PREVALENCE AND PATTERN OF CHRONIC KIDNEY DISEASE AND ITS ASSOCIATED RISK FACTORS IN AIYEPE, A RURAL COMMUNITY, OGUN STATE NIGERIA.

BY

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DECLARATION

The work reported in this dissertation was undertaken by me at Olabisi Onabanjo University Teaching Hospital, Sagamu. This dissertation has not been submitted either in part or whole to any other examination body in support of an application for another degree or qualification.

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ATTESTATION

I certify that Dr. Oyebisi, Olayanju Oyekunle carried out this project at the Department of Medicine, Olabisi Onabanjo University Teaching Hospital, Sagamu, Ogun State, Nigeria.

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DEDICATION

This project is dedicated to my parents, Comrade and Mrs. Raimi Ajibola Oyebisi and my wife Folasade Oyebisi.

TABLE OF CONTENT

LIST OF ABREVIATIONS

AKI	Acute kidney injury.
ADPKD	Autosomal dominant polycystic kidney disease.
ACR	Albumin creatinine ratio.
ARIC	Arteriosclerosis Risk in Community
BMI	Body mass index
CKD	Chronic kidney disease.
CVD	Cerebrovascular diseases.

CARI	Caring for Australians with renal impairment.
ESRD	End-stage renal disease.
GFR	Glomerular filtration ratio.
FSGS	Focal segmental glomerulosclerosis.
KDOQI	Kidney Dialysis Outcome Quality Initiative.
MRFIT	Multiple Risk Factors Interventional Trial.
MDRD	Modification of diet in renal diseases
NHS	National Health Scheme.
NICE	National Institute of Health and Clinical Excellence.
KEEP	Kidney Evaluation and Early Prevention Program
NHANES	National Health and Nutrition Examination Survey.
RRT	Renal replacement therapy.
USRDS	United State Renal Data System.
WHR	Waist hip ratio.
WC	Waist circumference.

SUMMARY

BACKGROUND: Chronic kidney disease (CKD)has now assumed epidemic proportion and hence a high priority as a disease of public health importance. The rise in the population of patients with end stage renal disease (ESRD) is partly related to the failure of early detection of the pre-clinical stages of CKD and its associated risk factors. Effective preventive and control strategies for CKD can only be achieved if based on baseline epidemiological data of the disease as derived from community studies. In Nigeria and indeed most sub-Sahara Africa, there is paucity of such hard data.

AIMS: The aim of the study was to determine the prevalenceof chronic kidney diseaseand its associated risk factors in Aiyepe community, as well asknowledge and awareness level of

thepopulation about CKD, with a view to designing appropriate preventive measures for the disease.

METHODS: It was a cross-sectional community-based studyinvolving 456 participants recruited through cluster and simple random sampling techniques. A pre-tested structured questionnaire was used to obtain information about demographic characteristics, level of awareness,knowledge and the disease risk factors with scores allotted for the knowledge. Bio-physical measurements of the participants were done with blood pressure measured using Omron digital sphignomanometer. Participants were screened for urinary albumin by dipstick and/or albumin creatinine ratio. Serum creatinine, fasting blood sugar and serum lipid profile were determined whileglomerular filtration rate was estimated using Cockroft and Gault formula from serum creatinine.The prevalence of CKD was defined as eGFR<60ml/min/1.73m^2 and or proteinuria persistent for atleast 3 months. The presence and frequency of associated risk factors, and their impacts were noted.

RESULTS: Four hundred and sixty-eight (468) participants were recruited and only four hundred and fifty-six (97.4%) completed the study. Males constituted 35.3% while 64.7% of the participants were females. Three hundred and forty seven (76.1%) of the participants were aged 60 years and below. The mean age ± standard deviation (SD) of the study population was 48.09(±15.7) years, and the age range was 18-80 years. Majority of the participants were petty traders and farmers.

Hypertension was seen in twenty eight percent (28.9%) of studied participants while only 4.2% were diabetic, of the diabetic population, 2.2% were known diabetic while 2% were newly diagnosed. The mean waist–hip ratio (WHR) of the participants was 0.94(±0.55) and it ranged from0.59 to1.46. The mean WHR of males was 0.91(±0.08) while that of females was 0.96 (±0.68). The mean BMI of the participants was 26.62 (±6.0) kg/m^2 with a range of 15.04 to 48.68 kg/m^2. The prevalence of overweight and obesity was found to be 24.4% and 30%

respectively.About 26.3% of the participantsindulged in alcohol consumption while 6.6%smoked cigarette. The prevalence of albuminuria in the study was 16.3% comprising of both macro-albuminuria (7.3%) and micro- albuminuria (9.0%) while 17(3.7%) of the participants had history of haematuria. The prevalence of CKD, as defined by eGFR< 60ml/min/1.73m^2 and/or proteinuria as defined by ACR> 300mg/g was 27.6%.

On logistic regression, age (OR-1.080, CI-95%, 1.059-1.102), female gender (OR-0.550, CI-95%, 0.320-0.945), BMI (OR-0.832, CI-95%, 0.785-0.882) and dyslipidaemia (OR-1.007, CI-95%, 0.978-1.037) were found to be predictive of CKD in this study.

CONCLUSION: The prevalence of CKD and itsassociated risk factors was high in Aiyepe community. Age, female gender, BMI, dyslipidaemia and poor knowledge all have impact on the prevalence of CKD in the community. All these need to be addressed.

CHAPTER ONE

1.0 INTRODUCTION

Chronic kidney disease (CKD) is defined as glomerular filtration rate <60ml/min per 1.73m^2 and/or kidney damage determined by abnormal findings in urine such as proteinuria, haematuria, abnormal imaging and/or histology lasting for 3 months or more.[1]

Chronic kidney disease is fast becoming a disease of public health importance as the disease may go on without any symptoms until substantial part of the kidney is destroyed. Once established, it is most often difficult to prevent renal failure and its consequences are premature death, poor quality of life and increased healthcare cost.[2]

In the United States (US), 13.1% of non-institutionalized adults were estimated to have CKD.[3] According to the latest U.S Renal Data System Annual Data Report of 2013, updated in October 2015, more than 615,000 Americans were being treated for end-stage renal disease (ESRD), of whom more than 430,000 are on dialysis and more than 185,000 have a functioning kidney transplant.[4] The surveys in Australia, Europe, and Japan reported the prevalence of chronic kidney disease to be between 6-16%.[5] Chronic kidney disease progresses relentlessly to ESRD but also with complications of reduced kidney function and increased risk of cardiovascular disease (CVD). Patients with CKD are more likely to die from CVD than to progress to ESRD.[6]

The Global Burden of Disease project report of 2014 indicates that diseases of the kidney and urinary tract add significantly to the global burden of disease and it was rated among the diseases that caused greater than 100,000 deaths per year in 2013.[7] Other diseases in this category are HIV/AIDS and diabetes.

There is a disparity in disease epidemiology with regards to age in sub-Saharan Africa when compared with other regions. Middle-aged and elderly populations are predominantly affected in developed countries, while in sub-Saharan Africa, younger adults at the peak of economic productivity aged between 20 to 50 years are affected with CKD.[8]

In Nigeria, there is no renal registry and there is paucity of hard data. Most studies are hospital based and report that end-stage renal disease (ESRD) constitutes about 8–10% of hospital admissions.[8,9,10]There are however a few community-based studies in Nigeria; Ulasi et al, Abioye-Kuteyi et al, Oluyombo et al, Nalado et al and Okoye et al reported 11.7%, 19.9%, 18.8%, 26% and 27.3% respectively in rural communities.[11-15] In Congo however, Sumaili et al,[16] reported a higher prevalence of 36% among the at-risk population.

Jones et al noted an increase in incidence of hypertension and diabetes mellitus leading to a surge in the prevalence of CKD in disadvantaged populations.[17] End stage renal disease (ESRD) has reached an epidemic proportion with more than 400,000 affected individual in the US and well

over 3.2 million worldwide with an annual increase rate of 6%;this staggering number represents the tip of iceberg because there is large number of undiagnosed pre-terminal CKD cases that may be 30-fold higher than that of ESRD.[18]

The 2006 United States Renal Data System (USRDS) report indicated that the number of cases of ESRD worldwide had grown from 970,436 in 1999 to 1,172,655 in 2004, representing a 21% increase and this rise in the population of patients with ESRD is partly related to the failure of early detection of the pre-clinical stages of CKD and its associated risk factors.[19] The population with ESRD has increased by about 9% and 4% per year in the United States of America and Japan respectively.[19,20] In developing countries, the number varies from less than 100 per million populations in sub-Saharan Africa and India to about 400 per million populations in Latin America and more than 600 per million populations in Saudi Arabia; these numbers may represent gross underestimation of the prevalence because of poor data collection and research.[21,22]

In the USA, the expected annual expenditure on ESRD will reach over 50 billion US dollars by the year 2030, this will be a huge challenge even for industrialized nations to surmount in the next one decade.[3] Renal services currently consume about 2% of the National Health Service (NHS) budget in the United Kingdom (UK) and the cost is rising with increased demand for renal replacement therapy(RRT).[23] If the reported rise in the prevalence of CKD is to be true for Nigeria, it would pose a more serious economic challenges. In Nigeria and other developing countries RRT is either not available or not affordable as less than 10% of patients can afford the cost of maintenance haemodialyis for more than 3months.[24,25] There is excessive pressure on the scarce healthcare resources therefore the knowledge of the prevalence, disease awareness and identification of CKD will be of utmost benefit in evolving or mounting preventive strategies.[26]

CKD can be detected early through a general population screening in about 58.7% to 89.7% of cases and such cases when detected early can be referred for specialist care which has been

reported to improve quality of life, delay progression and decreased morbidity and mortality and the need for renal replacement therapy (RRT).[26] It is a common observation in Nigeria and most developing countries that patients often present at ESRD or stage 4 of CKD when they require some form of RRT, a facility that is either not available or inaccessible due to its prohibitive cost.[25]

The outcome of ESRD in sub-Saharan Africa is very poor and this is principally a result of poor awareness of kidney disease in the community, late presentation to the hospital, limited capacity of health workers in kidney disease prevention amongst others.[27,28]

Therefore, a strategy for effective control of CKD and reduction of its burden would include early detection and identification of the risk factors through community-based screening programmes. This will provide opportunity for:

1. Determining the level of disease awareness.
2. Determining the prevalence and pattern of CKD, and its risk factors.
3. Modification of the risk factors to retard the progression of CKD and mitigate its associated complications.

1.1 JUSTIFICATION FOR THE STUDY

(a) In spite of the several reports on the prevalence of CKD in Nigeria, only a few are derived from community based studies, while fewerstudies comprehensively examined the risk factors in our environment, thus making effective and sustainable planning for the control of the disease difficult.

(b) A general weakness of the previously conducted studies was their failure to re-evaluate the subjects after three months to establish the presence of the renal abnormalities in keeping with the definition of CKD.

(c) In addition, the huge population of Nigeria (estimated to be 170million), necessitates that studies at different locations in the geographical regions be carried out to determine national prevalence data/statistics in the absence of a viable renal registry.

1.2 AIMS AND OBJECTIVES

MAIN OBJECTIVE

- To study the prevalence and pattern of CKD and its associated risk factors in a rural community of Ogun State, South-Western Nigeria.

SPECIFIC OBJECTIVES

- To determine the level of awareness of CKD.
- To determine the prevalence and the pattern of CKD in the community.
- To determine the frequency of the associated risk factors for CKD.
- To make recommendations for the prevention and control of CKD in our environment.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 DEFINITION AND CLASSIFICATION

Chronic kidney disease (CKD), also known as chronic renal disease, is a progressive loss in renal function over a period of at least three months. Chronic kidney disease is defined as kidney damage or glomerular filtration rate (GFR) below 60 ml/min per 1.73 m^2 for 3 months or more irrespective of the cause.[1] The symptoms of deteriorating kidney function are vague and non-specific, and might include malaise and a reduced appetite. Often, CKD is diagnosed as a result of screening of people known to be at risk of kidney disease, such as those with high blood pressure or diabetes and those with a blood relative with CKD. Chronic kidney disease may also

be identified when it leads to one of its recognized complications, such as cardiovascular disease, anemia or pericarditis.[29] This is the stage at which most of our patients present, when various life threatening complications have set in. This underscores the need for early detection.

The Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines have classified CKD into 5 stages.[1] This classification, although useful in simplifying the categorization of CKD, has its limitations, which include classifying people with isolated albuminuria as suffering from CKD, labeling mild and stable kidney damage as CKD, and not differentiating between age-related impaired kidney function and progressive disease-induced CKD which may overestimate the prevalence of CKD.[1]

In 2005, the Kidney Disease: Improving Global Outcomes (KDIGO) group suggested clarifications including the addition of the suffix T for patients with renal allografts and D to identify CKD stage 5 patients on dialysis.[30]

The U.K. National Institute of Health and Clinical Excellence (NICE) has modified, in 2008, the KDOQI CKD classification by subdividing CKD stage 3 into 3a and 3b, estimated GFR of 45 to 59 ml/min per 1.73 m2 and 30 to 44 ml/min per 1.73 m2, respectively.[31]The NICE CKD guidelines also stipulated that the suffix p be added to the stages in proteinuric patients. This refinement of the initial CKD classification by NICE assumes that there is a distinction between patients with GFR below 60 ml/min per 1.73 m2 and those with GFR below 45 ml/min per $1.73m^2$ in terms of prognosis and that the presence of significant proteinuria has to be acknowledged in the classification.[31]

Classification of CKD based on GFR as proposed by the Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines and modified by NICE in 2008 is shown in table below.[1,30,31]

Table 1. Stages of CKD.

Classification of CKD Based on GFR	
CKD Stage	**Definition**
1	Normal or increased GFR; some evidence of kidney damage reflected by microalbuminuria, proteinuria, and hematuria as well as radiologic or histologic changes
2	Mild decrease in GFR (89–60 ml/min per 1.73 m^2) with some evidence of kidney damage reflected by microalbuminuria, proteinuria and hematuria as well as radiologic or histologic changes
3 3A 3B	GFR 59-30 ml/min per 1.73 m^2 GFR 59 to 45 ml/min per 1.73 m^2 GFR 44 to 30 ml/min per 1.73 m^2
4	GFR 29-15 ml/min per 1.73 m^2
5	GFR <15 ml/min per 1.73 m^2; when renal replacement therapy in the form of dialysis or transplantation has to be considered to sustain life
The suffix p to be added to the stage in proteinuric patients (proteinuria >0.5 g/24h)	

GFR – glomerular filtration rate, p – proteinuria. CKD – chronic kidney disease.

2.2 THE BURDEN OF CKD

Chronic kidney failure used to be a disease of fatality. It is emerging as a disease of public health concern. The incidence of end-stage renal failure is increasing worldwide at an annual growth rate of 8%.[29] Data from most of the developing world are often unavailable, but given the prevalence of poor socio-economic factors, the incidence is likely to be greater.[28] Like all other developing countries of the world, there are no reliable statistics to assess the prevalence of kidney diseases in Nigeria. The few community based studies in Africa are regional and may be difficult to extrapolate because of geographical variations. Community-based studies on the prevalence of

CKD have been reported in some developed countries such as USA, Spain, Australia, China, and Norway.[32-36] The predominant CKD stage in all the studies was stage 3 CKD as in table 2.

Most patients with CKD die because of lack of funds, as very few can afford regular maintenance dialysis.[27] The outcome of CKD was revolutionized by the advent of dialysis and transplantation. This has led to reduction in morbidity and mortality; thus individuals with kidney disease tend to live long with better productivity. However this is only achievable in developed or resource-rich countries.[27] A study from Nigeria reported a median survival of 2 weeks in 760 patients presenting with end-stage kidney failure and only 6.8% of 556 of the patients who started haemodialysis could afford to continue for more than 12 weeks.[37] Peritoneal dialysis, though supposed to be cheaper than haemodialysis, is infrequently used in sub-Saharan Africa because of the high cost of fluids which necessarily have to be imported.[38] Kidney transplantation is even less common, with only four countries in sub-Saharan Africa routinely engaged in transplantations locally.[39]

Where renal replacement therapy is available, its cost is prohibitive, with costs ranging from US$7,000 to $55,000 per patient per year, largely on a fee-for-service basis.

Table 2: Studies on the prevalence of different stages of CKD

Reference	Country	Study population and design	No of Participants	Age range in years (mean age)	Urinalysis/ albumin-creatinine ratio.	Stages of CKD					All stages	CKD stage 3
						1	2	3	4	5		
Brown et al[30] 2005	USA	KEEP(community screening)	6071	18-101 (52)	Microalbuminuria	3.1	4.8	19.7	1.1		28.7	20.8
Coresh et al[18] 2003	USA	NHANES III(community study)	13323	≥ 20 (36.3)	Microalbuminuria	1.78	3.24	7.69	0.35	NA	13.07	8.04
Otero et al[31] 2005	Spain	EPIRCE (community-based epid. study)	237	≥ 20(49.58)	Microalbuminuria	3.5	5.3	5.3	0.4	0	12.7	5.1
Chadban et Al[33] 2003	Australia	AUSDIAB(population based cross sectional study)	11247	≥ 25	Proteinuria And Haematuria	0.9	10.9	10.9	0.3	0.003	14.1	11.2
Chen et Al[35] 2009	China	Community-based study	2596	≥18(58.4)	MAL	2.4	3.6	5.5	0.3	0.04	11.8	5.84
Halla et al[32] 2006	Norway	Population survey	65181	≥ 20 (50.2)	Microalbuminuria	2.7	4.2	0.16	0.16	NA	10.26	4.36
Sumaili et al[14] 2009	Congo	Community based	503	ADULT POPULA-TIONS	Proteinuria	2.0	2.4	7.8	0	0.2	12.4	8
Oluyombo et al[11] 2010	Ilie, Nigeria.	Community based	454	≥18	Proteinuria.	2.4	4.1	11.8	0.5	0.0	18.8	
Okoye et al[15]	Ogbona, Nigeria	Community-based	476	≥18	3.8	1.2	1.7	23.3	1.0	0.0	27.2	

KEEP - Kidney Evaluation and Early prevention programme. NHANES - National Health and Nutrition Examination Survey.

EPIRCE - Epidemiologic o de la Insufficiencies renal en Espana. AUSDIAB - Australian Diabetes, Obesity and Lifestyle Study.

Dialysis is often only available in tertiary health care facility and rarely as a component of primary health care system therefore, theexistingfacilities cannot meet the needs of the population.[40] In South Africa, one of the richest countries in Africa, more than 50% of potentially eligible patients are turned down for dialysis.[40]

If governments decide to offer any treatment, they must weigh the substantial opportunity costs, and decide how and whether to ration such expensive care. Even then, patients incur high out-of-pocket costs for transportation and medication. For many patients with kidney failure in sub-Saharan Africa, the stark reality is that the treatment expenditures are catastrophic, perhaps leaving several generations in debt, or the option of death. The first task is to understand the scale of the problem, which at present is largely invisible.

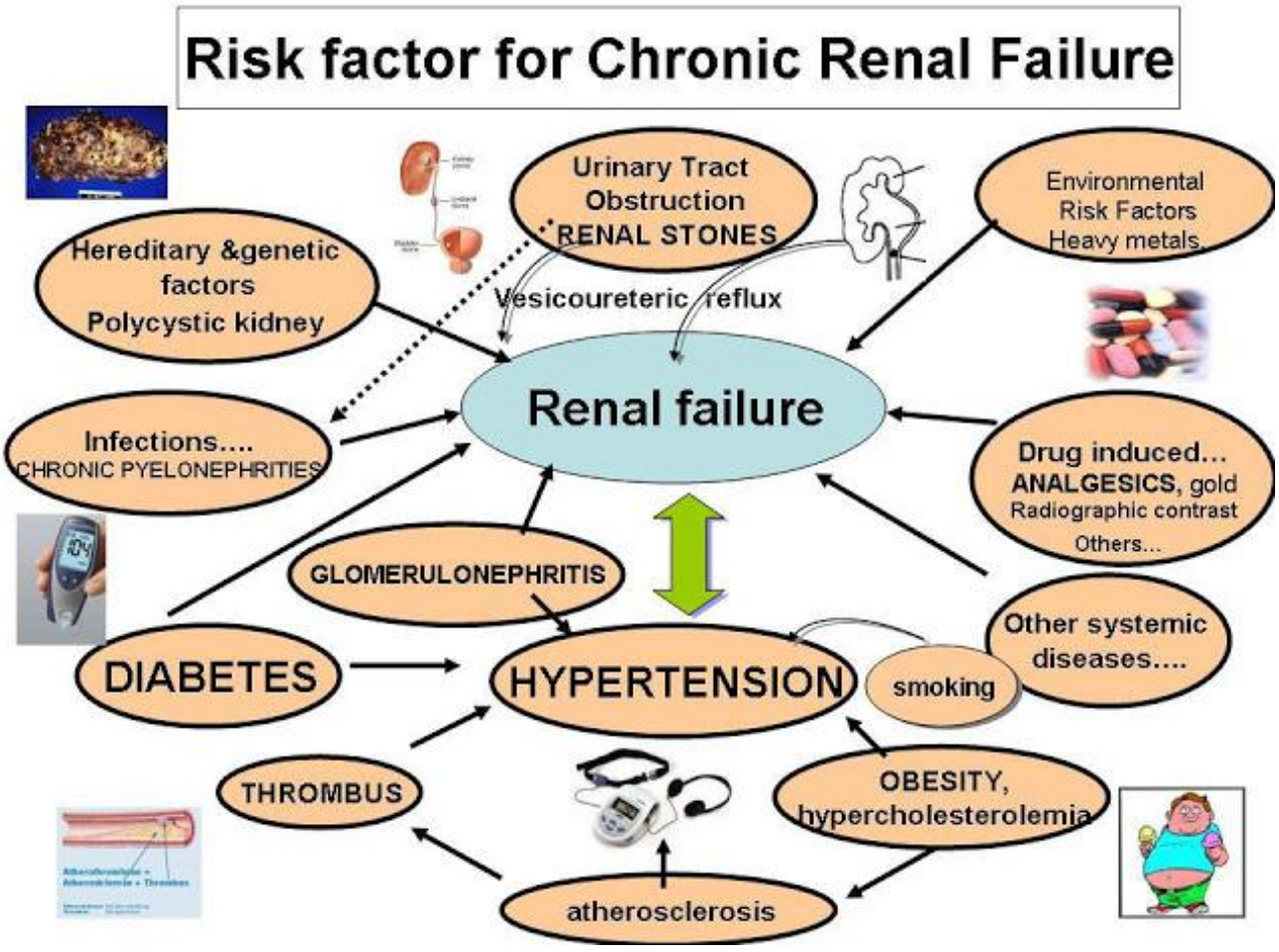
2.3 CAUSES AND RISK FACTORS FOR CHRONIC KIDNEY DISEASE

Chronic kidney disease is believed to be a 'multi-hit' process. Risk factors for CKD are grouped under susceptibility, initiation, and progression factors. Susceptibility factors predispose to CKD, initiation factors directly trigger kidney damage whereas progression factors are associated with worsening of already established kidney damage.[5,41] The aim of identifying susceptibility and initiation factors for CKD is to define individuals at high risk for development of CKD; with progression factors, the aim is to define individuals at high risk for worsening (CKD) kidney damage and subsequent loss of kidney function. These risk factors are further classified according to feasibility for intervention as modifiable and non-modifiable.[41]These are listed in figure 1.

1. Modifiable risk factors include hypertension, diabetes, dyslipidaemia, smoking, alcohol, obesity, infections.
2. Non-modifiable risk factors include age, gender, and ethnicity.

Known CKD susceptibility factors include genetic and familial predisposition, race (Afro-Caribbean, Indo-Asians), maternal-fetal factors (low birth weight, malnutrition in utero), age (elderly), and gender (male).[41,43] Beyond the susceptibility to CKD, additional initiation factors are likely to trigger disease. Once it is established, CKD (eGFR 60 ml/min) progression is influenced by a number of modifiable and non-modifiable risk factors.[43]

Figure 1: Risk Factors for CKD. (culled from kidneygroup.blogspot.com)



2.4 PATHOPHYSIOLOGY OF CHRONIC KIDNEY DISEASE

Chronic renal failure (CRF) and end-stage renal disease (ESRD) are functional diagnoses characterized by a progressive decrease in glomerular filtration rate (GFR).[1]

The pathophysiological events underlying the inception of every nephropathy are different but those involved in the progression of the disease are, to a certain extent, common to many nephropathies.[42,43] This may explain why, as different diseases progress, an increasingly common renal phenotype of tissue destruction, inflammation and scarring ensues, regardless of etiology.[43] Persistent insults to renal cells by the various agents eventually activate inflammatory and fibrotic responses that not only interfere with the repair processes, but also redirect the renal tissue status through similar mechanisms of irreversible degeneration.[44] Regardless of whether the disease starts mostly as a glomerular (chronic glomerulonephritis) or tubular insult, the initial cellular damage eventually activates responses that finally damage other nephron structures. This leads to a vicious circle, where nephrons progressively become sclerosed and are substituted by scar tissue. Cell damage and activation lead in all cases to inflammation and cytokine imbalance, which activates other cell types and contributes to unleashing fibrosis, mesangial and vascular contraction contributing to the reduced GFR, tubule degeneration and scarring.[43,44] The various stages provide opportunity for pharmacological intervention aimed at slowing down disease progression.

2.5 HYPERTENSIVE NEPHROPATHY

Hypertension is a serious health problem that results in major cardiovascular mortality and morbidity.[45] Systemic hypertension is an important cause, consequence, and presenting feature of CKD. It is one of the leading causes of ESRD worldwide and the second leading cause in the United States after diabetes.[19] It is a leading cause of CKD in Nigeria and most sub-Sahara Africa.[9,46] According to the United States renal data system, about 51–63% of all patients with

CKD are hypertensive and this number grows to 90% in patients over 65 years of age.[19] Some experimental and epidemiologic studies have shown that sustained hypertension is indeed a significant contributor to the progression of CKD in diabetic and non-diabetic nephropathies.[44] It is believed that the transmission of systemic hypertension into the glomerular capillary beds and the resulting glomerular hypertension contributeto the progression of glomerulosclerosis.[47] According to the 2011 US Renal Data System (USRDS) data, in the year 2009, hypertensive nephrosclerosis (HN) accounted for 28% of patients reaching end-stage renal disease (ESRD) and the rate of ESRD attributed to hypertension has grown to 8.7% since the year 2000.[48]

The term hypertensive nephrosclerosis traditionally has been used to describe a clinical syndrome characterized by long-term essential hypertension, hypertensive retinopathy, left ventricular hypertrophy, minimal proteinuria, and progressive renal insufficiency. Most cases are diagnosed based solely on clinical findings.[49] In fact, most of the literature dedicated to hypertensive nephrosclerosis is based on the assumption that progressive renal failure in a patient with long-standing hypertension, moderate proteinuria, and no evidence suggesting an alternative diagnosis characterizes hypertensive nephrosclerosis.[47,49,50]

A couple of important points have been made in different studies. First, among an unselected sample of community-based participants in the Framingham Heart Study, the combination of hypertension and a mild reduction in GFR was found to be an important risk factor for the development of new-onset kidney disease. Other factors noted were diabetes, obesity, smoking, and a low high-density lipoprotein cholesterol level. Second, systolic blood pressure (SBP) is a strong, independent predictor of a decline in kidney function among older persons with isolated systolic hypertension. This is a significant finding because most cases of uncontrolled hypertension in the United States are due to isolated systolic hypertension among older adults.[45]

Most patients reaching ESRD irrespective of the causes are hypertensive with nephrosclerosis being the classic finding in end-stage kidneys. Regardless of the etiology, once hypertension develops, a cycle of renal injury, nephrosclerosis, worsening of hypertension, and further renal injury is established. As a result, in a patient presenting with ESRD, determining whether nephrosclerosisis the cause or the consequence of chronic renal injury may be difficult.[44,49] Two pathophysiologic mechanisms have been proposed for the development of hypertensive nephrosclerosis. One mechanism suggests that glomerular ischaemia causes hypertensive nephrosclerosis which is a consequence of chronic hypertension resulting in narrowing of preglomerular arteries and arterioles, with a consequent reduction in glomerular blood flow.[49,50] Alternatively, glomerulosclerosis occurs because of glomerular hypertension and glomerular hyperfiltration. According to this theory, hypertension causes some glomeruli to become sclerotic and in an attempt to compensate for the loss of renal function, the remaining nephrons undergo vasodilatation of the preglomerular arterioles and experience an increase in renal blood flow and glomerular filtration. The result is glomerular hypertension, glomerular hyperfiltration, and progressive glomerular sclerosis.These mechanisms are not mutually exclusive, and they may operate simultaneously in the kidney.[49,51]

In patients with primary hypertension, hemodynamic studies frequently show a reduction in renal blood flow. The increased preglomerular vasoconstriction of the afferent arteriole and interlobular artery is thought, at least initially, to exert a protective effect in the glomerulus. With time, sclerosis of the preglomerular vessels causes further reduction in renal blood flow. The GFR is maintained because of increased intraglomerular pressure secondary to efferent arteriolar vasoconstriction and systemic hypertension. Eventually, glomerular ischemia and tubular ischemia develop. Considered together, these data suggest that hypertension precedes and accelerates arteriolar changes in the renal vessels.[49,51]

In the Multiple Risk Factor Intervention Trial (MRFIT), no changes in the reciprocal creatinine slope were observed in white people, but a significant loss in kidney function was observed in black people despite similar levels of BP control.[52] Similarly, secondary analyses from the Modification of Diet in Renal Diseases (MDRD) study demonstrated that at equivalent mean arterial pressures greater than 98mmHg, black patients had a reduction in their GFR at a rate of approximately 1 ml/min/year more than white patients.[45] APOL1 and MYH9genetic variants have been associated with increased risk of kidney disease in the AASK participants.[53]

2.6 DIABETIC NEPHROPATHY

The worldwide prevalence of diabetes mellitus (DM) has risen dramatically over the past two decades, from an estimated 30 million cases in 1985 to 177 million in 2000 and based on current trends, about 360 million individuals would have diabetes by the year 2030.[54] In Africa, the International Federation of Diabetes estimated in 2000 that about 7 million people were diabetic and it was projected that 17.2 million people will have diabetes by 2030 and this will be an increase of 80% which far exceeds the worldwide increase of 55%.**[54]** Although the prevalence of both type 1 and type 2 DM is increasing worldwide, the prevalence of type 2 DM is rising much more rapidly.[55] Until 40 years ago diabetes mellitus was said to be rare in sub-Saharan Africa. The estimated prevalence of diabetes in Africa is 1% in rural areas, up to 5 % to 7 % in urban sub–Saharan Africa, and between 8 % and 13 % in more developed areas such as South Africa and in populations of Indian origin.[56]

Diabetes has become the leading cause of ESRD in many countries of Western Europe, the United State, and Japan.[55] In the United States, the proportion of patients with diabetes as the cause of ESRD increased from 27% in 1988 to 36% in 1992 and 40% in 1995.[55] The reasons for this trend include:

(i) The increase in the prevalence of diabetes in the population.

(ii) The improvement in survival of patients with type 2 diabetes, and

(iii) The increasing acceptance of elderly polymorbid patients into renal replacement programs.

A similar trend of increasing prevalence of diabetes as a cause of ESRD has also been reported from Nigeria.[57] Diabetes accounts for 11% of patients with ESRD in Nigeria and 9%-15% in Kenya.[57,58] The increasing prevalence of diabetes in most populations is partly due to increase in the prevalence of obesity.[59] The rates of obesity have risen three-fold or more since 1980 in some areas of North America, the United Kingdom, Eastern Europe, the Middle East, the Pacific Islands, Australia, South-East Asia, and China with a similar trend in the developing countries.[60] Currently, more than one billion adults are overweight, with at least 300 million of them clinically obese.[60] A number of observations as well as randomized clinical trials have demonstrated during the last 25 years that tight diabetes control can potentially slow the rate of progression of diabetic microvascular complications, including diabetic nephropathy in both type 1 and type 2 diabetes mellitus.[54,61]

Diabetic nephropathy is the most common glomerulopathy, and the leading cause of ESRD in the USA and Europe.[54] In fact, about 50% of ESRD patients (in the USA) are diabetic.[54] It is the third leading cause ofESRD in Nigeria and most other developing countries.[9,57] It is important to consider that hyperglycemia is a primary initiator of diabetic nephropathy. Only 30% of patients with type 1, and 35–40% of patients with type 2 diabetes develop diabetic nephropathy irrespective of glycemic control.[61] Thevarious stages of DM nephropathy features hyperfiltration (elevated values of GFR) and occasional microalbuminuria, which may last approximately 5 years. During the next 20 years, microalbuminuria turns into progressively higher proteinuria, whereas GFR declines.[62] Finally, patient progresses to renal insufficiency with severe proteinuria, which eventually evolves into ESRD.[63] Very early, hyperglycemia induces

endothelial nitric oxide synthase (eNOS) expression in afferent arteries and glomerular capillaries, which leads to vasodilatation and increased GFR.[64] Progressively, glomerular distension causes endothelial dysfunction and hemodynamic alterations.[65]Loss of the glomerular basement membrane (GBM) electric charges and GBM thickening, decreased number of podocytes, foot process effacement and mesangial expansion have been shown to underlie the initial glomerular injury,which eventually leads to glomerulosclerosis.[64,65] Damage to podocytes is emerging as a critical event in glomerulosclerosis.[66] This has led to the notion that diabetic nephropathy is a disease of podocyte.[67]

2.7 CHRONIC GLOMERULONEPHRITIS (CGN)

Term "glomerulonephritis" encompasses a group of disorders with wide-ranging clinical presentations, severity, causes and immunopathogenetic mechanisms due to injury to, or inflammation of the glomerular capillary wall. The condition is characterized by irreversible and progressive glomerular and tubulointerstitial fibrosis, ultimately leading to a reduction in the glomerular filtration rate (GFR) and retention of uremic toxins. If disease progression is not halted with therapy, the net results are chronic kidney disease (CKD), end-stage renal disease (ESRD), and cardiovascular disease.[68]

In Nigeria, a tropical country with poor socio-economic indices and a weak health care delivery system, glomerulonephritis is certainly taking a major toll as the most common cause of ESRD especially in the younger adult.[9]

According to the report of a study carried out in Ile-Ife, Nigeria, chronic glomerulonephritis (CGN) was diagnosed clinically in patients that were aged about 30 years with past history of post-infectious glomerulonephritis, nephrotic syndrome, recurrent body swelling, with moderate to massive proteinuria.[27]

The leading causes of chronic renal failure among Nigerians have been documented to include glomerulonephritis, hypertension and diabetes mellitus and obstructive uropathy.[8,52] Several studies in Nigeria have documented chronic glomerulonephritis and hypertension as the commonest causes of ESRD.[9,57] In a study done by Nzegwu et al,[69] CGN was found to be the most common cause of ESRD. Similarly, in other developing countries, glomerulonephritis is still the prevalent cause of ESRD.[41] Ojo et al[70] in an autopsy study in Ile-Ife reported CGN to be the most common cause of CKD accounting for 40.9% of all causes and this is a reflection of high prevalence of infectious diseases in developing countries. In the United States, chronic glomerulonephritis is the third leading cause of ESRD and accounts for 10% of patients on dialysis after hypertension and diabetes.[48]

In Japan and some Asian countries, chronic glomerulonephritis accounted for as high as 40% of patients on dialysis.[71] However, recent data in Japanshowed a drop in the rate of chronic glomerulonephritis in patients on dialysis to about 28%.[71]The cause of this declining rate is not known but it may be due to better control of infections and infestations.

Despite the common occurrence of CGN, the basic etiology in the majority of adult patients with CGN remains ill-defined. The aetiology of CGN can be classified into two:

1. Primary (Idiopathic): This is due to the primary diseases of the kidney i.e. there is no identifiable systemic condition that could lead to the glomerulonephritis. Example includes minimal change disease, focal segmental glomerulosclerosis, IgA nephropathy etc.
2. Secondary: This is due to other systemic diseases which could be infection/infestation or non-infectious causes. The general notion is that of a post-infectious process, induced by a number of infective agents including;

(i) Bacteria such as streptococcal (throat or skin infections), Salmonella, seen widely across the continent;

(ii) Parasites - Plasmodium malariae in East and West Africa; FilariaLoaloa and Onchocercavolvolus

(West Africa) Schisotosomalmansoni and S.haematobium (North Africa, West Africa), viral - Hepatitis B – Southern Africa (Zimbabwe andNamibia, South Africa),

(iii) Hepatitis C (Egypt) and Human Immunodeficiency Virus (HIV) in (sub-Saharan Africa).'[72]

Parasitic nephropathy or glomerulopathy induced by parasites accounts for a large proportion of the nephritis encountered in Africa.[73] The well-recognized entities include quartanmalariae nephropathy (QMN) predominantly seen in West and East Africa, schistosomal nephropathy in North Africa (Egypt, Sudan), West Africa (Nigeria), filarial nephropathy (West Africa, Nigeria and Cameroon).[74]

Though less well defined, visceral leishmaniasis causes interstitial nephritis in North Africa. The renal lesions are thought to arise from host-parasite interactions, leading to a variety of complex adaptive immune responses fundamentally aimed at host's survival, and are triggered primarily by the recognition of "foreign" parasite antigens by the host's major histocompatibility complex (MHC) coded antigens.[75] A variety of ill-defined parasite antigens -structural and the non-structural proteins (which are in particular located on the surface membranes of the parasites) and the metabolic antigens are exposed to the host; they are recognized by the host's immune cells (macrophages/leucocytes/endothelial), and these in turn provoke certain immune responses.[75] These immune responses include;

(1) Formation of antibodies - which include non-specific antibodies, cross-reactive and auto-reactive antibodies.

(2) Formation of immune complexes, in circulation or in situ (in the kidney) and

(3)Activation of lymphocytes and interaction between macrophages and monocytes with production of mediators of injury,

(4) Effects on the resident cells in the kidney thereby manifesting as nephropathy.

The clinical features are in most cases those of chronic GN - in the form of asymptomatic proteinuria, the nephrotic syndrome and/or renal failure. Parasitic nephropathies share some distinct characteristics - these include

(1) A relentless progression to ESRD over a period of 3-7 years, (much shorter than seen with primary nephritides in Europe and America.

(2) Poor response to steroids and immunosuppressive.

(3) Limited effect of treatment of the initiating parasitic infection. Treatment aimed at clearing the parasites has limited benefit except in the early lesion. Trials of steroids, cyclophosphamide, azathioprine have recorded limited success as well in quartan malarial nephropathy.[74]

2.8 OBESITY

Obesity is a condition in which the natural energy reserve, stored in the fatty tissue of humans is increased to a point where it is associated with certain health conditions or increased mortality. Obesity represents a state of excess storage of body fat and could also be defined as an excess body weight for height.[60,76]

Several studies have linked obesity, and the associated metabolic syndrome, with increased risk of CKD.[77] Excessive body weight and a raised body mass index have also been linked to a faster rate of progression of CKD.[78] According to the Nigerian Demographic and Health Survey conducted in 2003, the prevalence of overweight and obesity was found to be 27.7% and 9.6%, respectively.[79] The rates of obesity have risen three-fold or more since 1980 in some areas of

North America, the United Kingdom, Eastern Europe, the Middle East, the Pacific Islands, Australia, Southeast Asia, and China.[76] A similar increase in the prevalence of obesity is also noticed in the developing countries and more worrisome is the increasing epidemic of childhood, obesity with increasing diagnosis of type 2 diabetes in children.[76]The increasing prevalence of type 2 diabetes in adults and children will in turn increase the prevalence of diabetic ESRD.[59]According to the WHO, an estimated 1 billion individuals are now classified as overweight or obese. In the USA, 35% of the adult populations are thought to be overweight and another 26% are classed as obese.[76] Obesity has been associated with the initiation and progression of glomerulonephritides. Obesity is also associated with focal segmental glomerulosclerosis (FSG).[78]

Obesity itself likely has independent effects on renal haemodynamics and individual with a low number of nephrons are likely to be the most susceptible to these changes.[77] Multiple mechanisms have been postulated whereby obesity directly impacts kidney disease, these includes hyperfilteration, increased glomerular capillary wall tension, and podocyte stress.[70]

2.9 LIPIDS

It is well known that dyslipidaemia represents an important risk factor for the development of cardiovascular disease (CVD) in the general population.[80] Many observational studies suggest that lipids may play a role in development and progression of glomerular injury.[80,81] Ravid et al[81] found that the level of cholesterol both at the onset and after a five year follow-up period was positively correlated with subsequent increase in urinary albumin excretion in microalbuminuric patient with Type 2 DM. In the Atherosclerosis Risk In Communities (ARIC) study, HDL, HDL-2 cholesterol and triglycerides have been shown to be significant predictors of a rise in serum creatinine while some other studies suggested an inverse relationship between serum cholesterol

values and mortality in ESRD individuals, a phenomenon also known as "reverse epidemiology"[82,83]

Dyslipidemia may contribute to glomerulosclerosis and tubule-interstitial fibrosis. A number of studies of diabetic and non diabetic nephropathies have confirmed by multivariate analysis that dyslipidemia is a risk factor for a faster rate of CKD progression.[82]

The mechanism of action is that circulating lipids bind to and become trapped by extracellular matrix molecules where they undergo oxidation increasing the formation of reactive oxygen species such as superoxide anion and hydrogen peroxide.[64] The resultant reduction in the actions of endothelium-derived vasodilator/growth inhibitors, such as prostacyclin and nitric oxide, with maintenance or increased formation of endothelium-derived vasoconstrictors/growth promoters such as angiotensin 11, endothelin-1, and plasminogen activator inhibitor-1, has significant vascular and renal pathophysiological consequences.[81] Macrophages-derived foam cells release cytokines that recruit more macrophages to the lesion and influence lipid deposition, endothelial cell function, and vascular smooth muscle cell proliferation. Glomerular cells mimic some of these characteristics, therefore similar pathogenetic mechanisms may contribute to the progression of atherosclerosis and CKD.[82,83]

There is a strong correlation between the rate of glomerular filtration rate decline and the plasma concentration of triglyceride rich apo B-containing lipoproteins, but no significant association with cholesterol rich apo B-containing lipoproteins.[84]

2.10 SMOKING

Smoking has been shown to increase the risk of albuminuria as well as that of progression of CKD.[85] Possible mechanisms whereby cigarette smoking may contribute to kidney damage include sympathetic nervous system activation, hypertension, the promotion of renal atherosclerosis,alterations in systemic and renal hemodynamics, and effects on endothelial

function and potential direct tubulotoxicity.[86] The association between smoking and stages of kidney disease earlier in thecontinuum is increasingly being recognized. Increasing evidence suggests that chronic smoking is a risk factor for progression of nephropathies.[86,87]

It has been implicated in all aspects of progression of renal disease in type 1 diabetics,[94] type 2 diabetics,[95]polycystic kidney disease.[88,89,90] Cigarette smoking also could cause renal dysfunction in subjects without documented renal disease, since the effective renal plasma flow is reduced in smokers, compared to non-smokers.[86] The exact influence of chronic smoking on the physiologic decline in renal function is unclear. It is also unclear whether the renal effects of smoking are reversible upon discontinuation of the habbit.[82] Chronic smoking, however, is associated with a marked risk of developing a proteinuria, which seems irreversible.[84]

Smoking shortens the interval from microalbuminuria to overt nephropathy, and accelerates progression of nephropathy and loss of glomerular filtration rate.[91]

2.11 ALCOHOL

The link between alcohol and hypertension is well established, yet the mechanism through which alcohol raises blood pressure remains elusive.[85] Possible mechanisms include an imbalance of the central nervous system, impairment of the baroreceptors, an increase of sympathetic activity, stimulation of the renin-angiotensin-aldosterone system, an increase in cortisol levels, an increase of intracellular calcium levels with a subsequent increase in vascular reactivity, stimulation of the endothelium to release endothelin or inhibition of endothelium-dependent nitric oxide production, and chronic subclinical withdrawal.[85] For control of hypertension, cessation or at least reduction of alcohol intake is the first step. Pharmacologic treatment should be withheld until after 2 to 4 weeks of abstinence from alcohol. Alcoholism can result in autonomic neuropathy and cardiomyopathy that can lead to a fall in blood pressure.[86]

2.12 ANALGESICS AND KIDNEY

Chronic analgesic nephropathy (AN) is a slowly progressive renal disease resulting from daily use for many years of mixtures containing at least two analgesics (e.g., aspirin, paracetamol, pyrozolones, phenacetin) and caffeine, codeine, and/or barbiturates, which may lead to psychological dependence and overuse.[92,93] The cumulative dose of analgesics required to cause renal impairment is about 4kg over 2 years.

The disease is characterized by capillary sclerosis, renal cortical atrophy, chronic interstitial nephritis, and papillary sclerosis/necrosis/calcifications.

In a number of cases, not related to the progression or stage of renal failure, the uro-epithelia can develop transitional cell carcinoma.[92] Phenacetin was present in all products used by patients described in the early reports of AN. This finding is the sole argument to support the generally accepted "phenacetin kidney" concept.[93] Experimental studies revealed, however, that aspirin and phenazone derivatives the drugs invariably taken with phenacetin all produce experimental nephrotoxicity more readily than phenacetin.[93] The most common renal disorder associated with non-steroidal anti-inflammatory drugs (NSAIDs) is acute kidney injury, largely reversible, as a result of the inhibition of renal vasodilatory prostaglandins in the clinical setting of a stimulated renin-angiotensin system.[94]

The prevalence of AN,is directly related to the pattern of analgesic consumption in different populations. In Nigeria the pattern of analgesic consumption and its contribution to renal disease is not known but Akinsolaet al[95] observed habitual use of analgesic in 78.2% of population studied in a semi-urban area in Ile-Ife. Abioye-Kuteyi et al[96] found a similar result (74.7%) in a rural area with unskilled workers who engaged in hard labour, especially famers being the most common abuser of analgesics. Older age, hypertension, concomitant use of diuretics or aspirin,

preexisting renal failure, diabetes and plasma-volume contraction is known risk factors for renal failure after the ingestion of NSAIDs. The frequency of analgesic nephropathy in patients with end-stage renal diseases (ESRD) varies greatly within and among countries. There is paucity of studies on AN in Africa including Nigeria where it was reported as a rare cause of chronic renal failure (CRF).[70] The prevalence varies from 1% in the United States to 22% in South Africa.[40] The prevalence in Nigeria has not been documented but Akinsola et al., classified AN as among the rare causes of CRF.[40,92] Underestimation of prevalence is likely because of lack of well-defined criteria of diagnosis. Analgesic nephropathy accounts formost CRF of unknown origin.[40] This could explain the paucity of reports of AN in Nigeria where the cause of CRF is not known in a significant number of patients.[40]

Analgesic nephropathyis more common in women and in the fourth to seventh decade. Usually, there is a preceding history of back or hip pain or headache, which leads to the daily use of analgesic. Okafor et al reported a case of AN in a 55year old Nigerian businessman who was being managed for osteoarthritis.[97] The highest prevalence rates of end-stage renal disease from analgesic nephropathy occur in South Africa (22%), Switzerland and Australia (20%), Belgium (18%), and Germany (15%).[98,99] In Belgium, the prevalence is 36% in the north and 10% in the South. In Great Britain, the rate is 1% nationwide; in Scotland it is 26%. In United States, the rate is 5% nationwide, 13% in North Carolina and 3% in Washington, DC.[48] Renal manifestations are nonspecific and consist of slowly progressive chronic renal failure with impaired urine concentrating ability, urinary acidification defects, and impaired sodium conservation. The diagnostic criteria for AN are[100]

1. History of daily use of analgesic for >5years.
2. Renal imaging showing small kidney/bumpy kidneys/papillary necrosis.
3. Proteinuria less than 3g/day.
4. Sterile pyuria.

The primary injury in analgesic nephropathy is medullary ischemia due to toxic concentrations of phenacetin metabolites combined with relative medullary hypoxia, aggravated by inhibition of vasodilatory prostaglandin synthesis.

2.13 TOXIC NEPHROPATHY

Toxic nephropathy is a general term used to categorize any adverse functional or structural changes in the kidney due to the effect of a chemical or biological product that is inhaled, ingested, injected, or otherwise absorbed, or that yields toxic metabolites with an identifiable adverse effect on the kidneys.[98] By extension, the concept of toxic nephropathy is occasionally applied to the adverse renal effects that occur when physiological substances circulate in concentrations greater or less than normal (e.g., hypercalcemic, hyperuricemic, or hypokalemic nephropathy).[98]

Nephron structures are extremely complex and therefore vulnerable in a variety of ways. Since many drugs and other substances are capable of causing serious kidney damage, and the list of potentially hazardous compounds grows yearly, it is important that the physician has a good working knowledge of the subject of toxic nephropathy. Various drugs and medicaments including analgesics and antibiotics, skin lightening creams have been incriminated as aetiological factors of chronic renal failure.[101]In our environment, ingestion of herbal concoction and zobo drink is common, and may contribute significantly to CKD.[102,103]

Mercury is found in alloy plants, mirror plants, and some batteries, and mercury intoxication usually occurs as a result of accidental exposure to mercury vapor. Although mercury has been shown to induce membranous nephropathy in experimental animals, the nephrotic syndrome is so uncommon in humans exposed to mercury that its etiologic role has been doubted.[98,104] Chronic lead nephropathy is usually identified when a source of high exposure is known as in occupational hazard or consumption of illicitly distilled spirits (moonshine).[105] Hyperuricemia is common

because of impaired uric acid excretion. Urine sediment is benign, and urinary protein excretion is less than 2g/day. Hypertension is almost always present, and in the absence of appropriate testing or a careful exposure history, lead nephropathy is often misdiagnosed as hypertensive kidney disease. Gouty arthritis affects about half of patients. Patients with chronic lead intoxication may occasionally manifest other signs, including peripheral motor neuropathies, anemia with "basophilic" stippling, and perivascular cerebella calcifications.

The incidence of nephrotoxicity from aminoglycosides has increased since their introduction in 1969, when the reported incidence of nephrotoxicity was 2% to 3%.[106]In 1993, the incidence was reported to be 20%, a figure that has changed little in the past decade, despite the proliferation of monograms and pharmacokinetic programs devised to prevent renal toxicity.[107]

Many hydrocarbons (HC) have been shown to be toxic to the tubular structures but epidemiological case control studies have suggested a causal link between the development of glomerulonepathy and chronic hydrocarbon exposure. Several cross-sectional studieshave described an association between glomerular and renal tubular disturbances and worksite hydrocarbon exposure. However, the pathophysiological mechanism of hydrocarbon-induced nephropathy remains unclear.[108]

Data in Africa are sparse but a study in Nigeria supports the hypothesis that hydrocarbon exposure may play a role in GN in Nigerian subjects and may have important implications for CRF prevention and management strategies.[103] The study found that the HC exposure was significantly higher in GN patients than in healthy controls irrespective of age and gender and increased the risk of GN-induced CRF more than four-fold. These findings support the hypothesis that the HC exposure may play a role in GN in Nigerian subjects and may have important implications for CRF prevention and management strategies.Decreased HC exposure may reduce the risk of developing GN. This is comparable to the report of Yaqoob et al.[109]

2.15 SOCIO-DEMOGRAPHIC FACTORS

CKD and ESRD have been found to be more common among certain ethnic groups, including Asians, Hispanics, Native Americans, Mexican Americans, and Australian Aborigines. It is clear that African- Americans experience a higher incidence of CKD and are over-represented in the dialysis population of the US.[100] This is probably due to low socio-economic status. Persons of low socio-economic status (SES) appear to be at increased risk of ESRD. The incidence of ESRD was found to be greater in geographic areas with less educated populations and lower household incomes.[111]

Age has been found to be a strong risk factor for CKD. The structural and functional impact of biologic aging on the kidney is most evident when stresses of inter-current insults, including infections, immunologic processes, drugs, toxins, or other organ failure, affect the patient. Donor kidneys demonstrate this change: kidneys older than 55 years of age are more likely to fail from chronic allograft nephropathy. The GFR reduction is progressive afterthe age of 30 and continues to decline steadily after the age of 60.[112] This implies that nephron loss may be part of ageing. The incidence of a decline in renal function over 5 years was greater among older patients with hypertension. In addition, the prevalence of end-stage renal disease (ESRD) is five times higher in the elderly than in young adults.[48]

Many studies suggest that male gender is associated with worse renal outcome. The age- and sex-adjusted incidence and prevalence of ESRD is greater in men than in women in the United States.[48,113] A Japanese community-based mass screening program observed that the odds ratio of developing ESRD (if baseline serum creatinine was greater than 1.2 mg/dL for males or 1 mg/dL for females) was almost 50% higher in men than in women.[52,113] Studies have reported a higher incidence of proteinuria and CKD among men in the general population, an increased risk of ESRD, or death associated with CKD among men in general population, a higher risk of decline

in renal function among male hypertensive patients, a lower risk of ESRD among female patients with CKD stage 3 and a shorter time to renal replacement therapy among male patients with CKD stages 4 and 5. Furthermore, meta-analysis of 68 studies that included 11,345 patients with CKD found a higher rate of decline in renal function in men.[52,114]

2.16 OTHER RISK FACTORS

Other factors associated with development of chronic kidney disease include (i) sickle cell disease, (ii) chronic pylonephritis, (iii) family history, (iv) obstructiveuropathy, (v) genetics etc. Clinically significant renal involvement occurs more frequently in sickle cell disease than in sickle cell trait or in combined hemoglobinopathies, which appears to be more common among patients with sickle cell trait.[115]Renal infarcts and papillary necrosis occur in either sickle cell disease or trait, with prevalence estimates of 30 to 40 percent in radiographic studies.[116] Among patients with sickle cell disease, the prevalence of proteinuria has been estimated to be 20 to 25 percent, and decreased kidney function has been reported in 5 to 30%.[117] Among patients with other sickling hemoglobinopathies, albuminuria and/or proteinuria has been reported in 8 to 30 percent (with the prevalence increasing with age), and decreased kidney function in six percent.[118] In the United States, sickle cell disease accounts for <1 percent of all new cases of end-stage renal disease.[52]

2.17 GENETIC CAUSES

Autosomal dominant polycystic kidney disease is a genetic disorder and the most common inherited kidney disease affecting 1 in 400 to 1000 live births in white populations.[119] Autosomal dominant polycystic kidney disease (ADPKD) often leads to progressive renal failure due in part to continued enlargement of the cysts.[120] The exact epidemiology is not known in black Africans. In Nigeria, a few cases have been reported in Ibadan and Enugu. In 1989, Akinsola et al[9] reported only one case of polycystic kidney disease out of 100 cases with chronic renal failure. Ojo et al[70]

in 1992, did not record a case of polycystic disease in an autopsy review of chronic renal failure. It is known to be multisystemic in that brain, liver, pancreas and heart have been reportedly affected.[120]

Autosomal recessive variety is hardly compatible with life, as fetal and neonatal death is the common place. Autosomal dominant variety has 2 types 1 and 11. Type 11 present late and progresses slowly to renal failure. PKD1 is located on chromosome 16 p 13.3 and accounts for majority (85%) of cases. PKD2 is located on chromosome 4 q 22 and accounts for 15% of ADPKD cases.[120]

Many studies show that polycystic kidney disease and chronic glomerulonephritis have high rates of progression to CRF and the Modification of Diet in Renal Disease(MDRD) study showed that polycystic kidney disease was the most progressive chronic renal disease with the mean rate of progression being 3.6ml/min/year faster than in patients with chronic glomerulonephritis or other nephropathies.[121] The greater contributory role of polycystic kidney disease in CRD progression may be partially explained by the fact that the growth rate and size of the cysts are probably the main factors affecting progression in polycystic kidney disease patients with reduced GFR.[120]

2.18 NATURAL HISTORY OF CHRONIC KIDNEY DISEASE

The natural history of CKD stages 1 and 2 remains to be fully defined. The rate of progression is variable but generally inexorable progress to renal failure or ESRD.

It has generally been assumed that the majority of patients with CKD stages 3b to 5 progress relentlessly to ESRD. This has recently been challenged as progression is variable, and a sizable percentage of these patients have stable kidney function or die prematurely of CVD.[122] A Canadian study showed the natural history of CKD stages 3 and 4 to be variable and reflects the patient's risk factor profile.[123] Many CKD patients with GFR below 60 ml/min per 1.73 m^2 die from cardiovascular or other causes before reaching ESRD.[6] A straight-line relationship is often

found between the reciprocal of serum creatinine (1/SCr) values or the estimated GFR and time. However, a significant percentage of patients do not progress in a predictable linear fashion and have breakpoints in their progression slopes, suggesting acceleration or slowing down of the rate of progression of CKD.[6] These breakpoints could be either spontaneous or secondary to events such as infections, dehydration, changes in the adequacy of systemic blood pressure control, and exposure to nephrotoxins, in particular nonsteroidal anti-inflammatory drugs (NSAIDs) or radio contrast agent, herbal concoction.[6] Attention has also been drawn recently to the impact of intercurrent acute kidney injury (AKI) events on the rate of progression of CKD. It is also important to appreciate that some patients with mild to moderate CKD have stable renal function for sustained periods.[6,124]

The rate of progression of CKD also varies according to the underlying nephropathy and between individual patients. Historically, the rate of decline in GFR of patients with diabetic nephropathy has been among the fastest, averaging around 10 ml/min per year. Control of systemic hypertension slows the rate of GFR decline to 5 ml/min per year, with further improvement (1 to 2 ml/min per year) expected in patients whose glycemia and hypertension are optimally controlled and in those treated with inhibitors of the renin-angiotensin-aldosterone system (RAS). In non-diabetic nephropathy, the rate of progression of CKD was 2.5 times faster in patients with chronic glomerulonephritis than in those with chronic interstitial nephritis and 1.5 times faster than in those with hypertensive nephrosclerosis.[124] The association of proteinuria and faster progression of CKD was highlighted in a number of studies. Relief of obstruction, discontinuation of nephrotoxic agents, and control of hypertension often stabilize renal function in a large percentage of patients. Patients with polycystic kidney disease and impaired renal function, CKD stage 3b and beyond may also have a faster rate of progression compared with other nephropathies.[124]

The rate of progression of CKD in the elderly has been associated with incident and progressive underlying cardiovascular disease. This is of interest as an increasing number of elderly patients reach ESRD, and renovascular disease has become one of the most common causes of ESRD in some countries.[122]

2.19 SCREENING FOR CHRONIC KIDNEY DISEASE

In view of the rising number of people suffering from ESRD and the perceived high prevalence of CKD in communities, interest has focused on the early detection of CKD and those at risk. Several guidelines for screening, mostly targeted to high-risk individuals, have been issued and implemented worldwide. These include the U.S. KDOQI, the U.K. CKD NICE, and the Australian Caring for Australasians with Renal Impairment (CARI) guidelines, to name a few.[1,3,125] There are a few differences as to the recommended targeted populations, but they invariably include individuals with hypertension and diabetes mellitus. Other groups include those with a family history of CKD, obese individuals, those with cardiovascular diseases (especially congestive heart failure), people with multisystem diseases, ethnic groups with high prevalence of CKD and those with urologic conditions such as nephrolithiasis.[126] The KDOQI guidelines additionally recommend screening those older than 65 years. Screening should consist of a urine albumin estimation as well as measurement of serum creatinine and estimation of GFR.[30,126,127] Overall, CKD screening would best be associated with broader national strategies and programs to minimize cardiovascular disease (CVD).[18]

The goal of a medical screening program is to recognize a disease in its pre-clinical phase so that intervention can occur at earlier stages for better outcomes.[128] Screening programs may also promote public awareness and education, encourage physician adherence to clinical practice guidelinesand serve as medical outreach to underserved populations. Such programs have benefits, risks, and costs.[2,30]

An evidence-based treatment regimen for patients with recognized CKD already exists and serves as a prerequisite for CKD screening programs. Screening for CKD occurs in many contexts, including during routine carewithin high-risk populationsand in the general population.[18,127] Population-based screening must ensure follow-up and successful referral of test-positive individuals for appropriate diagnosis, treatment, and counseling. In addition, because screening in these different contexts entails different risks and benefits, informed patient choice is essential to a successful screening program.[30]

2.20 DEFINITION AND TESTS FOR CKD SCREENING

Despite the publication of several practice guidelines in recent yearsthe effectiveness of early detection of CKD among adults in the general US population has not yet been studied.[1,48] The KDOQI guidelines defined the five stages of CKD, on the basis of renal damage as manifested by the presence of abnormal urinary albumin excretion (albuminuria) and the level of kidney function measured by GFR.[1]Chronic kidney disease is generally asymptomatic in its early stages. The pre-clinical phase may therefore not be detectable by usual testing,thus making the definition of CKD and choice of screening tests a more difficult issue.[30]

The measurement of albuminuria provides a sensitive marker of CKD from very early to more advanced stages of the disease process.[48] A 24-hour urine collection for the evaluation of albuminuria remains the gold standard; however, because of the inconvenience and errors associated with a timed urine sample, a spot urine sample using either albumin-specific dipstick or albumin-to-creatinine ratio is now an accepted screening method.[126]Houlihanet al[129]assessed the characteristics of the albumin-to-creatinine ratio as a screening test and found sensitivities >90% for both men and women, with excellent accuracy. Recently, both the Prevention of Renal and Vascular EndStage Disease (PREVEND) study group in Europe and Jafar et al[130]in an Indo-Asian population assessed the validity of urinary albumin concentration and the albumin-to-

creatinine ratio to detect individuals with albuminuria in subsequent 24 hour urine samples.[126,130] Both studies found the diagnostic performance of albumin concentration and albumin-to-creatinine ratio to be similar and acceptable with area under the receiver operator characteristics curve of 0.92 and 0.93, respectively, in the PREVEND study group versus 0.87 and 0.88 in the study by Jafar et al.[130]

The other option to screen for CKD is to measure GFR independent of the albuminuria status. Two common gold standard methods, plasma clearance of inulin and iothalamate infusions, available to measure GFR more accurately, are not appropriate for mass screening because they are expensive and take a few hours to complete. However, equations that estimate GFR and creatinine clearance from serum creatinine have been tested in several studies and are now recommended.[131] The most commonly used equations in adults are the Cockroft-Gault, the Modification of Diet in Renal Disease (MDRD) and CKD EPI. These equations have limitations, particularly because of the variability of the creatinine assay itself.[121,132,133] The National Kidney Disease Education Program has begun a creatinine standardization program to improve and standardize serum creatinine results generated by clinical laboratories for use in estimating equations.Several studies have assessed the reliability of such tests in different populations and have shown overall that the MDRD equation tended to underestimate true GFR, particularly in healthy individuals, whereas the Cockroft-Gault equation tended to overestimate true GFR, particularly in patients with CKD.[133] It should also be noted that even the gold standard methods of GFR measurement have intra-individual variation across laboratories and time as reported by Coreshet al.[131] In their study, test-to-test variability was inversely correlated with eGFR, particularly when renal function was >60 ml/min per 1.73 m^2. Thus, the balance of evidence for screening strategies is that GFR estimation at multiple time points, as recommended for proteinuria, may be warranted in a screening program.

2.21 AWARENESS OF CKD

Identification of CKD requires recognition of individual risk and appropriate laboratory testing (serum creatinine and/or urinary protein), since symptoms generally do not manifest in earlier stages of CKD; however, earlier-stage CKD can lead to several complications, such as anemia and bone mineral metabolism disorders, and poor outcomes, including cardiovascular events, morbidity, and mortality, in addition to progression to end-stage renal disease (ESRD), requiring dialysis or transplant for survival.[18] Despite these known adverse consequences of CKD, the majority of persons with the disease, especially prior to ESRD, remain unaware of their disease.[129,136] Awareness of CKD remains unacceptably low, despite recent attempts to increase awareness through dissemination of clinical practice guidelines and recommendations for patients with CKD or its risk factors to providers, community awareness events such as World Kidney Day, and free screening efforts for high-risk individuals like the Kidney Early Evaluation Program (KEEP).[30,110,129]

In the 1999 to 2004 National Health and Nutrition Examination Surveys (NHANES), only 8% and 41% of persons with CKD stages III and IV, respectively, self-reported their CKD.[18] Similarly, only 9% of patients with CKD and diabetes in a screening study were aware of their CKD status and only 5% of those with CKD and coronary heart disease self-reported CKD awareness in a cohort study.[137,138]

Alebiosu et al[139] reported low awareness of CKD among a community population in Ogun state. Low level of awareness was also reported by Oluyombo et al.[140] Earlier recognition of CKD could slow progression of CKD, prevent complications, and reduce cardiovascular-related outcomes.Additionally, early referral to a nephrologist has been shown to improve outcomes for those who progress to end-stage renal disease.[30,133]

CHAPTER THREE

3.0 METHODS AND SUBJECTS

3.1 STUDY AREA

The study was carried out at Aiyepe community, a circumscribed homogenous rural community in Odogbolu Local Government Area, Central Senatorial District of Ogun State. The village has a fairly stable population devoid of frequent influx and efflux of people due to its location and low economic activity. It is located about ten kilometers away from a major highway and the nearest sub-urban town is about five kilometers away. The population is about 13,650 a projection from 1991 population figure from National Population Commission.[66]The composition is predominantly of indigenous people and a few settlers from other tribes who are mostly peasant farmers and a few petty traders. The predominant religions are Islam and Christianity with a few traditional religion worshippers. It has a police post and a health center that serve the community. The nearest General Hospital is in Odogbolu, the Local Government Headquarter. It is bounded to the East by Odogbolu and to the North by Ikenne, to the west by Imota and south by Sagamu.

The town is divided into four major quarters namely Aba, Obiri, Odo-Olowu and Alakan quarters. Each has a traditional ruler and they coexist peacefully. These are represented in the sketched map of Aiyepe as shown in Appendix 1.

Aiyepe was chosen because of its fairly stable and homogenous population and no such study had been undertaken previously in this community.

3.2 STUDY DESIGN

A cross-sectional community-based study aimed at screening adults in rural community for CKD and its associated risk factors.

3.3 SAMPLE SIZE (Cochran formula)[141]

$N= (Zi – a)^2P(1-P)/d^2$

N – Minimum sample size.

a – significant level of effort tolerable for this study at 0.05 confidence level = 95%.

Zi – a =1.96 (from Z table).

P= best estimate of prevalence from literature review =10 - 18.8%[13]

D = absolute precision of 5%.

$N= (1.96)^2 * 0.188(1-0.188)/0.05*0.05$

= 235.

This was doubled to 470.

3.4 SAMPLING TECHNIQUES

A simple cluster sampling technique was used. The town was divided fairly equally into four clusters by the main road i.e. Imota-Odogbolu road from East to West and College and Ikenne road from South to the North. See Appendix 1.

A region was selected by simple random sampling method and in this region one out of 3 houses was selected. All individuals who fulfilled the inclusion criteria in the selected houseswere sampled.

3.5 STUDY PROTOCOL

Two indigenes from Aiyepe were recruited as field assistants to lead the research team to the individual houses. The researcher was involved in administering the questionnaire, bio-physical measurement and collection of samples. The participants were taken through a structured pre-tested questionnaire that seek information on knowledge, attitudes and practices regarding

CKD, socio-demography, family history and relevant past medical history of renal disease such as body swelling, frothy urine, haematuria, recurrent dysuria. (See Appendix 2).

Knowledge of CKD was graded as poor, fair, good and very good when participant scored 1-7, 8-15, 16-24, and 25 point and above respectively.[13]The maximum obtainable point was 37. See appendix 1. The knowledge question was adopted with little modification from Oluyombo et al.[13]

The questionnaire also addressed history of specific risk factors that have been well established and clinical features of CKD such as body swelling, haematuria, frothy urine, difficulty in passing urine, hypertension, diabetes mellitus, recurrent urinary tract infections, drug history (including analgesics, native drug concoction), cigarette smoking, alcohol intake, sore throat, septic skin rashes, parasitic infestations (e.g. filariasis, schistosomiasis) and exposure to hydrocarbon through occupation etc.

3.6 ETHICAL CONSIDERATION AND CONSENT

Ethical approval was obtained from Ethic and Research Committee of Olabisi Onabanjo University Teaching Hospital, Sagamu. (Appendix 3) Informed consent was taken from the individual subjects. (Appendix 4)

3.7 METHODOLOGY

3.7.1 HEIGHT - This was measured with the aid of a stadiometer. The subject's height was taken with shoes removed while standing on a flat surface, arm by the side, looked straight while backing the stadiometer. The measurement was taken to the nearest 0.1cm.[142]

3.7.2 WEIGHT - bathroom weighing scale (Hana, made in China) was used to measure the weight with the subject putting on light clothing and measurements were taken to the nearest 0.1kg.An equation [(weight in kilograms)/(square of the height in meters)] was used to calculate

the body mass index(BMI). A BMI of 30 or greater was defined as obesity, and those between 25 and 30 will be considered overweight. [142]

Obesity was graded as mild, moderate and morbidly obese when BMI was 30-34.9kg/m^2, 35-39.9kg/m^2 and ≥ 40kg/m^2 respectively. Underweight was defined as BMI <18.9 while normal BMI was between 19-24.9 [142]

3.7.3 WAIST CIRCUMFERENCE - This was measured with the aid of non-stretching tape measure. The measurement was taken while the subject stood erect with feet about 25 - 30cm separated. It was taken midway between the inferior margin of lowest rib and the iliac crest in a horizontal plane. The circumference was measured to the nearest 0.1cm at the end of normal expiration. A value of < or = 88cm and < or = 102cm was taken as normal for female and male respectively.[142]

3.7.4 HIP CIRCUMFERENCE - Measurements were taken using a non-stretching tape rule. Participants had their measurements done at the level of greater trochanters. The measurement was recorded to the nearest 0.1cm and waist hip ratio was calculated.[142]

Waist: Hip ratio of <0.9 and 0.85 was taken as cut-off points for men and women respectively. Abdominal obesity or central obesity was defined with waist-to-hip ratio over 0.9 for males and 0.85 for females.

3.7.5 BLOOD PRESSURE MEASUREMENT

Blood pressure was measured according to the guidelines presented in the Eight Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC 8) using electronic sphygmomanometer (Omron) with medium and large cuff sizes.[143,144] The blood pressure was measured in the left arm after participants have been seated for at least five minutes using sphygnomanometer. Participants who currently required anti-

hypertensive therapy to control their blood pressure or those with a systolic blood pressure (SBP) of 140mmHg or greater and/or diastolic blood pressure (DBP) of 90mmHg or greater at screening was reconfirmed after a third measurement (repeated every 15 min after rest) before they were accepted as hypertensive.[143] Pulse pressure was calculated as the difference between systolic blood pressure and diastolic blood pressures.

Mean arterial blood pressure (MABP) was calculated; MABP = 1/3 X pulse pressure + DBP.

3.7.6 FASTING BLOOD SUGAR

The fasting blood sugar was measured by a standardized Glucometer (Accuchek, Roche, UK) after an overnight fast. Subjects with a diabetic history or those with fasting blood glucose ≥126 mg/dL were categorized as diabetic.[137]

3.7.7 LIPID PROFILE

Venous blood sample about 5ml was taken after an overnight fast to determine the lipid profile which was assayed in Olabisi Onabanjo University Teaching Hospital, Sagamu.

Those with serum cholesterol >200mg/dL and serum triglyceride >150mg/dL at screening were interpreted as having hypercholesteraemia and hypertriglyceridaemia, respectively according to NCEP ATP guideline.[131]

3.8 SAMPLE COLLECTION, HANDLING AND ANALYSIS

3.8.1 BLOOD

The venous blood sample was taken from peripheral vein through an aseptic procedure. 5mls needle and syringe was used to take 5ml of blood sample into a 5mls lithium heparin tubes, centrifuged with the plasma separated in plain specimen bottles and stored at -20^{o} C. Serum creatinine estimation was done using modified kinetic Jaffe reaction (Alkaline picric acid method); RANDOX kit from RANDOX Laboratories Ltd. UK[145]

3.8.2 URINE COLLECTION AND HANDLING

Spot urine samples were collected in plastic universal containers and analyzed for the following;

1. Urinalysis was done using dipstick (Combi 10) for the presence of protein, red blood cells, white blood cells and nitrates.
2. Urine microscopy was carried out using OLYMPUS^{R} microscope to examine the urine of subjects whose dipsticks analyses were positive for red blood cells (1+ or greater) and white blood cells. This was to detect the presence of cellular components (red blood cells; presence and morphology, pus cells, casts, bacteria cells, schistosomahaematobium) and crystals.
3. Automated albumin: creatinine ratio was done using i-CHROMA^{TM}Microalbumin. (Boditech Med Incorporated, Republic of Korea) on urine samples that was negative for proteinuria with Combi 10 dipsticks.

   10µL of urine at room temperature was drawn with transfer pipette and added to the tube containing Buffer. It was mixed well by inverting repeatedly the tube. Then 75µL of the sample mixture was taken and loaded onto the well of a disposable Test Kit. It was left at room temperature for 12 min before inserting the device into the holder. The instrument automatically scans the test device and result was displayed on the screen of the i-CHROMA Reader.
4. Urine albumin: creatinine ratio of each sample was estimated and expressed in mg/g. A value equal to or greater than 300mg/g was regarded as positive.
5. Glomerular filtration rate (GFR) was estimated from serum creatinine using Cockroft and Gault equation which has been validated among Nigerians.[146]

Cr Clearance =$\frac{(140 - \text{Age (years)}) \times \text{Weight (kg)}}{\text{Plasma Cr (mg/dl)} \times 72}$(multiply by 0.85 if female)

3.9 INCLUSION CRITERIA

Adults who had resided in the community for at least 2 years.

3.10 EXCLUSION CRITERIA

Non consent.

Urinary tract infection.

Age, less than 18 years.

Individuals who have not resided in the community for up to 2 years.

Acute febrile illness.

Women that are menstruating.

Pregnant women.

3.11 EVALUATION CRITERIA

CKD was assessed based on the following:

1. The presence of albuminuria (using albustix) which is graded as follows:

1+ (30mg), 2+ (100mg), 3+ (500mg) and 4+ (>500mg)

Urinary albumin excretion assessed from spot urine sample, by calculating urinary albumin:creatinine ratio and the results were interpreted as follows:

Less than 30mg/g; Normal

Microalbuminuria: ≥30 to <300mg of albumin/g of creatinine.

Macroalbuminuria: ≥ 300mg of albumin/g of creatinine.

2. eGFR<60ml/min/1.73.

Based on the classification of chronic kidney disease (CKD) by the National Kidney Foundation using the K/DOQI guideline, patients were classified into five stages based on glomerular filtration rate (GFR).

The stages are:

Stage 1: GFR ≥ 90 ml/min/1.73m^2

Stage 2: GFR = 60-89 ml/min/1.73m^2

Stage 3a: GFR = 45-59 ml/min/1.73m^2

Stage 3b: GFR = 30-44 ml/min/1.73m^2

Stage 4: GFR = 15-29 ml/min/1.73m^2

Stage 5: GFR < 15 ml/min/1.73m^2

A urine dipstick test was done and positive test for leukocyte esterase or nitrite was taken as suggestive of the presence of urinary tract infection.

After the first screening for CKD, all studied subjects who had evidence of functional kidney abnormalities werethose with:

1. Albumin/creatinine ratio >300mg/g irrespective of GFR.
2. eGFR<60ml/min/1.73m^2

They had a repeat of their serum creatinine and urinalysis after 3months. Then only those consistently positive as described above were included in the CKD population. The aetiological factors as identified from the questionnaire, screening and physical examination were recorded.

Knowledge and awareness were assessed with questionnaires. Total mark obtainable for knowledge was 37. Knowledge was scored as poor, fair, good and very good when participant scored 1-7, 8-15, 16-24 and 25 or more respectively.[13]

3.12 STATISTICAL METHODS

All the statistical data were entered into the EpiData 3.0 for error checking before the SPSS 11.50 analysis. Descriptive analyses (in form of percentage, proportions, ratio and frequency as required) wereused to characterize the participant population by socio-demographic data (e.g. age, gender and education), health status (obesity, central obesity, hypertension, diabetes, albuminuria, haematuria, pyuria, eGFR, urinary albumin-to-creatinine, hypercholesteraemia, hypertriglyceridaemia, and nephrolithiasis) and lifestyle factors (smoking, alcohol consumption).

The participants that were consistently positive for indicators of CKD with the initial screening and at 3months wereidentified as having CKD and their proportion over all participants was noted as the prevalence of CKD.

The severity of the CKD was graded into 5 stages (1-5) according to KDIGO classification and the distributions were recorded. The pattern of the subjects' level of awareness was reported using frequency. The association of socio-demographic factors and grade of CKD with the awareness was determined using Students t-test for numerical data and Chi-square for categorical data.

P value of <0.05 was taken as statistically significant.

3.13 DEFINITION OF TERMS

The following are the definition of terms used in this project.

1. Chronic kidney disease: estimated glomerular filtration rate <60ml/min/1.73m2 or overt proteinuria or ACR >300mg/g persisting for ≥3 months.
2. Awareness of CKD was defined as responding "yes" to "Have you ever been told by a doctor or other health professional that you have weak or failing kidneys (excluding kidney stones, bladder infections, or incontinence)?" during the interview.
3. Hypertension was defined as having BP ≥140/90mmHg or was on regular use of anti-hypertensive.
4. Diabetes mellitus was defined as elevated fasting blood sugar of >126mg/dL or use of glucose lowering agents drugs or insulin.
5. Dyslipidaemia means any form of abnormalities in fasting serum lipid profile as defined by; total cholesterol ≥200mg/dL, triglyceride ≥150mg/dL, LDL≥100mg/dL, HDL ≤50mg/dL,
6. Proteinuria was defined as ACR > 300mg/g.
7. In this study, high level of education was regarded as secondary school education and above.

CHAPTER 4

RESULTS

4.1 DEMOGRAPHIC CHARACTERISTICS

4.1.1 Age and sex distribution

Four hundred and fifty-six subject of which 160 (35.1%) males and 296(64.9%) females were studied. The mean age ± standard deviation (SD) of the studied population was 48.1±15.7 years. The mean ages of male and female participants were 47.7± 17.1 years and 48.3± 14.9 years respectively. Three hundred and forty-six (75.9%) of the participants were aged 60 years and below. One hundred and twenty-five (27.4%) of the participants had CKD while three hundred and thirty-one (72.6%) did not have CKD. The mean age of CKD and non-CKD groups was 57.2(±15.1) year and 44.52±14.38 years respectively. (Table 3)

4.1.2 Educational status

One hundred and seventy-eight (36.8%) of the participants had secondary education while eighty three(17.5%) had tertiary education. The remaining participants had either primary or no formal education. (Table 3) A higher proportion of those with at least secondary education were in the age bracket 20-60 years compared to a majority of those without formal education who were in the older age group (older than 60years). This difference was statistically significant ($x2=116.410$, $p<0.001$). One hundred and fifty-one females (59.4%) had a higher level of education compared to one hundred and three males (40.6%), this difference was statistically significant. ($p<0.001$).

4.1.3 Religion

The sample population consisted of 172(37.7%) Christians and 270(59.2%) Muslims. The remaining 14 (3.1%) were traditional religion worshippers.

4.1.4 Occupation

The predominant occupation of the studied populationwas petty trading and farming while few were civil servants. Two hundred and seven (45.4%) engaged in trading, 152(33.3%) were farmers, 71(15.6%) were skilled workers, 16(3.5%) were civil servants and 10(2.2%) retired civil servants. (figure 2).

4.2 CLINICAL CHARACTERISTICS

4.2.1. History of hypertension and diabetes

Ninety-nine (20.5%) of participants had history of hypertension. Ninety-five (20.3%) of the participants had family history of hypertension. Three hundred and seventy-three (79.7%) of participants had checked their blood pressure at one time or the other. Ten (2.2%) of the participants had history of diabetes mellitus. Table 3 shows the medical history of the participant.

4.2.2 History of smoking and alcohol

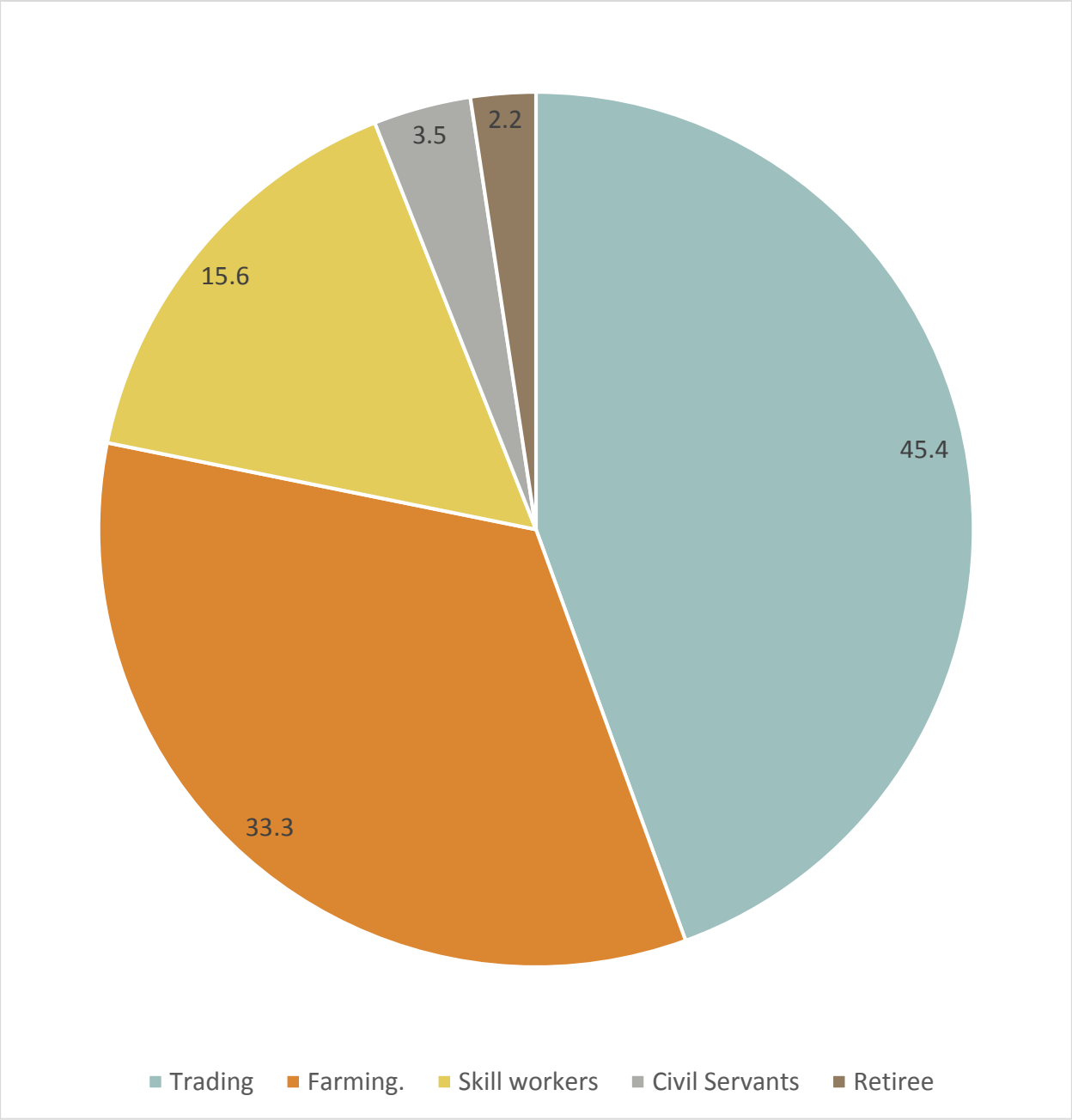
Thirty (6.6%) of the participants were current cigarette smokers, while 0.2% smoked marijuana (hemp). The number of sticks per day ranged from 1- 40 sticks.

One hundred and twenty (26.3%) of the participants consumed alcohol. Seventy three (62.4%) indulged in beer, sixteen (13.7%) took spirit, ten (8.5%) were palm wine drinkers while eighteen (15.4%) took different combinations of any of the above.(Table 3)

Table 3. Baseline socio-demographic and medical history of the participants

Baseline socio demographic and medical history of study participants.		Sex				
		male		female		total
		n	%	n	%	n
Age group (years)	<21	12	48.0	13	52.0	25
	21-40	47	36.7	81	63.3	128
	41-60	58	30.1	135	69.9	193
	>60	44	40.0	66	60.0	110
Level of education						
	nil formaledu	20	22.7	68	77.3	88
	primary	41	34.2	79	65.8	120
	secondary	58	34.5	110	65.5	168
	tertiary	42	52.5	38	47.5	80
History of diabetes	yes	4	40.0	6	60.0	10
	no	153	34.8	287	65.2	440
	don't know	4	66.7	2	33.3	6
History of hypertension	yes	39	34.5	74	65.5	113
	no	143	38.1	221	61.9	343
	don't know	0	0.0	0	0.0	0
Cigarettes smoke	yes	29	97.0	1	3.0	30
	no	130	30.5	296	69.5	426
	don't know	0	0.0	0	0.0	
Alcohol	yes	76	60.3	44	39.7	120
	no	87	25.9	249	74.1	336
	don't know	0	0.0	0	0.0	0
Haematuria.	yes	14	82.4	3	17.6	17
	no	146	33.3	293	66.7	439
	don't know	0	0.0	0	0.0	0

Figure 2. Occupational Distribution of the Participants



4.2.3 The use of herbal medications, analgesics and mercury containing soaps and creams

Four hundred and eighteen (91.7%) of the participants had used analgesics at one time or the other. Predominant analgesics used were NSAIDS and paracetamol. Three hundred and twenty-five (77.6%) used analgesics without prescription. Ninety-six (22.9%) took analgesics daily, two hundred and thirty-two (55.4%) took analgesics once in a month. Three hundred and seven (82.7%) took analgesics for more than six months.

Three hundred and fifty-eight (78.7%) of the participants had used herbal concoctions. Seventy-six (16.2%) had used it daily, forty-nine (10.5%) most days of the week and fifty-eight (12.4%) about twice a week. Ninety-six (22.9%) of participants used analgesics daily, thirty-seven (8.8%) used analgesics most days of the week, fifty-four (12.9%) had used analgesics twice a week while two hundred and thirty-two (55.4%) used analgesics once a month. Two hundred and eighty-four (84.5%) had used analgesic for more than six months.

One hundred and seventy-three participants (38.4%) used mercury containing soaps and/or creams. One hundred and thirty-five(73.8%) of them had used it for over six months.

4.2.4 Haematuria

Seventeen (3.7%) of the participants had history of haematuria. It was terminal in six (1.3%) and four (0.9%) had total haematuria. The remaining 7 participants could not remember if the haematuria was terminal or total.

4.2.5 Sore throat and skin rash

One hundred and sixty-seven (36.9%) of the participants had skin rash or sore throat in the past. History of body swelling and family history of CKD was obtained in 27(6.0%) and 9(1.9%) respectively.

4.3 ANTHROPOMETRIC MEASUREMENTS

4.3.1 Weight and Body Mass Index

The mean weight of the participants was 69±15kg, it ranged between 37kg to 125kg. The mean for maleswas 68±13kg whilethat of the females was 69.3±16.3kg.

The mean height of the participants was 1.61±0.09mand it ranged from 1.36m to 1.88m while the mean height for male and female were1.67±0.08mand1.57±0.07m respectively.

The mean BMI of the participants was 26.6±6.0kg/$m^2$and it ranged between 15.04kg/m^2 to 48.68kg/m^2 while the mean BMI formale and female were 24.3±4.3kg/m^2 and 27.9±6.5kg/m^2 respectively.

Nineteen (4.2%) were underweight, 192 (42.1%) had normal weight, 133(29.2) were overweight, 95 (20.8) had mild to moderate obesity while 17(3.7%) had morbid obesity. Table 4 shows BMI of the participants. The mean BMI of CKD and non-CKD group were 27.5±6.1kg/m^2 and 24.7±5.1kg/m^2 respectively.

4.3.2 Waist and Hip circumference

The mean waist circumference (WC) of the participants was 88.6±14.9cm and itranged between 30 to 125cm, while the mean WC of the males and females were 85.7±12.7cm and 90.3(±15.8)cm respectively.

The mean hip circumference of the participants was 98.3±16.8cm, itranged from 90cm to 146cm while the mean hip circumference of male and female were 94.4±11.4cm and 100.4±15.8cm respectively.

The mean waist-hip ratio of the participants 0.9±0.6 and it ranged from 0.59 to 1.46 while the mean for males and females were 0.9±0.1 and 0.96±0.9 respectively. (Table 4)

4.3.3 Blood Pressure Measurements

The mean SBP and DBP of the participant's was134.0±26.6mmHg and 80.3±14.8mmHg. The MAP±SD of the participant was 98.2±17.4mmHg. Mean arterial pressure for male was 96.8±15.5 and that of female was 99.0±18.4. There was no statistical significance between male and female MAP.

Table 4. Baseline Anthropometric Measurements of the Participants.

Anthropometric Measurements.	Male (n)	Female (n)	All participants (n)
HC (cm)	94.38±11.42	100.34±15.75	98.26±16.75
WC (cm)	85.65±12.66	90.27±15.75	88.64±14.89
WHR	0.91±0.08	0.96±0.68	0.94±0.55
Weight (kg)	68±13	69.32±16.32	68.91±15.01
BMI (Kg/m2)	24.34±4.25	27.86±6.54	26.68±5.94
BMI class (n/%)			
<18.5	9 (47.4)	10(52.6)	19
18.5-24.9	91 47.4()	101 (52.6)	192
25-29.9	47 (35.3)	86 (64.7)	133
30-34.9	14 (21.5)	51 (78.5)	65
35-39.9	1 (3.3)	29 (96.7)	30
≥40	1 (5.9)	16 (94.1)	18

HC - Hip circumference, WC - Waist circumference, WHR - Waist- Hip ratio, BMI - Body Mass Index.

4.4 LABORATORY PARAMETERS

4.4.1 Blood sugar

The mean fasting blood sugar of the participants was 93.41±32.0mg/dL and it ranged between 59 to 444mg/dL. Ten (2.2%) of the participants gave previous history of DM while nine (2.0%) of them were newly diagnosed. The total prevalence of DM in the study was 4.2%.

4.4.2 Haematuria and pyuria

Only 17(3.7%) of the participants had history of haematuria. Six (35.3%) had terminal haematuria, four (23.5%) total while seven (41.2%) could not remember. Pyuria was seen in four participants and all of them were females.

4.4.3 Serum lipids

The mean total cholesterol of the participants was 172.9±0.9mg/dL and it ranged between 102 to 290mg/dL, while the mean level for males and females were 165.8±32.7mg/dL and 176.3±36.6mg/dL respectively. The mean level for triglyceride among the participants was 127.2±46.1mg/dL and it ranged between 42 to 375mg/dL, while the mean level for males and females were 123.6±44.5mg/dL and 129.2±46.9mg/dL. The mean level for low density lipoprotein (LDL) among the participants was 98.2±30.7mg/dL and it ranged between 44 to 199mg/dL while the mean level for male and female participants was 92.9±26.7mg/dL and 101.1±32.3mg/dL. The mean level for high density lipoprotein (HDL) among the participants was 50.0±8.18mg/dL and it ranged between 31 to 76mg/dL while the mean level for male and female participants was 50.3±8.4mg/dL and 49.0±8.1mg/dL respectively.

4.5.1 Serum Creatinine and Estimated Glomerular Filtration Rate

The mean serum creatinine of the participants was 1.13mg/dL it ranged between 0.4 and 2.4mg/dL. The mean eGFR of the participants using Cockroft-Gault formula was 75.10±27.10

ml/min/1.73m^2 and it ranged between 20.3 to 168.6ml/min/1.73m^2. The eGFR of all the participants is as shown figure 3. The greater number of participants had their eGFR between 60 and 70ml/min/1.73m^2 as shown in figure 3.

After the first phase of the screening, 160 participants (34.2%) of the participants had eGFR<60ml/min/1.73m^2 and/or proteinuria. They were screened again after 3 months and 114(25%) of the participants had persistent eGFR<60ml/min/1.73m^2 while 12(2.6%) had persistent proteinuria. These cohorts were regarded as having CKD and were categorized according to KDOQI staging. Figure 4show the pattern of distribution of indicators of CKD.

4.5.2 Albuminuria

Thirty-four (7.3%) of the participants were found to have macro albuminuria as defined by positive dipstick or ACR>300mg/g, while 42(9.0%) had micro albuminuria as defined by ACR between 30-300mg/g. A total of seventy-six (16.3%) of the participants had albuminuria.

4.6 PREVALENCE OF CKD

4.6.1 Glomerular Filtration Rate and Proteinuria

The total of 456 participants completed the study. The prevalence of CKD as defined by eGFR< 60ml/min/1.73m^2 was 114 (25%) while proteinuria as defined by dipstick or ACR> 300mg/g was 12(2.6%) giving a total of 126 (27.6%) which was the total prevalence of CKD in the community studied.

The pattern of CKD according to Kidney Disease Outcome Quality Initiative (KDOQI) is as shown in the figure 4. Two subjects were in stage 1(1.6%), ten were in stage 2 (7.9%), sixty-five were in stage 3a (51.6%), forty-two were in stage 3b (33.3%), seven were in stage 4(5.6%) and no participant was in stage 5. The age distribution is as follows: <21 years was 5.5%, 21 –

40 year was 28.1%, 41– 60 years was 42.3% and >60 years was 24.1%. Table 4. The mean age also increased with the stages of CKD as shown in table5.

4.6.2 Albuminuria

The prevalence of albuminuria in the study was 16.3% comprising of both macro- and micro-albuminuria.

Figure 3. Distribution of eGFR in all participants

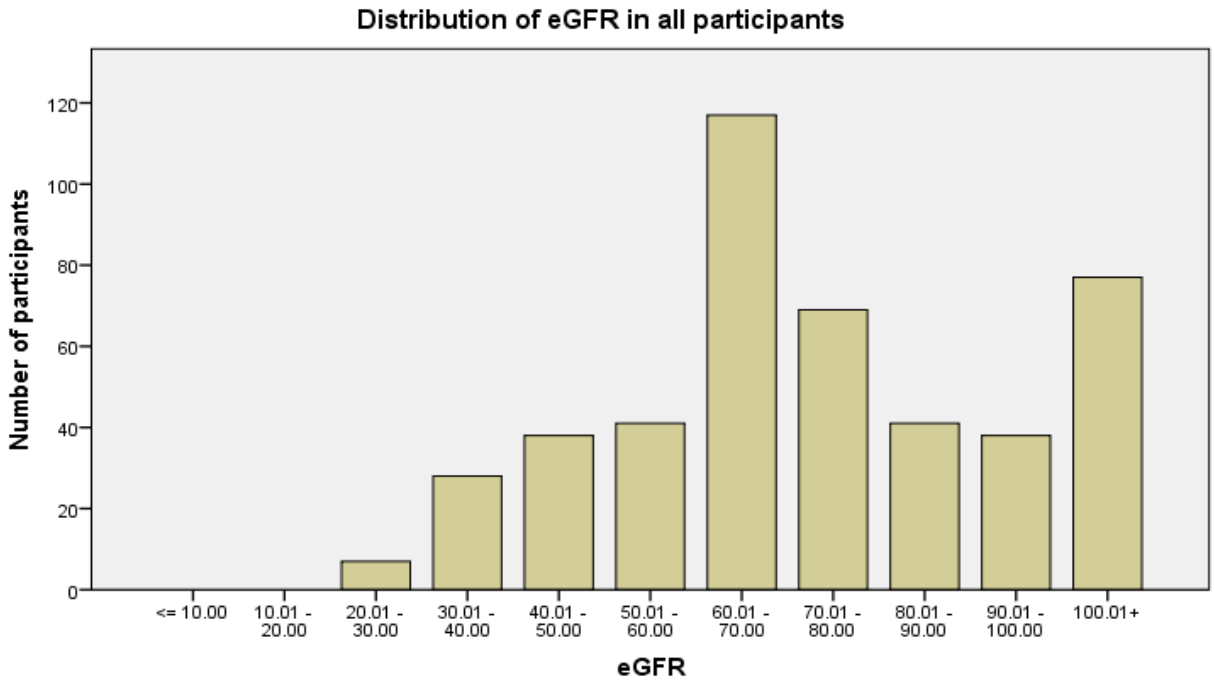


Figure 4. Pattern of CKD among the participants.

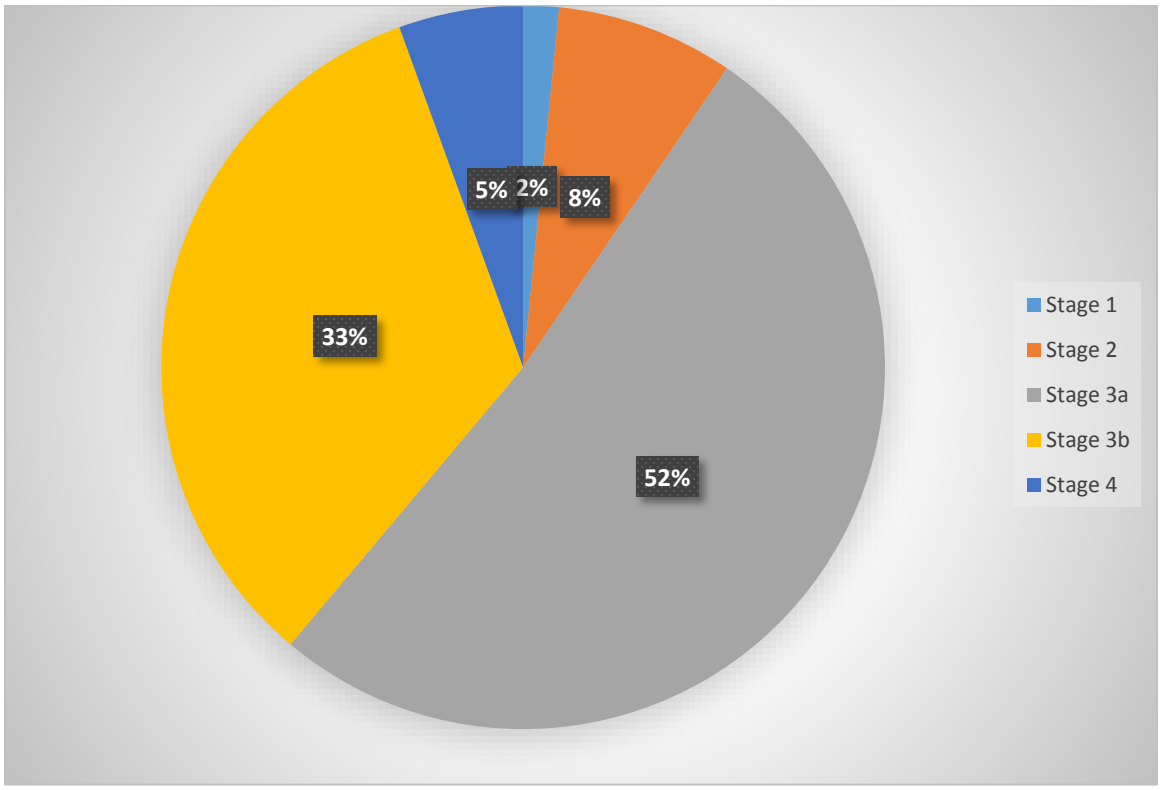


Table 5. Mean Age Distribution among Patients with CKD.

Stages of CKD		
	Mean Age	Count
1	44	2
2	46	10
3a	56	65
3b	62	42
4	69	7
5	0	0

4.7 RISK FACTORS FOR CKD

4.7.1 Educational Status, Age and Sex

The mean age of the CKD group was significantly higher than non-CKD group. ($p<0.001$)

There was a steady increase in percentage of participants with CKD from age 21year to 60years. Sixty-one (48.4%) of participants with CKD were above 60year of age as compared to forty-eight (14.5%) of participants without CKD and this difference was statistically significant. ($x^2 =62.011$, $p<0.001$). The severity of CKD also increased with age as 61.9% and 85.7% of those with CKD stages 3b and 4 respectively were aged above 60years and this difference was statistically significant. ($p=0.01$).

The participants with maximum of primary school education or its equivalent was regarded as having low level of education. Seventy-three (69.8%) of participants with CKD had low level of

education as compared to 36% of those without CKD which was statistically significant (x^2 =45.432, p<0.001).

Eighty-three (65.9%) participants with CKD were females compared to two hundred and fourteen (64.8%) participants without CKD, and this difference was not statistically significant. (p=0.837)

4.7.2 Knowledge and Awareness of Chronic Kidney Disease

Two hundred and ninety-nine (65.6%) of the participants have heard of CKD in the past (awareness). Fifty-nine (46.8%) of those that had CKD had no awareness as compared with ninety-eight (29.7%) of those without CKD and this was statistically significant. (p=0.001)

One hundred ninety-one (41.9%) of the participants had good knowledge while 136 (29.8%), 129 (28.3%) had fair and poor knowledge respectively.Eighty-five (67.5%) of participants with CKD had poor knowledge of CKD as compared with 180 (54.5%) of those without CKD and it was statistically significant. (p=0.032). The mean score of CKD group was significantly lower than that of non-CKD group. (p=0.002)

4.7.3 Hypertension

One hundred and thirteen (24.8%) of the participants had a history of hypertension. Forty-one (32.5%) of those with CKD had history of hypertension as compared to 72(21.8%) of theparticipants without CKD. This was statistically significant. (x^2=5.623, p=0.018).

Ninety-one (20.0%) had family history of hypertension. Newly diagnosed hypertensive was 18(3.9%)in the study. The total prevalence of hypertension was 28.7%. Forty-five (35.7%) of the CKD population had hypertension compared with non-CKD population and it was statistically significant. (p=0.049).The mean arterial pressure for CKD group was 100.6 (±20.2) mmHg as compared to non-CKD group with MAP of 97.2 (±16.1)mmHg, this difference was statistically

significant with p=0.007. The MAP and the systolic and diastolic blood pressures across the CKD groupsare as shown in the table 6.

Table 6. Mean Blood Pressure and Stages of CKD.

Stages of CKD	mean arterial Pressure	Systolic	diastolic
	Mean	Mean	Mean
1	100.00	131	85
2	98.17	132	80
3a	103.37	141	84
3b	97.27	135	78
4	95.48	135	75
5	-	-	-

CKD - Chronic kidney disease

4.7.4 Exposure to mercury soap, analgesics and herbs

Thirty-eight (30.2%) of the participants with CKD had used medicated soaps or creams.

One hundred and twenty (95.2%) of the participants with CKD used analgesics as compared with two hundred and ninety-eight (90.3%) of those without CKD, and the difference wasnot statistically significant. (p=0.088).

One hundred and five (83.3%) of those that had CKD took herbal concoctionsas compared to two hundred and fifty-three (76.9%) of those without CKD, but this difference was not statistically significant. (p=0.134)

4.7.5 Lipids

Ninety (20.6%) of the participants had elevated level of total cholesterol. Thirty-six (28.6%) of CKD population had high level of cholesterol compared to fifty-eight (17.6%) of the population without CKD and it was statistically significant (p=0.009).

One hundred and eighty-seven (41.0%) of the total population had elevated level of LDL. Sixty-six (52.4%) of CKD population had elevated level of LDL compared to one hundred and one (36.7%) of those without CKD and this difference was statistically significant (p=0.002).

One hundred and nine (23.9%) of the total population had elevated triglyceride. Twenty-eight (22.5%) of the CKD participants had high level of triglyceride compared to eight-one (24.5%)of those without CKD and this difference was not statistical significant. (p=0.603)

Forty-eight (10.5%) of the participants had low level of HDL. Fifteen (11.9%) of the CKD population had low level of HDL compared to thirty-three (10.0%) of those without CKD and thisdifference was not statistically significant. (p=0.553)

Two hundred and fifty-seven (56.4%) of the total population had dyslipidaemia. Eighty (63.5%) of the CKD population had dyslipidaemia compared to one hundred and seventy-seven (53.6%) of those without CKD. (p=0.056).

4.7.6 Alcohol and Smoking

One hundred and twenty (26.3%) of the participants indulged in alcohol consumption. Thirty-two (25.4%) of CKD population consumed alcohol compared to eighty-eight (26.7%) of the participants without CKD. It was not statistically different (p=0.783)

Thirty (6.6%) of the total population smoked cigarettes. Ten (7.9%) of the participants with CKD had history of smoking compared to twenty (6.1%) of those without CKD but it is not statistically different (p=0.480).

4.7.7 Haematuria

Seventeen (3.7%) of the total population had history of haematuria. Four (3.7%) of the participants with CKD had haematuria compared to thirteen (3.9%) of those without CKD.It was not statistically significant.(p=0.710)

4.7.8 Sore Throat/Skin rash and Body Swelling

One hundred and sixty-seven (36.9%) of the total population had history of sore throat/skin rashes. Forty-two (33.3%) of participants with CKD had history of sore throat compared to 24(7.3%) of those without CKD. (p=0.333) Three (2.4%) of the participants with CKD had history of body swelling compared to 123(28.9%) of those without CKD. (p=0.45)

4.8.9 Proteinuria

Twenty (62.8%) participants with overt proteinuria had reduced eGFR compared to 22.2% of those without proteinuria. (x^2=25.811, p<0.001)

Twenty-one (53.8%) participants with microalbuminuria (ACR 30-300m) had reduced eGFR compared to 19.0% of those without albuminuria. (x^2=24.976, p<0.001).

4.8.10 Diabetes Mellitus

Ten (2.2%) of the participants were previously diagnosed to have DM while nine (2.0%) were newly diagnosed. The total prevalence of DM in the study was 4.2%.

34.9% of those that have diabetes had CKD compared with non-diabetes participants. (p=0.264)

4.8.11 Body Mass Index

In this study, as the BMI increases the percentage of people with CKD decreases. Eight (50%) of the participants that were underweight, 71(37.6%) of normal weight, 28(21.1%) of overweight, 3(10.0%) of obese and 3(17.3%) of morbidly obese had CKD.The mean BMI decreases with severity of CKD. (table7).Seventy nine (62.6%) of participants with CKD were either underweight or normal weight compared to 125(38.8%) of those without CKD and it was statistically significant. (p<0.001).

4.9 Logistic Regression

The major risk factors identified as strong predictors of CKD having adjusted for all the risk factors identified in this study are gender as females are more likely to have CKD (OR-0.550, 95% CI, 0.320-0.945), age which shown that the older the subject the more likely to develop CKD (OR-1.080, 95%CI, 1.059-1.102), BMI which revealed that the subjects with obesity are more likely to have CKD (OR-0.832, 95% CI, 0.785-0.882) and also the dyslipidaemia (OR-1.007, 95% CI, 0.978-1.032). Table 8.

Table 7: CKD and the mean BMI

Grades of CKD	Mean BMI
1	28.24
2	27.11
3a	25.20
3b	23.54
4	21.82
5	-

CKD- chronic kidney disease, BMI – body mass index

Table 8. Risk factors for CKD among the participants

	B	S.E.	Wald	df	Sig.	OR	95% C.I.for EXP(B)	
							Lower	Upper
age	.077	.010	57.989	1	<0.001	1.080	1.059	1.102
Female gender	-.597	.276	4.690	1	.030	.550	.320	.945
HTN	-.084	.345	.060	1	.807	.919	.468	1.806
BMI	-.184	.030	38.658	1	<0.001	.832	.785	.882
knowledge	.007	.015	.229	1	.632	1.007	.978	1.037
dyslipdemia	-.522	.258	4.092	1	.043	.593	.358	.984

MAP	-.001	.009	.008	1	.930	.999	.981	1.018
Constant	.371	1.305	.081	1	.776	1.449		

BMI – body mass index, OR – odd ratio, CI – confidence interval, HTN – hypertension, MAP – mean arterial pressure.

CHAPTER 5

DISCUSSION

Chronic kidney disease has assumed high priority as a disease of public health importance. The prevalence is rising at an epidemic proportion posing serious health and economic challenges that is difficult to surmount even by the developed nations. The number of patients with ESRD that will need renal replacement therapy has grown astronomicallyworldwide despite the large pre-clinical stage of CKD.[5]The burden is not well appreciated due to lack of hard data because of absence of community-based studies and a national survey to actually determine the true prevalence of CKD and its associated risk factors.

Most available data in Nigeria are hospital based. The few community-based reports are regional and most have failed to comprehensively examine the risk factors for CKD.The first task in dealing with this disease is to understand the magnitude of the problem through a well-structured community-based study, to provide data for effective planning.

This study was therefore conducted to contribute to the available literature on the magnitude of CKD in our environment. It was conducted in Aiyepe community, a prototype of Nigerian rural community.

The prevalence of CKD from this study was 27.6%. The prevalence is high in this study compared to findings in most local studies, Ulasi et al,[11]Abioye-Kuteyi[12] and Oluyombo[13] reported 11.4%, 19.9% and 18.8% respectively. Thedifferences in prevalence may be partly because the report above used MDRD formula while this study and report by Okoye et al used the CG formula to estimate GFR. The difference may also bedue to geographical variation as the studies were done in different locations. The prevalence in this study is however lower than 36% that was reported by Sumaili et al in Congo.[16]

Compared to other studies outside Africa, this prevalence is similar to the finding of 28.7% in KEEP[32] but higher than that of EPRICE[33] NHANES[18] and AUDIAB[35] with 12.7%, 13.7%, and 14.1% respectively. The NHANES III was a large epidemiologic study performed to evaluate the health and nutrition of the US population while the KEEP is an ongoing community-based health-screening program that focuses on people at high risk for developing CKD.

There was preponderance of subjects in stage 3 of CKD in this study which was in agreement with most quoted local and international studies. About 50% of participants with CKD were in stage 3a. This could be an advantage for early intervention to retard the progression of the disease. It has been well documented that CKD progresses relentlessly toESRD from 3b. Also among the participants with normal eGFR, most of the participants had eGFR that ranged between 60 to 70 ml/min/1.73m, this is a pointer to a future serious problem as many more of the participants could develop CKD if prompt preventive interventions are not instituted in the community.

The cut-off for normal serum creatinine in an adult from laboratory that analyzed the samples is 1.5mg/dL. Using serum creatinine alone the prevalence of CKD was 6.6%. This is far lower than

using eGFR and proteinuria in this study. This is because serum creatinine does nor rise until stage 3 of CKD.

Proteinuria as a marker of kidney disease was also assessed. The participantsthat were negative for proteinuria were assessed for microalbuminuria. The prevalence of albuminuria in our study was 16.3%, with microalbuminuria being 9% and macroalbuninuria 7.3%. Most participants with stage 3 CKD had overt proteinuria. This prevalence is similar to some of the studies done in Nigeria, Oluyombo et al[13] reported 17.9%. This is higher than 3.8% reported by Okoye et al[14] and 7.7% by Ulasi et al.[11]It is also higher than 2.4% in AUSDIAB,[35] 9.3% in KEEP[32] and 7.2% in Dutch PREVEND.

The prevalence of proteinuria from this study is high even though higher values were reported from other studies in Africa. The figures from the developed countries were far lower than ours. This underscores the high prevalence of chronic glomerulonephritis which is ascribed to predominance of infections in Africa. Proteinuria is a strong progression factor for CKD and also a cardiovascular risk factor.[128]

Age is a well-known risk factor for renal disease.[112] The mean age of the participants was 48.1(±15.7) years and had a significant association with CKD. The prevalence of CKD increased with increasing age irrespective of the gender. Furthermore, 50% of participants aged 60 years and above had CKD. Majority of participants aged 60 years and above had more advanced CKD.This was probably due to the effect of aging on the kidney with accompanying reduced renal blood flow and possible presence of essential hypertension. The structural and functional impact of biologic aging on the kidney is most evident when cumulative stress of inter-current insults, including infections, immunologic processes, drugs, toxins, or other organ failure, affect the patient. Donor kidneys demonstrate this change as the donor-kidney of people older than 55

years tend to fail more often than that of those of younger age.[112] The eGFR usually drops by 1ml/min/1.73m^2 per annum from age 40years. In this study more females had CKD compared to males but the difference was not significant.

The prevalence of hypertension in our study was high. The prevalence was 28.7%. Newly diagnosed hypertensives comprised of18 (3.9%)while 113(24.8%) were known hypertensives with elevated BP or on medication. This is comparable to the findings by Oluyombo et al[13] who reported 26.7%.This value was lower than that of Amira et al[91] who reported a prevalence of 36.3% in an unselected population. Hypertensionis one of the leading causes of ESRD worldwide.[48] It is the second leading cause in the United States after diabetes.[48] It is the commonest cause of CKD in Nigeria and most sub-Saharan Africa.[50,69]According to the United States renal data system, about 51-63% of all patients with CKD are hypertensive.[48]

In the Multiple Risk Factor Intervention Trial (MRFIT), no changes in the reciprocal creatinine slope were observed in white people, but a significant loss in kidney function was observed in black people despite similar levels of BP control.[52] Similarly, secondary analysis from the Modification of Diet in Renal Diseases (MDRD) study demonstrated that at equivalent mean arterial pressures greater than 98 mm Hg, black patients had a reduction in their GFR at a rate of approximately 1 ml/min/y more than white patients.[45] Strong evidence links the progression of CKD to systemic hypertension in diabetic and non-diabetic nephropathies.[48]

The higher prevalence of hypertension in this study may be attributed to changing life style of Africans with its attendant high salt intake and obesity which may have impacted on the prevalence of hypertension.

The prevalence of DM in our study was 4.2%. A prevalence of 2% was reported in South West Nigeria in 1989[9] and by 2006 the figure had risen to 13.1% as reported by Alebiosu et al.[51] More

recently, Ulasi et al in South East Nigeria reported a prevalence of 10.8% among patients admitted with CKD. Diabetes accounts for 11% of patients with ESRD in Nigeria[16] The prevalence from the national expert committee on non-communicable diseases was 2.2% and it is similar to 2.6% reported by Amiral et al.[135] Our figure corroborate that of Oluyombo et al[13] who reported 3.7% but there was no correlation between diabetes and CKD in this study.

Several studies have linked obesity and the associated metabolic syndrome, with increased risk of CKD. Excessive body weight and a raised body mass index have also been linked to a faster rate of progression of CKD. According to the Nigerian Demographic and Health Survey conducted in 2003, 27.7% and 9.6% of participants were found to be overweight and obese respectively.[79] The incidence of focal and segmental glomerulosclerosis is higher in obese than in lean individuals and the progression of IgA nephropathy is thought to be faster in overweight patients.[78] Obesity is also associated with focal segmental glomerulosclerosis (FSG).[78] Obesity has been associated with the initiation and progression of glomerulonephritides.[77] The prevalence of obesity in our study was 30%, while 24.4% of subjects were overweightand these was statistically significant association between BMI and presence of CKD. This prevalence was far higher than the values for Nigeria Demographic and Health Survey quoted above but lower than 27.7% reported by Oluyombo et al.[13,79] The 30% overweight in our study is comparable to 27.7% reported in Nigeria Demographic Health Survey. This still underscores increasingly westernized way of life vis-à-vis the diet and lack of exercise along with sedentary way of life. Surprisingly, this study showed a higher prevalence of CKD with a decreasing BMI. Similar report was given by Ulasi et al.[11] The prevalence of CKD decreases with increase in BMI. About 50% of underweight had CKD while only about 18.8% of the obese participant had CKD.

The role of dyslipidemia in the pathophysiology of atherosclerotic disease in patients with impaired renal function remains controversial. Thus, some studies have shown a positive association between cholesterol values and the risk for cardiovascular events in CKD individuals whereas others failed to find any significant correlation.[81,83,84] In the Atherosclerosis Risk In Communities (ARIC) study, HDL cholesterol and triglycerides were shown to be significant predictors of a rise in serum creatinine.[81] In this study, total cholesterol and LDL had significant association with CKD while triglyceride and HDL did not. However, dyslipidaemia was observed in about 50% of the participants and it has a significant association with CKD.

About 54.3% of the participants had good education. Female had statistically significant higher level of education than male and the elderly people have statistically significant lower level of education. There was significant association between level of education and CKD. The prevalence of CKD was higher in participants with low level of education.Also participants with low level of education had more advanced CKD. This probably was due to poor health seeking attitude behaviour.

Two hundred and ninety-nine (65.6%) of the participants had awareness of CKD. This also impacted positively on the prevalence of CKD with statistical significance. Only 20.1% of those that have good awareness had eGFR<60 while 34.4% of those that never heard of CKD had CKD.

Likewise poor knowledge about kidney diseases was significantly associated with low eGFR in this study. Only 41.9% had good knowledge which is a little better than 30% reported by Oluyombo et al[140] and Alebiosu et al.[139] Most participants with good awareness got information through mass media. This is probably due to request for money for kidney transplant on radio, newspaper and television which is common among patients needing kidney transplant.

Tobacco use in the community studied was in various forms, smoking, chewing and snuffing. (2.9% snuffing and 2.2% chewing). Cigarette smoking prevalence was 6.6% and this is similar to 7.2% reported by Oluyombo et al.[13] Chronic smoking, however, is associated with a marked risk of developing a proteinuria.[85,87] Cigarette smoking and tobacco chewing was not associated with CKD in this study. This may be due to the fact that only a small percentage of the participants indulged in this habit.

Alcohol intake was found in 26.3% of participants but was not associated with CKD in this study. However, contrary to putative protective effect of moderate drinking, the link between alcohol and hypertension is well established.[85]Alcoholism can result in autonomic neuropathy and cardiomyopathy that can lead to a fall in blood pressure and CKD. For control of hypertension, cessation or at least reduction of alcohol intake is the first step.[86]

Consumption of herbal concoction and intake of analgesic did not have an association with CKD. However about 91.7% and 78.7% of the participants indulged in taking pain killer and herbal concoctions respectively. Almost all participant who indulged in the act consumed water based concoction which might probably reduce the toxic effects on the kidney. The use of mercury containing soap and cream was found to have association with CKD in our study.

CONCLUSIONS

There was high prevalence of chronic kidney disease in Aiyepe (27.6%) and this may be a reflection of prevalence of CKD in rural community in Nigeria.

There was also high prevalence of risk factorsfor CKD in the community particularly hypertension (28.9%),diabetes (4.2%), and proteinuria (16.3%).

Worthy of note is the high prevalence of dyslipidaemia (56.4%) and obesity (30%) in the community. All these are strong risk factors for cardiovascular diseases.

There was high intake of herbal concoctions in the community with unlimited access to analgesics especially NSAIDS and paracetamol. The high intake of un-recommended analgesics could be adduced to the nature of their work. This could be part of factors impacting on the high

prevalence of CKD in the community. Efforts must be geared towards correcting this unhealthy practice.

The level of education and awareness was fair and it reflected on the prevalence of CKD. Participants with good knowledge had a lower prevalence of CKD hence health education aimed at maintaining good kidney health should be encouraged.

This study provided a unique opportunity for intervention to retard the progression of CKD in majority of the participants. Unlike most other studies large numbers of affected people are in stage 3a of CKD (52%) which is easier and better to manage than the later stages through control of blood pressure,reduction of proteinuria, management of dyslipedaemia, avoidance of nephrotoxic drugs like analgesics and herbal concoctions as well as life style changes.

This finding of high prevalence of modifiable risk factors and CKD 3a strongly indicates that community screening would be a useful tool toward early intervention and slowing of CKD progression to end-stage renal disease.

RECOMMENDATIONS

CKD is a disease of public health concern. The high prevalence of CKD and its associated risk factors in our study is alarming because if they progress to ESRD it will pose a serious economic challenge to the individual and the nation. The only viable alternative is to halt the progression. It is therefore recommended as follows;

1. Education and awareness should be heightened in the community about CKD and its risk factors.
2. More health facilities should be provided for easy access to healthcare to curb the menace of self-medication and the use of herbal concoction.

3. Health personnel at health centers should be trained on how to recognize CKD and the risk factors and the need for prompt referral to nephrology facilities.
4. Dip stick urine test should be routine in our health centers and schools for early detection of proteinuria.
5. Treatment of risk factors like hypertension and DM should be made free or affordable by the government or through health insurance considering the socio-economic status of most individuals affected.
6. Nationwide epidemiological survey is advocated.

LIMITATIONS OF THE STUDY

1. The GFR was estimated using CG equation from serum creatinine with its attendant problems.

3. Some of the participants could not remember their age,and ages had to be estimated using land mark events.

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APPENDICES

Appendix 1: Sketch Map of Aiyepe village.


SKETCH MAP OF AYEPE
N
KALEJAYE
OLUPITAN STR
NKT
OBIRI QTRS
OLOWOPOREKU STR.
ABA QUARTERS
KALIBE STR.
OBIRI STR.
ROAD
IKENNE
ODE OLOWU QTRS
ATO QUARTERS
COLLEGE ROAD
ALAKARA QTRS
SOKARI STREET
ODOGBOLU
ROAD
Ayepe Central Mosque

APPENDIX 2

RESEARCH PROTOCOL ON STUDY OF THE PREVALENCE OF CHRONIC KIDNEY DISEASE

A. BIODATA

Informed consent Y/N

Identify number;

Age ----------

Sex ----------

Religion……

Occupation(Lastone)…….PreviousOccupation……..

Level of education – No-formal ☐ Primary ☐ Secondary ☐ Tertiary ☐ others

Arabic----------

For how long have you been living here? ----------

Reassurance: Explain the purpose of the research to the participant. Thank you for cooperation and for helping us. You can refuse to answer any question.

B. KNOWLEDGE AND AWARENESS.

(1) Have you ever heard of kidney disease? Yes ☐ No ☐ No Response ☐

(2) How did you hear about it? (a) Mass media ☐ (b) Health workers ☐

(c) Traditional healers ☐ (d) others not specified ☐

Answer the following questions on kidney?

(3) Where are the kidneys found in human being (a)chest ☐ (b) abdomen ☐

(c)Pelvic girdle ☐ (d) Other area ☐

(4) How many kidneys does an individual have? (a) 1 ☐ (b) 2 ☐ (c) 3 ☐ (d) Other ☐

(5) Does the number of kidneys vary between males and females? Yes ☐ No ☐

☐

Don't know

(6) Name functions of the kidney you know

i. ---------- ii. ----------

iii. ---------- iv Don't know

(7) To you, which of these features will suggest kidney disease?

(a) Pain in the sides of abdomen Yes ☐ No ☐ Don't know ☐

(b) Pain in lower abdomen Yes ☐ No ☐ Don't know ☐

(c) Painful Urination Yes ☐ No ☐ Don't know ☐

(d) Blood in urine Yes ☐ No ☐ Don't know ☐

(e) Frothy urine Yes ☐ No ☐ Don't know ☐

(f) Body swelling Yes ☐ No ☐ Don't know ☐

(g) Excessive Urination Yes ☐ No ☐ Don't know ☐

(h) Frequent Urination in the night Yes ☐ No ☐ Don't know ☐

(8) Do you think that these habits make one to be at risk of kidney disease?

(a) Cigarette smoking Yes ☐ No ☐ Don't know ☐

(b) Alcohol intake Yes ☐ No ☐ Don't` know ☐

(c) Use of herbal concoction Yes ☐ No ☐ Don't know ☐

(d) Eating too much salt Yes ☐ No ☐ Don't know ☐

(e) Eating lots of meat Yes ☐ No ☐ Don't know ☐

(f) Eating sweet foods Yes ☐ No ☐ Don't know ☐

(g) Lack of exercise Yes ☐ No ☐ Don't know ☐

☐

(f) Some pain killing drugs such as Aspirin, Paracetamol Yes ☐ No ☐ Don't know

(9) Can you tell me any laboratory test of kidney disease? Yes ☐ No ☐ Don'tknow ☐

if Yes, List them (i) ☐ (ii) ☐

(10) Can Kidney disease be healed? Yes ☐ No ☐ Don'tknow ☐

If yes, how?

(a) Spiritual means ☐

(b) Taking herbal concoction ☐

(c) Surgical operation ☐

(d) Drugs ☐

(e) Others ☐

(11) Have you heard about dialysis? Yes ☐ No ☐ Don't know ☐

(12) Have you heard of kidney transplant? Yes ☐ No ☐ Don't know ☐

(13) Have you ever heard about high blood pressure? Yes ☐ No ☐ Don't know ☐

If Yes, how long? ☐

(14) Can you tell me what high blood pressure cause? Yes ☐ No ☐ Don't know ☐

If yes, please list…….

C Risk Factors Assessment

(15) Have you been to the Hospital in the past one year? Yes ☐ No ☐

☐ ☐

(16) Have you ever been told by a doctor that you have diabetes? Yes No

If yes, how long?.....

(17) Which of these tests have you had done?

Blood pressure ☐

Urine test ☐

Blood Sugar ☐

Other blood test ☐ if yes state type

(18) Are you on treatment for diabetes? Yes ☐ No ☐

(19) Do you have family history of hypertension or has any of your family members suffered a stroke or sudden death? Yes ☐ No ☐ Don't know ☐

(20) Have you ever been told to have hypertension? Yes ☐ No ☐

(21) Do you have family history of diabetes? Yes ☐ No ☐ Don't know ☐

(22) Do you smoke cigarettes? Yes ☐ No ☐ If yes what type? ……

How many sticks per day?.....

(23) Do you use Snuff? Yes ☐ No ☐

(24) Do you chew tobacco leaves? Yes ☐ No ☐

If yes, How long? ----------

(25) Do you drink alcohol? Yes ☐ No ☐

If Yes, What brand (a) beer ☐ (b) spirit ☐ (c) palm wine ☐ (d) combined ☐

What quantity? (a) week ☐ average? ☐

For how long? ----------

(26) Do you take pain killing drugs? Yes ☐ No ☐

If yes which one. …

If Yes how often (i) daily ☐ (2) most days of the week ☐ (3) about twice a week ☐

(4) once or less in a month. ☐

Is it on prescription by a doctor/ health worker? Yes ☐ No ☐

For how long (1) less than 6months ☐ (2) >6months. ☐

(27) Do you take traditional medicine (Herbal concoction)? Yes ☐ No ☐

If yes, how often (1) daily ☐ (2) most days of the week ☐ (3) about twice a

week ☐ (4) once or less in a month. ☐

(28) For how long? (1) less than 6months ☐ (2) >6months. ☐

What type of herbs do you use?

(29) Do you use slimming herbs? Yes ☐ No ☐

(30)Have you ever taken Zobo drink? Yes ☐ No ☐

If yes how often (a) Daily ☐ (b) >2ce/week ☐ (c) 1ce/week ☐ Others ☐

(31) Do you use medicated soap/ cream? Yes ☐ No ☐

Which type? Name please. ----------

For how long (1) less than 6months ☐ (2) >6months. ☐

(32) Have you had blood in urine in the past? Yes ☐ No ☐

If Yes, (a)is it at the end of urine ☐ b) continuous throughout the urine stream. ☐

if yes, how old were you then?.....

(33) Do you know if you were born at 9months ☐ less than 9months ☐

>9m of pregnancy? ☐

(34) Are you a twin? Yes ☐ No ☐

(35) Were you told if you were very small at birth? Yes ☐ No ☐

(36) Were you told if you were very big at birth? Yes ☐ No ☐

(37) Have you had sore throat/skin rash in the past? Yes ☐ No ☐

(38) Have you had body swelling in the past? Yes ☐ No ☐ Don't know ☐

(39) Do you have history of kidney disease in any of your siblings or parents?

Yes ☐ No ☐ Don't know ☐

(40) Have you ever engaged in any of the following occupations?

(a) Battery charging. ☐ (b) Auto-mechanic. ☐ (c) Furniture making. ☐

(d) Spraying. ☐ (e) Fuel station attendant. ☐ (f) House painting. ☐

(41) Do you use insecticides sprays? at house? C☐ farm ☐

If yes, for how long……

(42) Do you protect yourself by wearing protective boot, gloves and face mask Yes ☐ No ☐

D CLINICAL ASSESSMENT (to be done before 12noon)

Blood Pressure (5 min after subject might have seated)

Systolic 1 Diastolic 1 Weight (kg) ----------

2 2

3 3 Height (m) ----------

Waist circumference (cm) = Hip circumference (cm) =

BIOCHEMICAL VALUES

Urinalysis –Protein, RBC WBC Glucose Nitrates

Casts Crystals Cells

Urine microscopy ----------

Proteinuria.

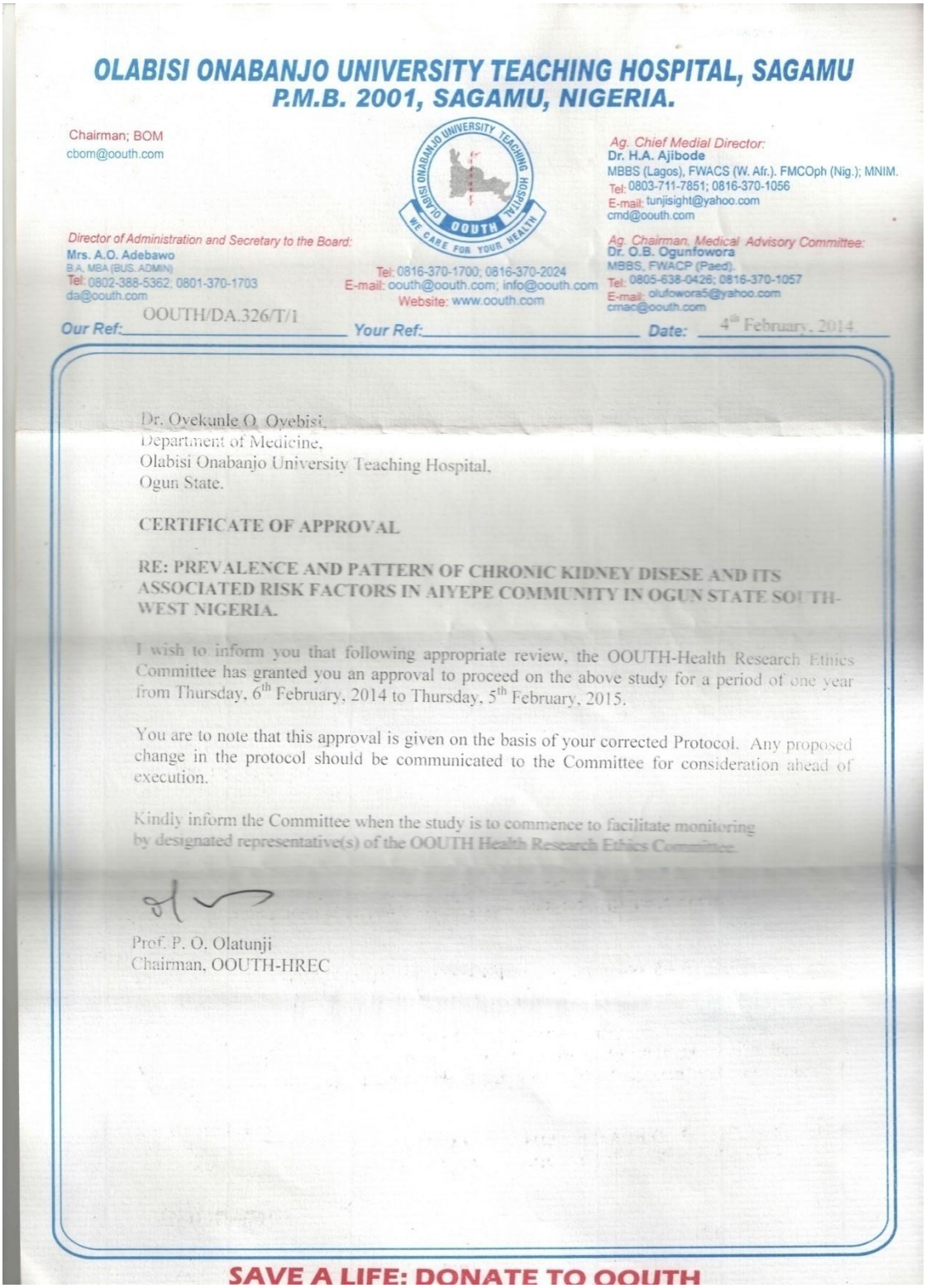
Blood sugar (fasting) and or HbA1c Albumin: creatinine ratio

Serum creatinine-- Serum Alburm Alburm: Creatinine ratio

Urine creatinine--- Creatinine clearance (ml/min) --

Urine albumin---- Packed cell volume (%) ……

Appendix 3: Ethical approval



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Our Ref: OOUTH/DA.326/T/1 Your Ref: Date: 4th February, 2014

Dr. Oyekunle O. Oyebisi,
Department of Medicine,
Olabisi Onabanjo University Teaching Hospital,
Ogun State.

CERTIFICATE OF APPROVAL

RE: PREVALENCE AND PATTERN OF CHRONIC KIDNEY DISESE AND ITS ASSOCIATED RISK FACTORS IN AIYEPE COMMUNITY IN OGUN STATE SOUTH-WEST NIGERIA.

I wish to inform you that following appropriate review, the OOUTH-Health Research Ethics Committee has granted you an approval to proceed on the above study for a period of one year from Thursday, 6th February, 2014 to Thursday, 5th February, 2015.

You are to note that this approval is given on the basis of your corrected Protocol. Any proposed change in the protocol should be communicated to the Committee for consideration ahead of execution.

Kindly inform the Committee when the study is to commence to facilitate monitoring by designated representative(s) of the OOUTH Health Research Ethics Committee.

Prof. P. O. Olatunji
Chairman, OOUTH-HREC

SAVE A LIFE: DONATE TO OOUTH

APPENDIX 4: Consent form

CONSENT FORM

I_____ have been duly informed about the study titled Prevalence and Pattern of Chronic Kidney Disease and its associated risk factor in Aiyepe, South-West Nigeria by Dr. Oyebisi Oyekunle O. of OOUTH, Sagamu, Ogun State, the coordinator of the research.

I have had the opportunity to ask questions and my questions had been answered to my satisfaction.

I hereby agree to participate in this study and I know that my participation is voluntary and that my refusal will not affect my treatment in anyway.

I consent to being examined clinically and have some urine and blood test done on me.

I agreed that the findings be made public provided my identity is not revealed.

Name of participant……..

Signature and date……

I confirm that I have given an explanation on the purpose, benefits, natures and hazards of this study to the above named participant who has agreed to participate.

Name of Researcher……

Signature and date……..