwide, it is noted to be a major cause of CKD among black populations and has a faster progression to ESRD[41] in them.

From United State Renal Data System (USRDS) hypertension was reported as a primary diagnosis in 27% of patients starting dialysis[42], South-African Dialysis and Transplant Registry (SADTR)[29] reported 45.6%, Matekole *et al.*(Ghana)[43,44] reported 48.7% and in Nigeria, Afolabi *et al.*[38,45] reported 29.8% and Amira *et al.*[32] reported 36.3% respectively, while Ulasi *et al.*[46] reported 15% and Kadiri *et al.*[47] reported 38.9% respectively. Among relatives of CKD patients on haemodialysis Tsai *et al.*[17] reported 27% with hypertension and Wei *et al.*[19] reported the prevalence of hypertension in FDRs of CKD patients as 17.0%. APOL1 mutation exclusively found in individual of African origin confer a higher risk of ESRD attributable to hypertension.[36]

Controlling hypertension is the most important intervention to slow the progression of renal disease. Any anti-hypertensive agent may be appropriate but angiotensin-converting enzyme inhibitors (ACEI) are particularly effective in slowing progression of renal insufficiency in patients with and without diabetes mellitus and angiotensin receptor blockers (ARBs) have been shown to have a renoprotective effect in diabetic nephropathy, independent of reduction in blood pressure.[48] Early detection and effective treatment of hypertension to target levels is essential.

2.6 Diabetes Mellitus and Chronic Kidney Disease

Increasing prevalence of diabetes mellitus has resulted in an upsurge of CKD. Globally, the number of people with diabetes mellitus is expected to rise from 194 million in 2003 to 333 million in 2025.[24] Most of this epidemic is projected to be in developing countries.

Diabetes mellitus is a common cause of CKD and accounts for a large part of the rise in ESRD in North America, about 50% of patients on RRT in United States and 20% of patients in United Kingdom have diabetes mellitus.[20] Report from United Kingdom Prospective Diabetes Study (UKPDS)[49] shows that from diagnosis of diabetes mellitus progression to gross renal dysfunction occurred at 2.3% per year and the prevalence of microalbuminuria (MA) 10 years post diagnosis of diabetes mellitus was 24.9%. Diouf *et al.* (Senegal)[50] reported 20.7% of CKD patients with primary diagnosis of diabetes mellitus. In Nigeria, Arogundade *et al.*[38,50] reported 3.1% and subsequently Ulasi *et al.*[46] *reported* 13.2% of CKD patients found to have diabetes mellitus. Wei *et al.*[19] reported a prevalence of 5% diabetes mellitus among FDRs of CKD patients. Diabetes mellitus nephropathy susceptibility locus for type1 has been identified on chromosome 3 and chromosome 3, 10, and 18 for type 2 while both types share similar site on 3q.[51]

Effective control of blood glucose and blood pressure reduces the renal complications of diabetes mellitus as meticulous control of blood glucose has been conclusively shown to reduce the development of microalbuminuria by 35% in type I diabetes. Control of blood pressure with a variety of anti-hypertensive agents, including ACEI, has been shown to delay the progression of albuminuria in both types 1 and type 2 diabetes.[52]

2.7 Obesity and Chronic Kidney Disease

Obesity independently or as a component of metabolic syndrome (hypertriglyceridemia, hypercholesterolemia, hypertension, hyperglycemia and obesity)[53] is an important global public health problem. Current estimates indicate that more than 1.3 billion adults worldwide are either overweight or obese. It is an important risk factor for diabetes mellitus and hypertension, the two most common etiologies of CKD.[53] Kambham *et al.*[54] reported that overweight and obese individuals have higher prevalence of CKD independent of association with hypertension and diabetes mellitus, Chagnac *et al.*[55] reported that obesity apart from being associated with several risk factors for CKD, is also known to be associated with detrimental renal haemodynamics leading to glomerulomegaly and obesity-related glomerulopathy-focal segmental glomerulosclerosis (ORG-FSGS) which is now a recognized disease entity. Hsu *et al.*[56] reporting a large population study evaluating the risk for ESRD (over 20 years) showed that increased body mass index (BMI) was an independent risk factor for progression to ESRD in obese individuals compared to those with normal body weight. Also, BMI over 35kg/m^2 has been considered a contraindication to renal transplant in some centers,[57] while Bergtrom *et al.*[58] reported that increased BMI is equally strongly associated with an increased risk of renal cell cancer. In Nigeria, Amira *et al.*[32] detected proteinuria in 4.9% of obese subjects, while Nalado *et al.*[10] reported that among obese subjects screened 11.7% had CKD. Rebecca *et al.*[59] reported 17.3% obese among patients with ESRD and 23% have positive family history of ESRD. Tsai *et al.*[17] reported 27.6% of relatives of CKD patients to have BMI over 27kg/m^2.

Obesity itself may increase CKD risk by increasing the metabolic demands on the kidney, which lead to higher glomerular capillary pressures and glomerular hypertrophy, targeting obesity is

beneficial not only for better control of hypertension and diabetes mellitus, but also possibly helps stabilization of CKD.[55,57]

2.8 Protenuria and Chronic Kidney Disease

Proteinuria previously considered a marker of renal disease is itself pathogenic and is the single best predictor of disease progression,[49] Renal impairment usually progresses through several stages; microalbuminuria, macroalbuminuria and overt proteinuria in chronic renal insufficiency and ESRD.[60] Remuzzi *et al.*[61] demonstrated that proteinuria induced tubulointerstitial injury through increased transglomerular flow of protein, increased cytokine production and inflammatory mediators recruitment leading to interstitial inflammation, glomerulosclerosis, fibrosis, tubular atrophy and reduced GFR regardless of the underlying nephropathy.

Prevention of Renal and Vascular End-stage Disease (PREVEND)[62] study among others have demonstrated that albuminuria is CVD risk factor independent of GFR, hypertension or diabetes mellitus. Proteinuria is a recognized factor favouring CKD progression.[63-65] Gouda and Tsai *et al.* reported prevalence of microalbuminuria of 10.6% [17,18] in relatives of CKD patients, and Wei *et al.* reported prevalence of 12.9% among FDRs of CKD patients, 14% in CGN relatives, 15.8% in relatives of hypertensive patients and 8.6% in relatives of diabetics[19].

Several studies have shown significant benefit in reduction of proteinuria in treatment of CKD patients, Ramipril Efficiency In Nephropathy (REIN)[66] study, Reduction in ENdpoint with the Angiotensin Antagonist Losartan (RENAAL)[67] study among many others demonstrated that ACEIs or ARBs reduced proteinuria, doubling of creatinine, ESRD and death in diabetic and non-diabetic nephropathy.[66-69]

2.9 Life-style and Chronic Kidney Disease

Some harmful life-style has been associated with CKD, notably excessive alcohol ingestion, smoking, and recreational drug use.[70-74] It was reported that induction of renal injury can occur through many pathways including association with systemic hypertension, glomerular hypertension, proteinuria, hyperlipidaemia, renal microvascular injury, growth factors and cytokine activation, ultimately leading to fibrogenesis and renal scarring[70].

Several studies such as Multiple Risk Factors Intervention Trial (MRFIT),[75] and PREVEND[62] among many others have documented significant association of particularly smoking with increased risk for ESRD. Zaghloul *et al.* reported that of the FDRs of CKD patients found to have albuminuria 26.2% are smokers.[18]

2.91 Nephrotoxins

Most notable among these entity include; Chinese herb nephropathy (Aristolochia fangchi, A.clematis, A.manshuriensis), NSAIDs, bleaching creams and many undefined local herbs and traditional medications.[38] It has been reported that nephrotoxin can cause a slowly progressive decreased kidney function.[76,77] Wei *et al.* reported that nephrotoxin, particularly Chinese herbs containing aristolochic acid, was independently associated with occurrence of albuminuria (ORs = 2.08,95% CI:1.19-3.62) in FDRs of CKD patients.[19]

2.92 Clinical Features

When renal function deteriorates slowly, patients may remain asymptomatic until glomerular filtration rate is 20ml/min or less. Nocturia, due to loss of concentrating ability and increased osmotic load per nephron, is often an early symptom. Thereafter, due to wide spread effects of renal failure, symptoms and signs may develop related to almost every body system. Patients may present with complaints which are not renal in origin, such as tiredness or breathlessness. ESRD patients appear ill and anaemic. There may be unusually deep respiration, anorexia and nausea. Later hiccoughs, pruritus, vomiting, muscular twisting, fits, drowsiness and coma.[33,78] Most patients in Nigeria present in late stage of the disease.[79]

2.93 Laboratory Investigations

Investigations include; serum urea, electrolytes and creatinine, fasting blood sugar, Uric acid, phosphate, albumin, calcium, urine profile (protein, creatinine clearance, electrolytes) lipid profile, urinalysis, renal ultrasound scan, and skeletal survey among others.[78]

2.94 Treatment

1. Lifestyle Modification:

Lifestyle modification such as healthy diet, weight reduction, exercise, avoidance of smoking and excessive alcohol consumption has been shown by a number of trials to considerably reduce the incidence of type 2 diabetes in overweight individuals with impaired glucose tolerance, likewise can also be effective in preventing hypertension and metabolic syndrome.[75,80] Smoking, excessive alcohol consumption and recreational drugs, have been linked to the development of ESRD.[70-74]

2. Pharmacological Approaches:

The control of risk factors for CKD such as hypertension and diabetes mellitus has been shown to be a very important intervention to reduce both albuminuria/proteinuria, and the subsequent progression of CKD. Also, the control of albuminuria/proteinuria is an important factor in slowing the progression of diabetic and non-diabetic CKD. For that, antihypertensive approaches based on the inhibitor/ blockage of the renin-angiotensin system (RAS) have been recommended in diabetes mellitus and nephropathy patients.[66-69] Treatment of hyperlipidaemia with 3-hydroxy-3-methylglutaryl co-enzyme A reductase inhibitor (statins) has been shown to be protective in experimental models of CKD.[48] In patients with CKD, a systematic interventions review suggested that lowering lipid levels might have a beneficial impact on the rate of progression of renal insufficiency, likewise other interventions including blood pressure control, RAS manipulation, glycaemic control, and cessation of smoking have the added advantage of cardio protection in susceptible patients with CKD.[75,80]

Treatment of ESRD, involves the use of complex and more expensive programs such as dialysis or kidney implantation (RRT). Such subjects could undoubtedly be detected in an earlier phase by screening for risk factors and markers of renal dysfunction.[18,50]

3. Renal Replacement Therapy:

Haemodialysis remains the most common modality of management with very few units offering peritoneal dialysis.[29] In the developing countries, very few can afford regular maintenance dialysis and renal transplantation is often not affordable nor available.[7,18] Nearly two million people currently are receiving haemodialysis worldwide, 60% of whom are treated in five countries (USA, Japan, Germany, Brazil and Italy), 20% are treated in 100 developing countries that make up 50% of world population.[81] Chronic haemodialysis became available in Nigeria in 1981 and the country now has about 40 dialysis units and majority are in public hospitals in major cities.[7] Healthcare is not adequately funded in the developing world, particularly for expensive and chronic treatment such as renal replacement therapy.[18]

2.95 Prevention

The incidence of ESRD is increasing, hence the need for RRT, this poses a growing healthcare and financial problem. Therefore, there is an urgent need to develop preventive strategies. Screening for risk factors may help to detect subjects at risk for progressive renal and CVD at an early stage, in which preventive strategies can be started and are expected to be efficacious. Such screening needs to be performed at least in subgroups at increased risk, such as relatives of CKD patients, diabetics and hypertensives, also in older age above 50years, and subjects with a family history of diabetes, hypertension and renal disease.[13-19] Such targeted screening has been shown to be more cost effectiveness than general population screening of CKD.[18]

CHAPTER THREE

3.0 METHODOLOGY: SUBJECTS, MATERIALS AND METHODS

3.1 Study Site

The study was conducted from January, 2015 to October, 2015 in the Nephrology clinic and Haemodyalisis unit at Aminu Kano Teaching Hospital (AKTH), Kano-Nigeria. A tertiary referral health centre, which has a capacity of 500 beds, the hospital was established in 1988 and is located in the North-Western geopolitical zone of Nigeria. It has 14 clinical departments including laboratory medicine with modern diagnostic facilities and equipment. Under the Department of Medicine of the hospital is the Medical Outpatient department which include the Nephrology clinic that caters for Nephrology and hypertensive cases with an average turnover of about sixty patients per week and the *Alhassan Dantata Haemodialysis Unit* which has 14 functioning haemodialysis machines and a total of 80 patients on maintenance HD, on a daily basis 10-16 patients undergo dialysis in the unit. The hospital serves as a referral center for Kano, Jigawa, Bauchi, Katsina, Gombe, Yobe, and Zamfara states. Patients are also referred from Sokoto, Maiduguri, Jos and Niger Republic for services such as kidney transplant or haemodialysis for patients with Hepatitis B, C or HIV infection.

3.2 Study Design

The study was a cross-sectional study.

3.3 Study Population

The study population comprised of adult (18years and above) FDRs (full parents, full siblings and offspring) [19] of the study probands (CKD patients attending AKTH through the renal clinic which runs every Monday and those on maintenance HD which operates morning, evening and night sessions every day of the week) who consented to the study.

3.4 Selection Criteria

3.4.1 Inclusion Criteria for the Study Subjects

- Age 18 years and above
- Individuals who consent to be part of the study.
- Confirmed as FDR (full Parent, Child or full Sibling) of the study proband.

3.4.2 Exclusion Criteria for the Study Subjects

- Age below 18 years.
- Individuals who refuse consent to be part of the study.
- Non-first degree relatives (half siblings, half parents, cousins, and other $2^{nd}/3^{rd}$ degree relatives).
- On-going menstruation or pregnancy until after menstruation or after delivery.
- On-going febrile illness until treated and resolved.
- On-going symptomatic urinary tract infection until treated and resolved

3.5 Ethical consideration

Approval for the study was obtained from the ethical committee of Aminu Kano Teaching Hospital prior to the commencement of the study (Appendix I). Individual informed consent was sought from each FDR before being enlisted for the study (Appendix II). The provision of the HELSINKI declaration was also respected.

3.6 Sample Size Determination

The minimum sample size required was determined using the formula[82]:

$$\mathbf{n=Z^2pq / d^2}$$

n= minimum sample requirement

Z= standard normal deviation at 95% confidence limit= 1.96

p = estimated prevalence rate of CKD in FDRs of CKD patients reported in previous literature- 29.7% [19].

q= 1-p

d= precision of the study= 0.05

n= $(1.96)^2$ x 0.297 x (1-0.297) / $(0.05)^2$

= 3.84 x 0.208 / 0.0025

n= 320

If 5% non-response (drop-out) is assumed, the minimum of; 320+16=336 Adult FDRs of CKD patients who consented and satisfied the inclusion criteria will be sampled.

3.7 Sampling Technique

The study started by invitation of all the study probands, comprising of all patients on maintenance HD in the haemodialysis unit (80) and all CKD patients being manage and follow up in nephrology outpatient clinic of AKTH (140), giving a total of 220 probands. Series of health talks was held and they were informed about the purpose of the study and the benefits of early detection of CKD and its modifiable risk factors in their families, all were asked to invite their adult FDRs for participation in the study and free screening after submitting the names of invitees. Relatives of about 95% of the CKD patients responded. Participants who satisfied the inclusion criteria were recruited by the researcher until the required sample size was obtained.

A systematic sampling technique was used by means of calculating the sampling fraction and sampling interval from the sampling frame obtained from the list of total number of adult FDRs (930) submitted by all probands and the calculated sample size.

Sampling fraction = calculated Sample Size/Sampling Frame

which was equal to 336/930, about 1/3.

The Sampling Interval = Reciprocal of Sampling Fraction = 3.

During selection of the participants, from the calculated sampling interval (3), every eligible third responder was recruited after randomly selecting the first participant by balloting. The participants were then screened for presence of CKD and determinants of CKD to determine its prevalence and risk factors.

3.8 Materials and Equipment

3.8.1 Materials and supplies

1) Validated study Questionnaire. 2) Cotton wool. 3) Fluoride oxalate specimen containers. 4) Universal specimen containers. 5) Lithium heparin specimen containers. 6) Disposable Gloves. 7) Sterile needles and syringes 8) Methylated spirit 9) Stationaries-papers, pen, staplers etc. 10) Urine test strips (H_{11}-$_{MA}^{TM}$).

3.8.2 Equipment

1) Littman's stethoscope. 2) Sphygmomanometer [Accoson, UK]. 3) Weighing scale for weight measurement [ZT-120 Health Scale]. 4) Stadiometre for height measurement 5) Autoanalyzer Cobas Integra 400 Plus (Roche Diagnostic Corporation, Mannheim, Germany). 6) Computer with SPSS/PASW version 16.0 statistical software.

3.9 Study Procedure

Following the ethical clearance (Appendix I), the study procedure was first explained to all the participants and a signed written informed consent (Appendix II) was obtained from individual. A structured questionnaire (Appendix III) was administered to each of the participant recruited for the study by the researcher and trained assistants.

The International Society of Nephrology-Commission for Global Advancement of Nephrology-chronic Kidney disease, Hypertension, Diabetes and Cardiovascular diseases in Developing Countries (ISN-COMGAN-KHDC) programme on prevention and surveillance of chronic non-communicable diseases, designed the adapted questionnaire which was piloted and validated to our setting by ISN-COMGAN Research subcommittee in 2004.

The questionnaire has three sections; (1) Section on personal data of the respondents. (2) Section on medical history of the subjects. (3) Section of clinical examination and laboratory evaluation.

The section (1) of the questionnaire was used to obtained data on socio-demographic status such as age, sex, type of relation, occupation, tribe, religion, marital status, education level and lifestyle behavior like cigarette smoking and alcohol ingestion were completed for each subject, also history on use and duration of substances known to be nephrotoxic such as non-steroidal anti-inflammatory drugs (NSAIDs), herbs or traditional remedies and mercury containing or bleaching cosmetics were recorded. Personal and family medical history such as hypertension, diabetes mellitus, recurrent sore throat and previous skin rashes were completed using section (2). And section 3 was used to complete blood pressure, anthropometric and biochemical data that were measured to assess for potential risk factors as subsequently described.

3.10 Physical Measurements

1. Anthropometric measurements:

Height was measured with a stadiometre. It consists of a metric tape affixed to a vertical surface such as a wall and a movable block attached to the vertical surface at a tight angle that can be brought down to the crown of the head. The subject stood without shoes with the heels together and back as straight as possible; the heels, buttocks, shoulders and head touching the wall. With the weight of the subject evenly distributed on both feet, the head was positioned in the Frankfurt horizontal plane, with the arms hanging freely by the sides and the palms facing the thigh. The subject will be asked to inhale deeply and maintain a fully erect position. The movable block is brought down until it touches the head with sufficient pressure applied to compress the hair. The measurement was recorded to the nearest 0.1 centimetres. The weight was measured using a standard weighing scale- platform–beam scale or its equivalent. The beam of the platform scale is graduated so that it can be read from both sides. The subject stands then stood over the centre of the platform with the body weight distributed between both feet. Weight was then recorded in kilogrammes to the nearest 0.1 kilograms. Body mass index (BMI) was then calculated as the ratio of measured weight to the square of the measured height (kg/m^2).

2. Blood pressure measurement:

Blood pressure was measured with the patient in the sitting position using a well calibrated Accoson mercury sphygmomanometer after subject has rested for 5 minutes. Blood pressures in both arms were measured in turn, and the arm with the higher value was used for this study. The arm to be measured was supported at the level of the heart by resting it on the consultation table. An appropriate sized cuff (with the bladder encompassing more than two-thirds of the arm) was

then wrapped snugly (allowing a finger into it) around the arm about 2.5 centimetres above the antecubital fossa, with the midline of the bladder over the brachial artery pulsation. The cuff was inflated rapidly to about 70 mmHg and then by 10 mmHg increments while palpating the radial pulse. The reading at which the pulse disappears and then subsequently reappears during deflation is noted. With the bell of the stethoscope over the brachial artery pulsations, the cuff was rapidly inflated to a pressure 20-30 mmHg above the level previously determined by palpation. The cuff was then deflated at 2 mmHg/second while listening for the first Korotkoff sounds, and was then deflated rapidly after the last Korotkoff sound. The systolic blood pressure recordings were taken at phase I Korotkoff sounds, while the diastolic blood pressure was recorded at phase V Korotkoff sounds (when they disappear) or at phase IV Korotkoff sounds (becomes muffled) when the difference between phase IV and phase V is more than 20 mmHg. The BP recordings were recorded to the nearest 2 mmHg.

3.11 Laboratory measurement

Ten milliliters of venous blood samples were taken from all participants after an overnight fast of at least 8 hours for determination of levels of fasting plasma glucose using fluoride oxalate sample bottles, serum creatinine and fasting serum lipids using lithium heparin sample bottles by the researcher and research assistants in the haemodialysis unit consulting rooms. All blood samples were taken to the chemical pathology laboratory immediately after which they were centrifuged to separate the plasma and then stored at 4^0 C till they were analyzed using Autoanalyzer Cobas Integra 400 Plus (Roche Diagnostic Corporation, Mannheim, Germany) in the Chemical pathology laboratory by a laboratory scientist using the manufacturer's protocol. Ten milliliters of midstream early morning spot urine was also obtained in a universal specimen container from each participant and tested using semi quantitative urine dipsticks (H_{11}-$_{MA}^{TM}$) for

proteinuria (tetrabromophenol blue), haematuria (diisopropylbenzenedihydroperoxide) and microalbuminuria (sulfonephthalein) by the same laboratory technician in the chemical pathology laboratory using the manufacturer's protocol.

Serum creatinine (Scr) obtained was used to calculate eGFR using the Cockroft-Gault Equation[1,2].

Crcl (ml/min per 1.73m^2) = 140-Age (years) x weight (Kg)/72 x Scr (mg/dl). For female multiply by a factor of 0.85.

According to National Kidney Foundation-Kidney/Dialysis Outcomes Quality Initiative (K/DOQI) and Kidney Disease Improving Global Outcomes (KDIGO), CKD is kidney damage or GFR <60ml/min per 1.73m^2, irrespective of cause persisting for three months or more. Kidney damage was ascertained by the presence of microalbuminuria/proteinuria and or haematuria which was repeated after 3 months to confirm for CKD as defined.

3.12 Definition of Terms

1) CKD is kidney damage or GFR <60ml/min per 1.73m^2, irrespective of cause persisting for three months or more.[1,2] Kidney damage ascertained by the presence of albuminuria and or haematuria persisting for 3 months in the index study.

2) Diabetes mellitus defined as FBS ≥7.0 mmol/l or previously diagnosed diabetes mellitus by a physician or on hypoglycaemic agents.[24]

3) Hypertension considered to be present when a person's systolic BP is consistently 140 mmHg or greater and or diastolic BP is consistently 90mmHg or greater, previously diagnosed hypertensive by physician or currently on antihypertensives.[25]

4) Obesity: Was defined based on WHO guidelines as the body weight (kg) of an individual divided by the square of the height in metres, expressed in kg/m^2. Subjects with BMI <18.5 were classified as underweight and those with BMI of 18.5-24.9 were classified as having normal weight. Those with BMI of 25.0-29.9 and ≥30.0 were classified as overweight and obese respectively.[53]

5) Dyslipidaemia: This was defined using adult treatment panel III (ATP III) guidelines, when one or all of the following are found; [53] Total cholesterols > 200mg/dl (5.2mmol/l), LDL >100mg/dl (2.6mmol/l), Triglycerides>150mg/dl(1.7mmol/l) and HDL<40mg/dl (1.03mmol/L) in men or <50mg/dl (1.30mmol/L) in women.

6) Microalbuminuria defines the urinary excretion of albumin in a range of 30-299mg/24hrs.[78]

7) Proteinuria: Urinary protein excretion greater than 300 mg/24hrs.[78]

8) Haematuria: Defined as ≥3 RBCs per HPF in at least 2 samples, dipstick detect peroxidase activity in RBCs.[78]

9) Smoking Status: Current Smoker: >1 cigarette/day, Ex-smoker: stopped smoking ≥ 2 years ago.[70]

10) Educational level: According to years spent in full time education. Low level <10 years and high level >10 years.[87]

11) Alcohol; consumption of ≥ of 60g of alcohol in a week by men and ≥30g by women was taken as significant. One unit of alcohol (8g) was considered as equal to half pint of beer, one glass of wine and 25ml, (one single measure) of spirit.[73]

12) Nephrotoxic substances (NTS); Comprising excessive use of NSAIDS, mercury containing cosmetics, bleaching creams and herbal remedies that are potentially damaging to the kidneys.[18,76]

13) Recurrent sore throat (RST); generally, define as seven episodes of sore throat in the preceding year or five episodes in each of the preceding two years. Strep throat if untreated one to two weeks after infection may lead to kidney damage.[78]

14) Previous skin rash (PSR); Describing a non-bullous impetigo, a contagious, itchy bacterial skin infection, most common among children, caused commonly by streptococcus pyogenes if untreated three-four weeks after infection may lead to kidney damage.[78]

15) Systematic sampling; Is a type of probability sampling method, in which sample members from a larger population (sampling frame) are selected according to a random starting point, and a fixed periodic interval (sampling interval) calculated by dividing the population size by desired sample size.[82]

16) Proband; Refers to the affected family member who seeks medical attention for a possible genetic disorder.[39] In the index study, definition includes all ESRD patients on maintenance HD in the haemodialysis unit and all CKD patients being managed and followed up in nephrology outpatient clinic of AKTH.

17) First Degree Relative; Defined by Wright coefficient of relationship (r) value of 0.5, where r is defined as the fraction of homozygous due to genetic composition. Thus a parent, child and siblings has a (r) value of r=0.5.[40]

18) Age groups; Young age refers to age of 18 to 45 years; middle age refers 46 to 60 years while elderly refers age >60 years.[1]

3.13 Data Analysis

The data from each participant obtained from the administered questionnaire, physical and biochemical measurements were collated and entered into the Statistical Software Package (SPSS) version 16.0 for analyses.

Qualitative data were described as frequencies, proportions or percentages. The variables were further cross-tabulated and assessed for association using Pearson's Chi-square test. Quantitative data were reported as means and standard deviations. The quantitative variables were further subjected to test of significance using Student t-test. Fisher exact test was used in cells that had variables less than five. Multivariate logistic regression analysis was further used to determine the independent risk factors of CKD in the study population. In all cases P- values < 0.05 was considered significant.

CHAPTER FOUR

4.0 RESULTS

4.1 Composition of Study Population

The study was conducted between between January 2015 and October 2015. There were a total of 462 participants from individual families, 350 (75.7%) fulfilled the inclusion criteria and were recruited into the study while 112 (24.2%) of which 52 with age less than 18 years and 60 that are non-first degree relatives (including half siblings, half parents, cousins and other $2^{nd}/3^{rd}$ degree relatives) were excluded, 341 completed the study while the remaining 9 dropped out of the study, yielding a response rate of 97.5%.

There were 234 (68.6%) males and 107 (31.4%) females in the study given a ratio of 3:2 as depicted in figure 1.

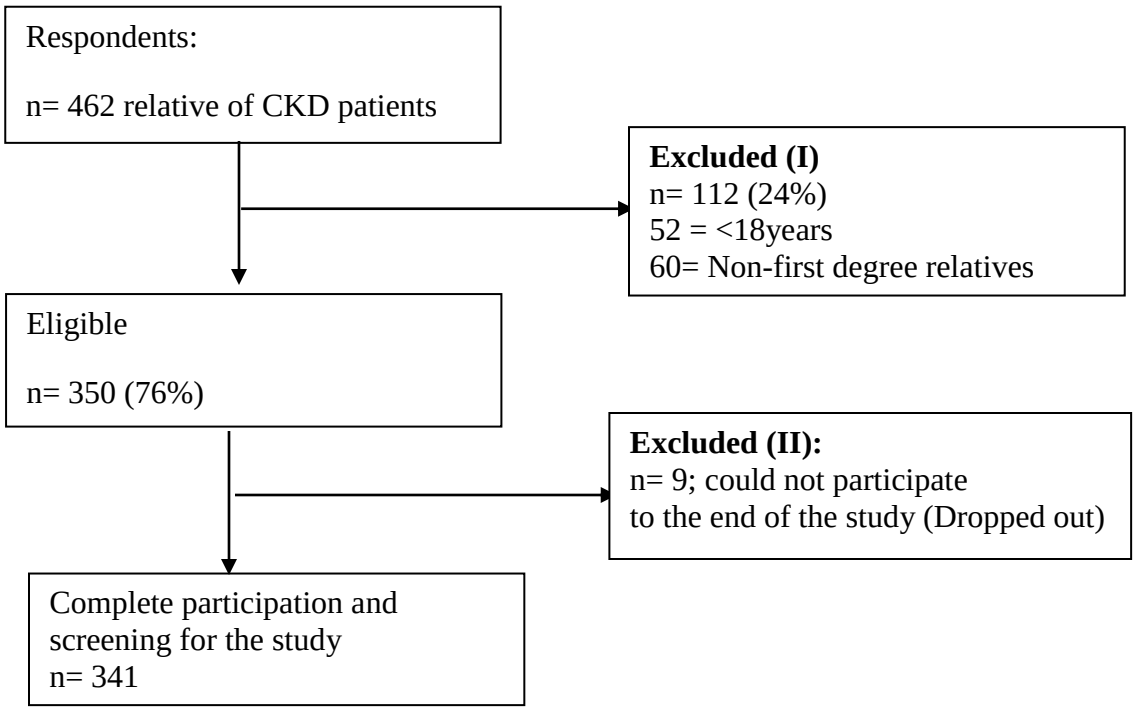

Figure 1: Recruitment flow chart of the Participants.

4.2 Socio – demographic characteristics of Participants.

4.2.1 Distribution of Participants by Age and Gender

The mean age of study participants ± (SD) was 33.04 ± 10.88years (range: 18 to 74 years). The mean age of males was 31.30 ± 10.42years and mean age of females was 36.82 ± 10.96years. There was statistically significant difference (p= 0.003) in the mean age of the participants based on gender, with females more likely to be older. Majority of the participants of 86.2% were in the "young" age group (18 to 45 years), the "middle" age group (46 to 60 years) account for 11.7% while the "elderly" (more than 60 years) account for 2.1%. There was significant difference in the distribution by gender of the participants (χ^2=11.743, p<0.000), with 68.6% of the participants being males. The age and gender distribution of the participants is shown in Table 2.

Table 2: Distribution of Participants by Age group and Gender

Age (years)	**Gender**		**Total N (%)**
	Male n (%)	**Female** n (%)	
Young age (18-45)	211 (61.9)	83 (24.3)	294 (86.2)
Middle age(46-60)	18 (5.3)	22 (6.4)	40 (11.7)
Elderly (>60)	5 (1.4)	2 (0.7)	7 (2.1)
Total	234 (68.6)	107 (31.4)	341(100.0)

χ^2=11.743, p<0.000

4.2.2 Distribution of Participants by Occupation, Marital status, Educational level and Tribe.

A substantial proportion of the participants (48.7%) comprising full-time house wives and students were unemployed, and 26.4% engaged in business, while civil servants accounted for 19.6%, and the remaining 5.3% were self employed including farmers, artisans, traders and commercial transporters.

Majority, 268 (78.6%) of the participants were married, 45 (13.2%) were single, 20 (5.9%) divorced, while 8 (2.3%) were widowed.

Sixty eight (19.9%) of the participants [female 39 (11.4%) and male 29 (8.5%)] had low level education, while 273 (80.1%) had high level education.

Majority, 240 (70.4%) of the participants were Hausas, 19 (5.6%) were Yorubas, 17 (5.0%) were Igbos, and the remaining 65 (19.0%) were from other tribes which comprise of Fulani, Babur, Nupe, Ebira, Idoma, and Kanuri. Distribution of participants by occupation, marital status, educational level and tribe is as shown in Table 3.

Table 3: Distribution of Participants by Occupation, Marital status, Educational level and Tribe.

Variables	Gender		Total N (%)
	Male n (%)	**Female** n (%)	
Occupational status:			
Business	83 (24.3)	7(2.1)	90 (26.4)
Civil servant	52 (15.2)	15 (4.4)	67 (19.6)
Self employed	12 (3.5)	6 (1.8)	18 (5.3)
Unemployed	87 (25.5)	79 (23.2)	166 (48.7)
Marital status:			
Married	187 (54.8)	81 (23.8)	268 (78.6)
Single	30(8.8)	15(4.4)	45(13.2)
Divorced	12(3.5)	8(2.4)	20(5.9)
Widowed	5(1.4)	3(0.9)	8(2.3)
Educational level:			
High level	205(60.1)	68(20.0)	273(80.1)
Low level	29(8.5)	39(11.4)	68(19.9)
Tribe:			
Hausa	159(46.6)	81(23.8)	240(70.4)
Yoruba	18(5.3)	1(0.3)	19(5.6)
Igbo	8(2.4)	9(2.6)	17(5.0)
Others	49(14.3)	16(4.7)	65(19.0)

4.2.3 Distribution of the Participants by Type of Relationship.

Majority, 145 (42.5%) of the participants were children of the CKD patients, 125 (36.7%) were siblings, while 71 (20.8%) were parents of the CKD patients. The distribution of participants by type of relationship is as shown in Table 4.

Table 4: Distribution of Participants by Type of Relationship.

Type of Relation	**Gender**		**Total N (%)**
	Female n (%)	**Male** n (%)	
Child	35 (10.3)	110 (32.2)	145 (42.5)
Sibling	33 (9.7)	92 (27.0)	125 (36.7)
Parent	39 (11.4)	32 (9.4)	71 (20.8)
Total	107 (31.4)	234 (68.6)	341 (100.0)

4.3 Clinical and Laboratory Characteristics of Participants.

4.3.1 Clinical Characteristics of Participants.

Of the 341 participants, 16.1% reported recurrent sore throat, while 16.4% reported past skin rashes. Eighty six out of 341 participants reported excessive use of nephrotoxic substances (including one or combination of NSAIDS, medicated soap, bleaching cream and herbal concoction) giving a combined prevalence of 25.2%.

Majority (76.8%) of the participants reported family history of hypertension, while 35.8% reported family history of diabetes mellitus, 12.6% took alcohol, while 18.5% were current smokers.

Mean body mass index was 25.62±5.19 Kg/m^2 and 16.4% were obese. Of the 341participants 88 (19 newly diagnosed) were hypertensive giving a prevalence of 25.8%. Table 5 shows the clinical characteristics of the study participants.

Table 5: Clinical Characteristics of Participants.

Variables	Status		Total N (%, mean ±SD)
	Present n (%)	**Absent** n (%)	
Medical history:			
Recurrent Sore Throat	55 (16.1)	286(83.9)	341 (100.0)
Past Skin Rashes	56 (16.4)	285 (83.6)	341 (100.0)
NTS	86 (25.2)	255 (74.8)	341 (100.0)
FHTN	262 (76.8)	79 (23.2)	341 (100.0)
FHDM	122(35.8)	219(64.2)	341 (100.0)
Current Smokers	63 (18.5)	278 (81.5)	341 (100.0)
Alcohol	43(12.6)	298 (87.4)	341 (100.0)
Phys. Measurement:			
SBP (mmHg)	341(100.0)		126.83±20.12
DBP (mmHg)	341(100.0)		78.78±11.63
Weight (Kg)	341(100.0)		67.42±12.83
Height (m)	341(100.0)		1.62±0.80
BMI (Kg/m^2)	341(100.0)		25.62±5.19
Hypertension	88(25.8)	253(74.2)	341 (100.0)
Obesity	56(16.4)	285(83.6)	341 (100.0)

n: number of participants in a category expressed as number (%), N: total number of participants or value for a variable expressed as number (%) or means ± SD, NTS: nephrotoxic substances, FHTN: family history of hypertension, FHDM: family history of diabetes mellitus, SBP: systolic blood pressure, DBP: diastolic blood pressure, BMI: body mass index, Phys. Measurement: physical measurement.

4.3.2 Laboratory Characteristics of Participants.

Mean value for total cholesterol (TC) and triglycerides (TG) was 4.38±1.15 mmol/l and 1.19±0.58 mmol/l respectively, while that of high density lipoprotein (HDL) and low density lipoprotein (LDL) cholesterol were 1.09±0.58 mmol/l and 2.68±0.94 mmol/l respectively, and 6.5% were found to have dyslipidaemia (one or combination of high TC, TG, LDL or low HDL).

Of the 341 participants 129 had microalbuminuria and 85 had proteinuria giving a prevalence of 37.8% and 24.9% respectively.

Mean FBS was 5.18±3.10 mmol/l and 49 (6 newly diagnosed) of the 341 participants were diabetic giving a prevalence of 14.4%.

The mean value for SCr and eGFR was 94.50±57.30 µmol/l and 93.37±34.31 ml/min respectively. Of the 341 participants 58 had reduced eGFR (<90 ml/min). Table 6 shows the laboratory characteristics of the participants.

Table 6: Laboratory Characteristics of Participants.

Variables	Status		Total N (%, mean ±SD)
	Present n (%)	**Absent** n (%)	
Microalbuminuria	129 (37.8)	212 (62.2)	341 (100.0)
Proteinuria	85 (24.9)	256(75.1)	341 (100.0)
Haematuria	45 (13.2)	296 (86.8)	341 (100.0)
TC (mmol/l)	341(100.0)	-	4.38±1.15
HDL (mmol/l)	341(100.0)	-	1.09±0.36
LDL (mmol/l)	341(100.0)	-	2.68±0.94
TG (mmol/l)	341(100.0)	-	1.19±0.58
FBS (mmol/l)	341(100.0)	-	5.18±3.10
SCr (µmol/l)	341(100.0)	-	94.50±57.30
eGFR(ml/min)	341(100.0)	-	93.37±34.31
Diabetes mellitus	49 (14.4)	292(85.6)	341 (100.0)
Dyslipidaemia	22 (6.5)	319 (93.5)	341 (100.0)
Reduced eGFR (<90ml/min)	58 (17.0)	283 (83.0)	341 (100.0)

n: number of participants in a category expressed as number (%), N: total number of participants or value for a variable expressed as number (%) or means ± SD, TC: total cholesterol, TG: triglycerides, HDL: high density lipoprotein, LDL: low density lipoprotein, FBS: fasting blood sugar, SCr: serum creatinine, eGFR: estimated glomerular filteration rate.

4.3.3 Chronic Kidney Disease Screening Test Results among the Participants.

The initial CKD screening test results and the repeat test after 3 months, showed that of the 129 participants who had MA, 90 persisted giving a prevalence of 26.4%. And of the 85 participants who had proteinuria, 70 persisted giving a prevalence of 20.5%. Of the 45 participants with haematuria, 30 tested positive for haematuria on repeat test giving a prevalence of 8.8%.

The mean value (repeat test) for SCr and eGFR was 162±55.02 µmol/l and 70.52±35.61 ml/min respectively. Of the 97 participants 39 (25 males and 14 females) had eGFR >90 ml/min of which 32, 12 and 8 had persisted MA, proteinuria and haematuria respectively.

Also, 30 participants (8 males and 22 females) had eGFR between 89 to 60 ml/min of which all and 12 had MA, proteinuria and haematuria respectively.

Likewise, 16 participants (6 males and 10 females) had eGFR between 59 to 45 ml/min of which all and 6 had MA, proteinuria and haematuria respectively.

Similarly, 10 participants (4 males and 6 females) had eGFR between 44 to 30 ml/min of which all and 2 had MA, proteinuria and haematuria respectively. And the remaining 2 participants (a male and a female) who had eGFR between 29 to 15 ml/min, all had MA, proteinuria and haematuria respectively. Table 7 shows the CKD screening test results among the participants.

Table 7: Chronic Kidney Disease Screening Test Results among the Participants.

Variables	Screening Result Status		Total N (%)
	Initial n (%)	**After 3 months** n (%)	
Microalbuminuria	129 (37.8)	90(26.4)	341 (100.0)
Proteinuria	85 (24.9)	70 (20.5)	341 (100.0)
Haematuria	45 (13.2)	30 (8.8)	341 (100.0)
Scr (µmol/l)	94.50±57.30	162±55.02	341 (100.0)
eGFR (mmol/l)	93.37±34.31	70.52±35.61	341 (100.0)
Reduced eGFR	62(18.2)	58(17.0)	341 (100.0)
Renal Impairment	129 (37.8)	97 (28.4)	341 (100.0)
Stages by eGFR:			
>90		39(11.4)	341 (100.0)
89-60		30(8.8)	341 (100.0)
59-45		16(4.7)	341 (100.0)
44-30		10(2.9)	341 (100.0)
29-15		2 (0.6)	341 (100.0)

N: total number of participants expressed as number (%), n: number of participants or value for a variable expressed as number (%) or means ± SD, SCr: serum creatinine, eGFR: estimated glomerular filtration rate, Reduced eGFR: <90ml/min, Renal impairment: presence of ≥1 of MA, PROT, HAEM, Red. eGFR

4.4 Prevalence of Chronic Kidney Disease.

4.4.1 Prevalence of Chronic Kidney Disease among the study Participants.

Of the 341 participants 97 (including 39 with normal eGFR >90 ml/min but with persisted MA, proteinuria and haematuria. And 58 with persistently reduced eGFR in addition to persisted MA, proteinuria and haematuria) had CKD giving a prevalence of 28.4% among the study population using Cockcroft and Gault equation for estimated glomerular filteration rate and evidence of renal damage (MA, proteinuria and haematuria). There were more female participants with CKD 53 out of 107 with a prevalence of 49.5%, when compare with the male participants, 44 out of 234 giving a prevalence of 18.8%. This difference in prevalence based on gender was found to be statistically significant ($p<0.000$). Table 8 summarizes the prevalence of CKD among the study participants.

Table 8: Prevalence of CKD among the study Participants by Gender.

CKD	**Gender**		**Total N (%)**
	Male n (%)	**Female** n (%)	
Present	44 (18.8)	53 (49.5)	97 (28.4)
Absent	190 (81.2)	54 (50.5)	244 (71.6)
Total	234 (100)	107 (100)	341 (100.0)

$\chi^2=24.06$, $p<0.000$

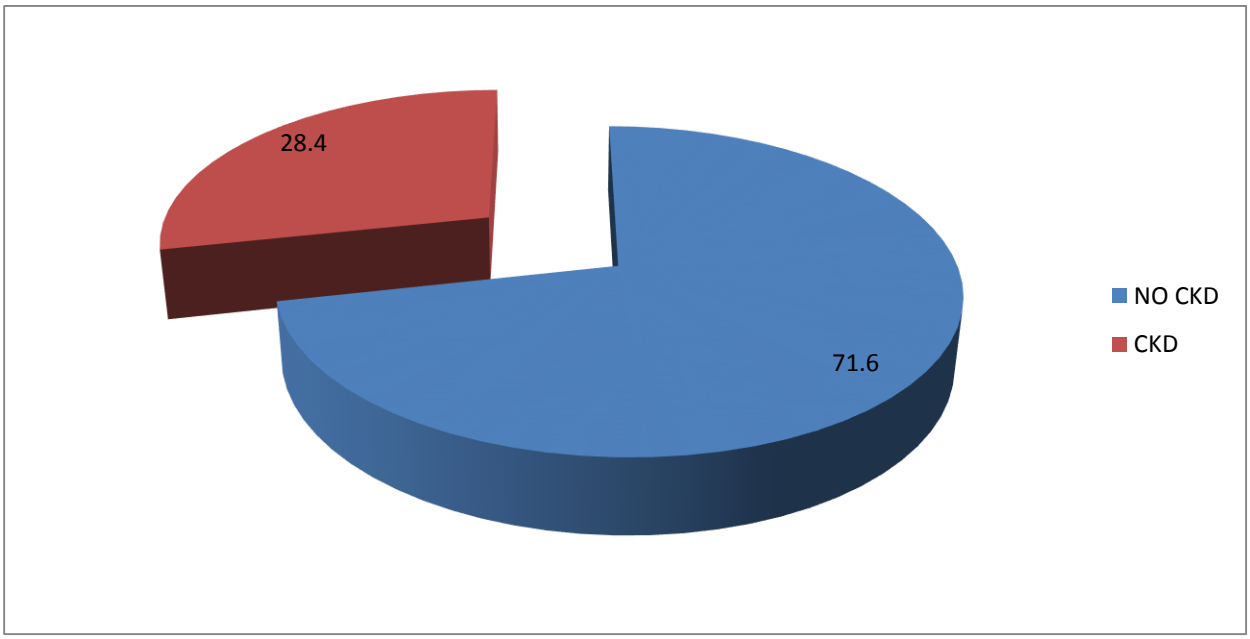

Fig 2: Pie Chart showing overall Prevalence of CKD among study Participants.

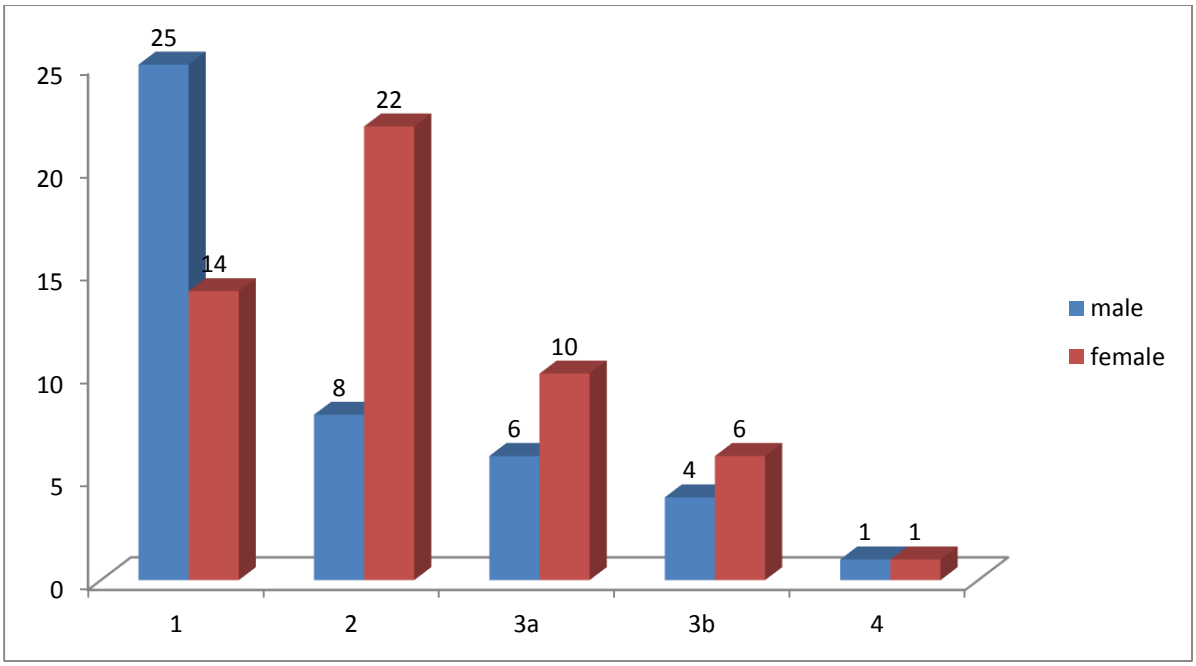

Fig 3: Bar chart showing different stages of CKD among the study Participants.

4.4.2 CKD across Socio-demographic, Clinical and Laboratory Characteristics of Participants.

4.4.2.1 Prevalence of CKD by type of Relationship.

The study showed that of the 71 parents that participated in the study, 52 (73.2%) had CKD, while 23 had CKD out of 125 siblings with prevalence of 18.4% and 22 had CKD out of 145 children of CKD patients giving a prevalence of 15.2%. The prevalence was higher among FDRs who were parents compared to the siblings and children. This difference in prevalence based on type of relationship was found to be statistically significant ($p<0.000$) as shown in the table 9.

Table 9: Prevalence of CKD by type of Relationship.

CKD	**Type of Relationship**			**Total N (%)**
	Parent n (%)	**Sibling** n (%)	**Child** n (%)	
Present	52 (73.2)	23 (18.4)	22 (15.2)	97 (28.4)
Absent	19 (26.8)	102 (81.6)	123 (84.8)	244 (71.6)
Total	71 (100)	125 (100)	145 (100)	341 (100)

$\chi^2 = 18.73$, $p<0.000$

4.4.2.2 Prevalence of CKD among the Participants by Age.

The study showed an increasing trend in the prevalence of CKD with increasing age, from 20.4% in the young (18-45 years) to 77.5% in middle age (46-60 years) and 85.7% in the elderly (age > 60 years). This increasing trend in prevalence of CKD with increasing age was found to be statistically significant (p<0.000) as shown in table 10.

Table 10: Prevalence of CKD among the Participants by Age.

CKD	**Age Category**			**Total** N (%)
	Young n (%)	**Middle age** n (%)	**Elderly** n (%)	
Present	60 (20.4)	31 (77.5)	6 (85.7)	97 (28.4)
Absent	234 (79.6)	9 (22.5)	1 (14.3)	244 (71.6)
Total	294(100)	40 (100)	7 (100)	341 (100)

χ^2 =27.90, p<0.000

4.4.2.3 Prevalence of CKD by Educational status.

In the study there was a higher prevalence of CKD among participants with low level of education (57.4%). This difference in prevalence based on educational status was found to be statistically significant ($p<0.001$) as shown in table 11.

Table 11: Prevalence of CKD by Educational status.

CKD	**Educational status**		**Total N (%)**
	High level n(%)	**Low level** n(%)	
Present	58 (21.2)	39 (57.4)	97 (28.4)
Absent	215 (78.8)	29 (42.6)	244 (71.6)
Total	273 (100)	68 (100)	341 (100)

χ^2 =3.51, p<0.001

4.4.2.4 Distribution of CKD by Clinical Characteristics of Participants.

Of the 86 participants who reported use of nephrotoxic substances 35 had CKD giving a prevalence of 40.7%. Sixty percent of participants who were hypertensive, had CKD ($p<0.001$). Of the 56 participants with obesity 25 had CKD giving a prevalence of 44.6%. Table 12 summarizes distribution and prevalence of CKD by clinical characteristics of the participants.

Table 12: Prevalence of CKD by Clinical Characteristics of Participants

Characteristics	Category	Total (N)	Prevalence of CKD n (%)	Test stat (χ^2)	P-value
RST	Yes	55	17 (30.9)	0.19	0.652
	No	286	80 (27.9)		
PSR	Yes	56	20 (35.7)	1.25	0.067
	No	285	77 (30.2)		
NTS	Yes	86	35 (40.7)	6.25	0.001*
	No	285	62 (24.3)		
FHTN	Yes	262	86 (32.8)	1.65	0.052
	No	79	11 (13.9)		
FHDM	Yes	122	51 (41.8)	1.33	0.058
	No	219	46 (21.0)		
CS	Yes	63	23 (36.5)	1.32	0.061
	No	278	74 (26.6)		
Alcohol	Yes	43	15 (34.8)	1.02	0.069
	No	298	82 (27.5)		
HTN	Yes	88	53 (60.2)	21.92	<0.001*
	No	253	44 (17.4)		
Obesity	Yes	56	25 (44.6)	18.18	<0.001*
	No	285	72 (25.2)		

N: total number of participants in a category, n: number of participants with CKD (%), RST: recurrent sore throat, PST: past skin rashes, NTS: nephrotoxic substances, FHTN: family history of hypertension, FHDM: family history of diabetes mellitus, CS: current smoker, HTN: hypertension.

4.4.2.5 Distribution of CKD by Laboratory Characteristics of Participants.

Twenty six out of 49 participants (53.1%) who were diabetic had CKD (p<0.001). Of the 45 participants with haematuria 30 had CKD with prevalence of 66.7%, while participants with microalbuminuria and proteinuria had a prevalence of CKD of 73.8% and 82.4% respectively. Table 13 summarizes CKD distribution and prevalence by laboratory characteristics of the participants.

Table 13: Prevalence of CKD by Laboratory Characteristics of Participants.

Characteristics	Category	Total (N)	Prevalence of CKD n (%)	Test stat (χ^2)	P-value
DM	Yes	49	26 (53.1)	14.22	<0.001*
	No	292	71 (24.3)		
DL	Yes	22	7 (31.8)	1.36	0.056
	No	319	90 (28.2)		
HAEM	Yes	45	30 (66.6)	11.47	<0.001*
	No	296	67 (22.6)		
MA	Yes	129	90 (70.0)	22.28	< 0.001*
	No	212	7 (3.3)		
PROT	Yes	85	70 (82.3)	26.64	<0.001*
	No	256	27 (10.5)		

N: total number of participants in a category, n: number of participants with CKD (%), MA: microalbuminuria, DM: diabetes mellitus, DL: dyslipidaemia, HAEM: haematuria, PROT: proteinuria.

4.5 Risk factors for Chronic Kidney Disease.

4.5.1 Distribution of Potential Risk factors for CKD among the study Participants.

The study showed that 76.8% and 35.8% of the participants reported family history of hypertension and diabetes mellitus respectively, while 25.8% and 14.4% of the FDRs had hypertension and diabetes mellitus respectively. Twenty five percent of the participants reported history of consumption of potentially nephrotoxic substances (NTS). Microalbuminuria, proteinuria and haematuria were found in 37.8%, 24.9% and 13.2% of the FDRs respectively. Table 14 shows the distribution of potential risk factors among the study participants.

Table 14: Distribution of Potential Risk factors for CKD.

Variables	Status		Test X^2	p-value
	Present n (%)	**Absent** n (%)		
RST	55 (16.1)	286 (83.9)	0.31	0.580
PSR	56 (16.4)	285(83.6)	1.48	0.519
NTS	86 (25.2)	255(74.8)	14.91	0.000*
FHTN	262 (76.8)	79 (23.2)	4.64	0.031*
FHDM	122 (35.8)	219 (64.2)	8.14	0.004*
Current smoker	63 (18.5)	278 (81.5)	1.85	0.501
Alcohol	43 (12.6)	298 (87.4)	1.51	0.220
Hypertension	88 (25.8)	253 (74.2)	26.74	0.000*
Diabetes mellitus	49 (14.4)	292 (85.6)	12.49	0.001*
Dyslipidaemia	22 (6.5)	319 (93.5)	3.79	0.052
Obesity	56 (16.4)	285 (83.6)	2.66	0.055
MA	129 (37.8)	212 (62.2)	37.72	0.000*
Proteinuria	85 (24.9)	256 (75.1)	39.60	0.000*
Haematuria	45 (13.2)	296 (86.8)	9.38	0.002*

Data expressed as number (%), n: Number of participants out of 341 overall participants, RST: recurrent sore throat, PST: past skin rashes, NTS: nephrotoxic substances, FHTN: family history of hypertension, FHDM: family history of diabetes mellitus, MA: microalbuminuria, P*= statistically significant.

4.5.2 Distribution of Potential Risk factors for CKD among the Participants by Gender.

In the study, the female participants were older with mean age of 36.82±10.95 years compared to male participants with mean age of 31.30±10.42 years, and the difference was statistically significant ($p<0.000$). Also a statistically significant higher proportion of male participants 172 (50.4%) reported a family history of hypertension when compared to 90 (26.4%) for the female participants ($p<0.003$), likewise 18.2% of the males were current smokers when compared to 0.3% of the female participants ($p<0.000$). Similarly, the female participants had significantly higher weight and more likely to be obese compared to their male counterparts with mean weight and body mass index of 71.21±16.50 Kg and 28.20±6.39 Kg/m^2 as against 65.69±10.33 Kg and 24.44±4.03 Kg/m^2 respectively ($p<0.000$). There was statistically significant difference in the higher proportion of female participants with hypertension 47 (13.8%), diabetes mellitus 26 (7.6%) and proteinuria 50 (14.6%) when compared to that of their male counterparts. Table 15 compares the potential risk factors among the study participants by gender.

Table 15: Distribution of Potential Risk factors for CKD among the Participants by Gender.

Variables	Gender		Test stat	p-value
	Male n (%)	**Female** n (%)		
Age (years)	31.30±10.42	36.82±10.95	t= - 4.464	0.000*
RST	36(10.5)	19(5.6)	X^2=0.31	0.580
PSR	31(9.1)	25(7.3)	X^2=0.48	0.190
NTS	42(12.3)	44(12.9)	X^2=0.91	0.570
FHTN	172(50.4)	90(26.4)	X^2= 4.64	0.031*
FHDM	72(21.1)	50(14.7)	X^2=0.14	0.054
Current Smokers	62(18.2)	1(0.3)	Fishers	0.000*
Alcohol	33(9.7)	10(2.9)	X^2=1.51	0.220
Hypertension	41(12.0)	47(13.8)	X^2= 26.74	0.000*
Obesity	24(7.0)	32(9.4)	X^2=20.66	0.000*
MA	63(18.5)	66(19.3)	X^2= 3.72	0.054
Proteinuria	35(10.3)	50(14.6)	X^2=39.60	0.000*
Haematuria	22(6.5)	23(6.7)	X^2= 0.90	0.266
Diabetes mellitus	23(6.8)	26(7.6)	X^2=12.49	0.000*
Dyslipidaemia	11(3.3)	11(3.3)	X^2= 3.79	0.052

Data expressed as number (%) or means ± SD, N: total number of participants for whom data is contributory for the variable in the table, RST: recurrent sore throat, PST: past skin rashes, NTS: nephrotoxic substances, FHTN: family history of hypertension, FHDM: family history of diabetes mellitus, MA: microalbuminuria.

4.5.3 Distribution of Potential Risk factors for CKD by type of Relationship.

In the study, a statistically significant higher proportion of parents of CKD patients 14.6% had hypertension when compared to that of the siblings 6.2% and that of the children 5.0% ($p<0.000$). Likewise, 7.3% of the parents were diabetics, when compared to 4.4% of the siblings and 2.7% of the children of the CKD patients ($p<0.000$). There was statistically significant difference in the higher proportion of parents with obesity 30 (8.8%), microalbuminuria 58 (17.0%) and proteinuria 44 (12.9%) when compared to that of the siblings and that of the children of CKD patients. Table 16 compares the potential risk factors among the study participants by type of relationship.

Table 16: Distribution of Potential Risk factors for CKD by type of Relationship.

Variables	Type of Relationship n (%)			Total N (%)	Test(X^2)	P
	Child	Parent	Sibling			
RST	34 (10.0)	10 (2.9)	11 (3.2)	55 (16.1)	10.92	0.004*
PSR	15 (4.4)	25 (7.3)	16 (4.7)	56 (16.4)	13.4	0.000*
NTS	18 (5.3)	35 (10.2)	33 (9.7)	86 (25.2)	14.5	0.000*
FHTN	104 (30.5)	60 (17.6)	98 (28.7)	262 (76.8)	4.65	0.098
FHDM	40 (11.7)	40 (11.7)	42 (12.4)	122 (35.8)	2.66	0.188
Current smoker	22 (6.5)	8 (2.3)	33 (9.7)	63 (18.5)	3.71	0.196
Alcohol	14 (4.1)	9 (2.6)	20 (5.9)	43 (12.6)	2.45	0.293
Hypertension	17 (5.0)	50 (14.6)	21 (6.2)	88 (25.8)	34.13	0.000*
DM	9 (2.7)	25 (7.3)	15 (4.4)	49 (14.4)	23.49	0.000*
Dyslipidaemia	5 (1.5)	10 (3.0)	7 (2.0)	22 (6.5)	3.87	0.055
Obesity	8 (2.3)	30 (8.8)	18 (5.3)	56 (16.4)	17.45	0.000*
MA	31 (9.1)	58 (17.0)	40 (11.7)	129 (37.8)	36.57	0.000*
Proteinuria	24 (7.0)	44 (12.9)	17 (5.0)	85 (24.9)	36.07	0.000*
Haematuria	14 (4.1)	23 (6.8)	8 (2.3)	45 (13.2)	29.47	0.000*

Data expressed as number (%), n: Number of participants out of 341 overall participants, N: Total number of participants contributory to the variable, RST: recurrent sore throat, PST: past skin rashes, NTS: nephrotoxic substances, FHTN: family history of hypertension, FHDM: family history of diabetes mellitus, MA: microalbuminuria, P*= statistically significant.

4.5.4 Distribution of Potential Risk factors for CKD by Age.

There was statistically significant difference in the higher proportion of the young participants with hypertension 48 (14.1%), diabetes mellitus 27 (7.9%), obesity 36 (10.5%), microalbuminuria 88 (25.8%) and proteinuria 55 (16.1%) when compared to that of the middle aged and that of the elderly participants. Table 17 compares the potential risk factors among the study participants by age category.

Table 17: Distribution of Potential Risk factors for CKD by Age.

Variables	Age Category n(%)			Total N (%)	Test(X^2)	P
	Young	Middle age	Elderly			
RST	45 (13.1)	5 (1.5)	5 (1.5)	55 (16.1)	1.90	0.390
PSR	35 (10.2)	15 (4.4)	6 (1.8)	56 (16.4)	15.83	0.000*
NTS	58 (17.0)	21 (6.2)	7 (2.0)	86 (25.2)	22.68	0.000*
FHTN	221 (64.8)	35 (10.3)	6 (1.7)	262 (76.8)	3.32	0.190
FHDM	97 (28.5)	22 (6.5)	3 (0.8)	122 (35.8)	7.58	0.023*
Current smoker	57 (16.7)	5 (1.5)	1 (0.3)	63 (18.5)	1.19	0.551
Alcohol	36 (10.5)	6 (1.8)	1 (0.3)	43 (12.6)	0.261	0.880
Hypertension	48 (14.1)	33 (9.7)	7 (2.0)	88 (25.8)	36.65	0.000*
DM	27 (7.9)	19 (5.6)	5 (0.9)	49 (14.4)	15.53	0.000*
Dyslipidaemia	8 (2.4)	10 (2.9)	4 (1.2)	22 (6.5)	19.56	0.000*
Obesity	36 (10.5)	17 (4.5)	3 (1.4)	56 (16.4)	27.12	0.000*
MA	88(25.8)	35 (10.2)	6 (1.8)	129 (37.8)	26.58	0.000*
Proteinuria	55 (16.1)	24 (7.0)	6 (1.8)	85 (24.9)	32.19	0.000*
Haematuria	31 (9.1)	12 (3.5)	2 (0.6)	45 (13.2)	13.11	0.001*

Data expressed as number (%), n: Number of participants out of 341 overall participants, N: Total number of participants contributory to the variable, RST: recurrent sore throat, PST: past skin rashes, NTS: nephrotoxic substances, FHTN: family history of hypertension, FHDM: family history of diabetes mellitus, MA: microalbuminuria, P*= statistically significant.

4.6 Multivariate Regression Analysis for Independent risk factors of CKD.

The multivariate regression analysis to determine independent risk factors for chronic kidney disease was performed on independent variables that were statistically significant which included age (elderly), type of relation (parent), gender (female), occupational status (unemployed), educational status (low level), PSR, NTS, FHTN, FHDM, hypertension, diabetes mellitus, dyslipidaemia, obesity, haematuria, microalbuminuria and proteinuria. Age (OR 3.433, 95% CI 1.069 – 9.732), Gender (OR 3.690, 95% CI 1.102 – 11.436), Hypertension (OR 6.870, 95% CI 2.993 – 18.216), Diabetes mellitus (OR 5.118, 95 % CI 2.592 – 12.563), Obesity (OR 3.766, 95% 1.106 – 6.613) and Proteinuria (OR 4.102, 95 % CI 1.814 – 14.604) were significant independent risk factors obtained in this study which are recognized risk factors for CKD. While type of relation, occupational status, educational level, PSR, NTS, FHTN, FHDM, haematuria and microalbuminuria were not statistically significant after logistic regression as shown in table 18.

Table 18: Multiple Logistic Regression for CKD Risk factors among study Participants

Variable	Odds Ratio	95% CI	P value
Age (elderly)	3.433	1.069 – 9.732	0.010*
TOR (parent)	1.457	0.436 – 3.781	0.343
Gender (female)	3.690	1.102 – 11.436	0.001*
Occupation	1.050	0.842 – 2.309	0.368
Educational level	0.793	0.428 – 1.705	0.479
HTN	6.870	2.993 – 18.216	0.000*
Obesity	3.766	1.106 – 6.613	0.010*
DM	5.118	2.592 – 12.563	0.000*
Proteinuria	4.102	1.814 – 14.604	0.001*
PSR	0.931	0.315 – 2.420	0.980
NTS	2.919	1.278 – 4.670	0.052
FHTN	1.969	0.539 – 3.928	0.095
FHDM	1.152	0.617 – 2.357	0.492
Dyslipidaemia	1.739	0.158 – 3.453	0.099
Haematuria	1.056	0.064 – 2.562	0.377
MA	2.580	1.104 – 4.751	0.055
Constant	0.000		0.000

CHAPTER FIVE

5.0 DISCUSSION

1. Introduction

The global epidemic of CKD has posed a major public health problem, Indeed, the incidence and prevalence of CKD has increased in recent years in both developed and developing countries including in sub-Saharan Africa (SSA),[50,83,84] this is associated with increased morbidity, mortality and prohibitive cost of care particularly in developing countries. Major contributory factors for this ominous picture include limited capacity of health facilities for CKD screening and surveillance, late referral to hospital, limited renal replacement therapy (RRT), and poor awareness of kidney disease in the community.[50,83,85] This situation prompted the International Society of Nephrology Commission for the Global Advancement of Nephrology (ISN-COMGAN) to make the fight against CKD one of its priorities, by promoting awareness, early detection, and effective treatment.[86] Likewise, the massive sensitization of governmental, non-governmental and community on CKD prevention in SSA,[50] by the African Association of Nephrology (AFRAN) and recently, the guidelines for the detection and management of CKD by Nigerian association of Nephrology,[84] aim at stepping up the campaign against the rising tide of CKD.

Universal screening of the general population would be time-consuming and expensive and has been shown to be not cost effective unless selectively directed toward the high risk groups.[87] Recommendations have been reported by the Kidney Disease Improving Global Outcomes (KDIGO) Conference regarding strategies for implementation of screening and surveillance for CKD in developing countries.[88] Similarly, the International Society of Nephrology Consensus Workshop statements on prevention of kidney diseases, National Kidney Foundation (NKF)[89]

and the Nigerian Association of Nephrology.[84] Target population recommended for screening using screening tools such as Urine test for proteinuria and a blood test to estimate GFR include Patients with hypertension, diabetes, Families of patients with CKD, Patients with hyperlipidaemia, obesity, metabolic syndrome, Smokers, patients who have had potentially nephrotoxic substance and those with age greater than 60 years.[87] Data are still emerging on studies to screen high risk population for CKD such as the first-degree relatives of CKD patients in Nigeria for the presence and risk factors of CKD. This study will therefore contribute to the knowledge on prevalence of CKD, its risk factors and other clinical characteristics in families of patients with CKD specifically the FDRs in view to improve the prevention of CKD and reduce its burden in our environment.

2. Prevalence of Chronic Kidney Disease (CKD)

The prevalence of CKD among the first degree relatives of patients with CKD at AKTH, in this study was 28.4%. This was the first study to specifically screen the FDRs of CKD patients for CKD, its risk factors and other clinical characteristics in Kano, to our knowledge. This prevalence was higher when compared with the prevalence of CKD among general population in the same region, Nalado *et al.* found overall prevalence of CKD in adult population in Kano to be 26.0%.[10] Although, this community study is limited by the fact that it is a one-time screening process and is thus a prevalence of CKD markers in the community.

However, the prevalence in the index study was slightly lower than that reported from Southern China by Wei *et al*,[19] who reported a prevalence of CKD among FDRs of CKD patients to be 29.7% compared with a prevalence of 12.1% among the general population in the same region.[90] The prevalence of CKD in this study is higher than those reported from similar studies in the

U.S and Taiwan (11.1 to 23%).[15-17] This could be because of the fact that in developing countries including SSA, low level of literacy and education, low level of access to medical care, extreme poverty, poor awareness of kidney disease in the community, limited CKD screening and surveillance program, limited health care resources and RRT are major contributory factors leading to late presentation, poor outcomes, limiting opportunities for preventive interventions and these were considered a major means that increases the growth of CKD and ESRD population in developing countries.[27,50,83]

Similarly, this high prevalence may be caused by differences in screening methods. However, this prevalence among FDRs in the U.S and Taiwan with the index study are in concordance and higher compared with prevalence obtained in the general population (10 to 16%).[91-93]

3. Socio – demographic characteristics of subjects.

In this study there were more males (68.6%) than females (31.4) which is similar to findings of Bagchi S. et al[94] in India who also reported a male preponderance (54%), however this is contrary to the female preponderance reported in China (58%) and Taiwan (54%),[17,19] this may be partly explained by the increased financial demand required for the management of CKD and ESRD in our environment where most female relatives are full-time house wives and unemployed.

The mean age in the index study (33.04±10.42 years) was lower when compared with the mean age reported from other studies in Egypt (39.12±14.29 years), Taiwan (38.40±13.80 years) and China (41.30±14.20 years).[17-19]

The finding of substantial proportion with low level of education and unemployment was similar to the findings of Zaghloul *et al.* in Egypt[18] but at variance to the findings across the U.S,[15,16]

which may be as a result of widespread poor socioeconomic status and poverty in developing countries particularly SSA,[27,50,83] including Nigeria.

4. Risk factors and other Clinical characteristics of CKD.

The commonest risk factor for CKD in this study was hypertension (25.8%), a finding that is in tandem with reports from previous studies in south western Nigeria (24.3%),[95] Egypt (25.2%), U.S (21.4%) and Taiwan (27%),[15-18] however the study from India (30%)[94] and Argentina (42%)[97] shows a much higher prevalence which could be explained by population growth and rate of urbanization.[87]

Diabetes mellitus is another risk factor that was also common (14%) in this studied population this was higher when compared to the findings from previous studies conducted by Raji *et al.* (9%),[95] Zaghloul *et al*. (11%),[18] Tsai *et al.* (5%)[17] and Jurkovitz et *al* (7%)[15] this may be explained by variation in socio-cultural background, lifestyle, diet, urbanization as well as differences in screening methods.

The index study also showed a substantial proportion (25%) of FDRs of CKD patients who consumed potentially nephrotoxic substances particularly traditional herbal concoction and NSAIDs, however, we could not state which of the remedies in the herbal concoction are nephrotoxic since studies of their composition are lacking, but this proportion was however higher than that reported in the studies conducted in China (8%)[19] and Taiwan(9%)[17] this may be explained by poor literacy, reduced awareness of kidney disease and poverty that compelled most populace to seek unorthodox treatment in our environment.

CKD has increasingly become a geriatric disease,[87] old age was another significant risk factor in this study 85% of the elderly participants screened had CKD, which is in congruent to the

findings reported in the studies conducted in Egypt, U.S, U.K, China and Taiwan.[14,17-19,96] where analyses showed that older age is significant independent risk factors for CKD.

Obesity was seen in 16.4% of the study participants which was similar to the findings reported in studies conducted in south western Nigeria (17.4%)[95] and Georgia (17.3%),[15,16] but this prevalence is lower than that reported from previous studies conducted in Egypt (46.7%),[18] Taiwan (28%)[17] and Argentina (62%),[97] which may be explained by variation in socio-cultural background, urbanization, lifestyle, genetic interaction as well as differences in ethnicities and screening methods.

Cigarette smoking was another important risk factor for CKD among the FDRs of CKD patients, the finding of 18.5% prevalence rate which was similar but in lesser proportion to what was reported from previous studies by Zaghloul *et al*. (40%),[18] Wei *et al*. (23%),[19] Tsai *et al*. (21.4%)[17] and Inserra *et al*. (35%).[97]

Another significant finding in this study which was the preponderance of female FDRs of CKD patients with CKD (49.5%) and in congruent to the findings of previous studies conducted in Taiwan, India and China,[17,19,94] where female sex is a significant independent risk factor for CKD, this may be partly explained by the clustering of multiple comorbid conditions seen in them.

Dyslipidaemia was another important risk factor for CKD among the study participants which was seen in lower proportion (6.5%) when compared to the findings reported by Bagchi *et al*. (18.8%),[94] Tsai *et al*. (19.9%)[17] and Wei *et al*. (43%).[19]

Family history of hypertension (FHTN) and FHDM was present in 77% and 36% of the study participants respectively which was slightly lower than that reported from the studies conducted

in Egypt and Taiwan.[17,18] RST and PSR was also present in about 17% of the FDRs of CKD patients which was slightly higher than what was reported by Wei *et al.*[19] Haematuria was present in 13% of the study population which was slightly lower than that reported from the study conducted in southern China.[19] MA and proteinuria (≥ 1+) was also present in 38% and 25% of the FDRs of CKD patients respectively which was higher than prevalence reported in KEEP (Kidney Early Evaluation Program)[96,98-101] in U.S, KEAPS (Kidney Evaluation and Awareness Program in Sheffield)[14] in U.K, this difference may be explained by the variability of the methodology used to assess the indicators, differences in race or ethnicity as well as the comorbid conditions of the studied population.

CHAPTER SIX

6.0 LIMITATIONS OF THE STUDY, CONCLUSIONS AND RECOMMENDATIONS.

6.1 Limitations of the Study

1. The diagnosis of albuminuria, proteinuria and haematuria was based on semi-quantitative urine dipstick with more prognostic than diagnostic value.
2. Unexamined impact of infection and infestation on the results of urine analysis, due to limited fund, microscopic confirmation for haematuria and standard quantitative nephelometry for albumin as well as throat swab culture and anti-streptolysin O titre could not be done. However, these drawbacks were minimized by repeat urine test, delayed investigation of participants with fever, dysuria and ongoing menstruation until resolved and the use of early morning spot urine which has been shown to be a reliable index of albuminuria in various studies.[17]
3. The study design was cross-sectional and has a drawback such as difficulty in determination of precise outcome for the screened participants.
4. Misclassification of educational level of participants with only Koranic education.
5. Unmatched study participants with a control group from a population without family history of CKD.
6. Limited number of family representatives, as the screening study only involved FDRs but not all the relatives of CKD patients. And many half siblings, half parents, second and third degree relatives were excluded.
7. Susceptibility of systematic sampling technique to selection bias.

6.2 Conclusions

1. Despite the limitations, findings in the index study showed that the prevalence of CKD among the FDRs of CKD patients in Kano, was 28.4%, which was higher than that of the general population in same region, similarly, clinical and laboratory characteristics of CKD including proteinuria, haematuria, MA and reduced estimated GFR were also found in high proportion as such suggesting that FDRs of CKD patients also have high risk of CKD.
2. The predominant risk factors for CKD in this study were hypertension, diabetes mellitus, NTS, old age, obesity, female gender, dyslipidaemia and cigarette smoking, while the independent risk factors were hypertension, diabetes mellitus, old age, proteinuria and female gender.
3. The benefit of targeted health screening program cannot be overemphasized, by identifying numbers of persons with hypertension, diabetes mellitus and CKD at various stages that are previously undiagnosed, and those with poorly control risk factors among the studied population that were counseled and referred appropriately for intervention.

6.3 Recommendations

1. The need for creation of local or international funding assistance (as in existence with HIV or TB infections) to support the program of prevention of CKD and control of some of its risk factors, incorporation of public health education series, also for the increase in distribution for a wider coverage to both the rural and urban health centers of the current guidelines for the detection and management of CKD.
2. A comprehensive and long term population-based screening, using a multistage sampling technique (that will give each individual family representatives equal chance), with matching of the study subjects with a control group from the population in the community without family history of CKD.
3. Genetic testing for possible genes associated with CKD using techniques such as bidirectional deoxyribonucleic acid (DNA) sequencing, Transcriptional profiling, Expression quantitative trait mapping and mapping by admixture linkage disequilibrium (MALD) is needed for a definitive conclusion.
4. In a developing countries with less funding of health sector and widespread poverty among the populace, It will be desirable to have an implementable national policy on prevention and surveillance of CKD with incorporation of health screening targeting FDRs of CKD patients, persons with hypertension, diabetes mellitus, obesity, elderly individuals, those that had NTS, persons with CVD, previous kidney injury, dyslipidaemia, albuminuria and haematuria, using available and affordable tools such as spot urine sample for standard dipstick test (MA, protein, RBCs) and serum creatinine to estimate GFR all of which need a repeat confirmatory test if positive at least three months apart and to be carried out by Doctors, Nurses and other trained health care professionals.

Persons detected to have CKD should be referred to experienced general medical practitioners for further evaluation, intervention and follow up, further referral to Nephrologists for management depending on severity of CKD, its risk factors and likelihood of CKD progression. And if no abnormality on initial screening tests, frequency for targeted individuals should be yearly.

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APPENDIX I

ETHICAL CLEARANCE

AMINU KANO TEACHING HOSPITAL

P. M. B. 3452, ZARIA ROAD, KANO.

(☎: 07068297399,) www.akth.org.ng, E-mail: enquiries@akth.org.ng, email: (akthkano@yahoo.com)

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NHREC/21/08/2008/AKTH/EC/1091

AKTH/MAC/SUB/12A/P-3/VI/1191 **16th December, 2013**

Dr. Abbas S. Bello
Internal Medicine
AKTH, Kano

Ufs:

The Head of Department
Internal Medicine
AKTH, Kano

ETHICAL APPROVAL

Further to your application in respect of your research proposal titled "Prevalence and Risk Factors of Chronic Kidney Disease among First Degree Relatives of Patients with Chronic Kidney on Maintenance Haemodialysis at Aminu Kano Teaching Hospital, Kano". The Committee has reviewed your proposal and noted same as a Prospective Study.

In view of above, Ethical approval is hereby granted to conduct the research.

However, the approval is subject to periodic reporting of the progress of the study and its completion to the Ethical Committee.

Regards

Bara'atu Kabir (Mrs)
Secretary, Research Ethical Committee
For: Chairman

APPENDIX II

CONSENT FORM

Dear Participant,

I am Dr Abbas S. Bello of the Department of Medicine, Aminu Kano Teaching Hospital, conducting a study in this unit with the aim of determining the prevalence and risk factors for chronic kidney disease among first degree relatives of patients with chronic kidney disease in Aminu Kano Teaching Hospital, Kano.

I am requesting your consent to take part in this study by providing the required information. This study if conducted successfully will give us the prevalence and risk factors of chronic kidney disease in relatives of patient with chronic kidney disease.

Note that:

1. Your participation is voluntary
2. You can withdraw from the study whenever you decide
3. The results of the tests will be explained to you
4. If you are found to have an abnormality you will be given the opportunity for treatment or referred as the case may be.
5. No adverse or punitive measure will be taken against you if you decline to participate in the study.

If you consent to participate in this project, please append your signature below.

Signature of participant……

Right thumb print…….

Date…….

Signature of the Researcher……..

Date…….

Thank you for your cooperation.

APPENDIX III

QUESTIONNAIRE

SECTION A: PERSONAL DATA

INITIALS: _____

SERIAL NUMBER: _____

AGE: _____

SEX: M ( ) F ( )

EDUCATION: PRY( ) SEC( ) TER ( ) Others ( )

OCCUPATION: _____

RELIGION: Islam_____ Christianity_____ Others_____

TRIBE_____

MARITAL STATUS: Single____ Married_____ Divorced____ Widowed____

ADDRESS: _____

PHONE NUMBER: _____

INITIALS OF INDEX PATIENT_____

FILE NUMBER OF INDEX PATIENT_____

RELATIONSHIP WITH INDEX PATIENT: CHILD( ) SIBLING( ) PARENT( ) OTHERS( )

SECTION B: MEDICAL HISTORY

Recurrent sorethroat? YES ( ) NO ( )

Recurrent skin rashes? YES ( ) NO ( )

Are you a known hypertensive? Yes_____ No_____ If yes, specify treatment _____

Are you a known diabetic? Yes_____ No_____ If yes, specify treatment _____

Dysuria? Yes_____ No_____

Froathy Urine? Yes____ No____

Haematuria? Yes____ No____

If yes, Initial? _____ Terminal? _____ Total? _____ When?

Current Pregnancy? Yes____ No_____

Last menstrual period? _____

Family history of hypertension? Yes_____ No_____

If yes, specify Father_____ Mother_____ Both ____ Others_____

Family history of diabetes mellitus? Yes_____ No_____

If yes, specify Father_____ Mother_____ Both_____ Others_____

Cigarette smoking? Yes_____ No_____

Number of stick per day? _____

How long? _____

Alcohol ingestion? _____

What specific type? _____

Bottles per day? _____

How long? _____

Use of Analgesic drugs? Yes_____ No_____

Specific drug? _____

Number of tablets per day? _____

How long?

Herbal preparation? Yes_____ No_____

What specific substance? _____

Use of medicated soap? Yes____ No_____

What type? _____

How long? _____

SECTION C: PHYSICAL EXAMINATION

Weight_____

Height_____

BMI = Weight / Height^2 _____

Blood pressure in mmHg Right arm_____ / Left arm_____

SECTION D: INVESTIGATION

Urine analysis

Microalbuminuria

Proteinuria

Red blood cells

Blood investigations

Serum creatinine concentration in mmol / litre_____

Estimated GFR in ml/min_____

Fasting Blood Sugar (FBS) in mmol/Litre_____

Lipid Profile

Tchol_____

LDL_____

HDL_____

Triglyceride_____

Second visit (3months later)

Blood pressure in mmHg Right arm_____ / Left arm_____

Repeat Urine analysis

Microalbuminuria

Proteinuria

Red blood cells

Repeat Serum creatinine concentration in mmol / litre_____

Repeat Estimated GFR in ml/min_____