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PREVALENCE OF AND FACTORS ASSOCIATED WITH CHRONIC KIDNEY DISEASE IN OSTEOARTHRITIS PATIENTS AT KENYATTA NATIONAL HOSPITAL

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A dissertation submitted in partial fulfilment of the requirements for the degree of Master of Medicine in Internal Medicine

DECLARATION

This dissertation is my original work and has been presented as a prerequisite to the award of a master's degree in Internal Medicine of the University of Nairobi. All resources and materials used or quoted have been indicated and acknowledged appropriately. This dissertation has not been presented for any degree to any other university.

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LIST OF ABBREVIATIONS AND ACRONYMNS

ACEI:	Angiotensin-Converting Enzyme Inhibitors
ACR:	American College of Rheumatology
AD:	Antidiabetics
AH	Antihypertensive
AIDS:	Acquired Immunodeficiency Syndrome
AIN:	Acute Interstitial Nephritis
AOR:	Adjusted Odds Ratio
ARBs:	Angiotensin Receptor Blockers
AS:	Anti-statins
ATN:	Acute Tubular Necrosis
BMI:	Body Mass Index
CG:	Cockcroft-Gault
CI:	Confidence Interval
CIN:	Chronic Interstitial Nephritis
CKD-Epi:	Chronic Kidney Disease–Epidemiology
CKD:	Chronic Kidney Disease
COR:	Crude Odds Ratio
COX-2:	Cyclooxygenase-2
CREDIT:	Chronic Renal Disease in Turkey
CVDs:	Cardiovascular Diseases
DBP:	Diastolic blood pressure
eGFR:	Estimated Glomerular Filtration Rate
ESRD:	End-Stage Renal Disease
EULAR:	European League against Rheumatism
GFR:	Glomerular Filtration Rate
GPAQ:	Global Physical Activity Questionnaire
HIV:	Human Immunodeficiency Virus
IHD:	Ischaemic Heart Disease
IQR:	Interquartile Range

JNC:	Joint National Committee
KDIGO:	Kidney Disease Improving Global Outcomes
KEEP:	Kidney Early Evaluation Program
KNH:	Kenyatta National Hospital
LDL:	Low-Density Lipoprotein
LMIC:	Low-Middle Income Countries
MDRD:	Modified Diet Renal Disease
NSAIDS:	Non-steroidal Anti-inflammatory Drugs
OA:	Osteoarthritis
RA:	Rheumatoid Arthritis
SBP:	Systolic blood pressure
SD:	Standard Deviation
SSA:	Sub-Saharan Africa
US:	United States
USD:	United States Dollar
WHR:	Waist-Hip Circumference
YLD:	Years Lived with Disability

DEFINITION OF KEY TERMS

Osteoarthritis: A degenerative joint disorder arising from biochemical breakdown of articular cartilage and surrounding joint structures.

Chronic Kidney Disease: Progressive loss of kidney function that can occur over many years.

Creatinine: A waste product produced by metabolism of creatine during normal breakdown of muscle tissue and excreted in urine.

Proteinuria: Excess protein in urine.

Estimated Glomerular Filtration Rate: A test to measure level of kidney function and determine your stage of kidney disease calculated using blood creatinine level, age, weight and gender.

Prevalence: Proportion of a given population with a particular condition at a specific point in time.

Physical Activity: Any bodily activity produced by skeletal muscles that requires energy expenditure. Measured through Metabolic Equivalents (METs) (i.e. the ratio of a person's working metabolic rate relative to their resting metabolic rate); which are commonly used to express the intensity of physical activity. Can be moderate-intensity (3-6 METs) or vigorous-intensity (>6 METs).

ABSTRACT

Background: Chronic Kidney disease (CKD) is a global health problem with increasing prevalence especially in Sub-Saharan Africa. It has a high morbidity and mortality. CKD and Osteoarthritis (OA) are related as they both increase with age and are associated with comorbidities e.g. hypertension, obesity, dyslipidaemia and diabetes. However, there is limited evidence on the prevalence of CKD and associated risk factors among OA patients.

Objectives: To assess the prevalence and factors associated with chronic kidney disease in osteoarthritis patients attending rheumatology and orthopaedic clinics in Kenyatta National Hospital.

Method: A cross-sectional study was conducted between November 2019 and January 2020. Patients aged 18 years and above; being followed up in the rheumatology and orthopaedic clinics at KNH with a diagnosis of knee, hip, spine and hand osteoarthritis based on the American College of Rheumatology (ACR) criteria were included. CKD was defined as an estimated Glomerular Filtration (eGFR) of less than or equal to 60ml/min/1.73m^{2}and/or proteinuria of 30mg/dl detected on urinary dipstick for three months or more. Descriptive statistics were used to describe the participants. The association between participants' characteristics and CKD prevalence were assessed using chi-square test. Factors associated with CKD among osteoarthritis patients were analysed using bivariate and multivariable logistic regressions.

Findings: The overall prevalence of CKD among patients with osteoarthritis was 61.9% (95 %CI:56.4–66.3) as per eGFR using Cockcroft Gault (CG) formula. Most were in CKD stage 3 at 59.2% with 45.5% in G3a and 13.7% in G3b. 1.1% were in stage 1, 38.3% in stage 2 and 1.4% were in CKD stage 4 and 5. Only 12.1% of the respondents had persistent proteinuria and thus most of the patients had low and moderate risk for CKD progression at 38% and 38.2% respectively.Only12.1% and 11.6% had high and very high risk for CKD progression. The CKD prevalence increased with age, being highest among older adults (65+ years). The prevalence was higher among men than women (65.9%, 95% CI: 54.7–75.5 vs.60.2%, 95% CI: 54.4–65.7).The factors associated with CKD in OA were old age, hypertension, poor and fair self-rated health and use of more than one medication (NSAID/ACEI/ARB) which

increased the odds of CKD while moderate physical activity and overweight/obesity reduced the odds of CKD.

Conclusion: This study provides evidence that osteoarthritis is associated with a high prevalence of CKD. However, most of the patients are asymptomatic and in low and moderate risk category based on KDIGO nomenclature. OA patients should be considered a high-risk group for CKD given their older age, chronic use of NSAIDs and high prevalence of comorbidities e.g. hypertension, overweight/obesity which are known risk factors for CKD. Screening for CKD in OA patients should therefore be done routinely as is the case in other high-risk groups e.g. diabetes.

CHAPTER ONE: INTRODUCTION AND PROBLEM STATEMENT

1.1 Introduction

Chronic kidney disease is a recognized global public health problem whose effects are felt across different socioeconomic divides. It directly resulted in an estimated 1.23 million deaths in 2017. It was the 12th leading cause of death globally in 2017. In addition to deaths resulting from CKD, impaired kidney function puts individuals at a higher risk for cardiovascular disease. In 2017, 1.36 million deaths were attributable to cardiovascular disease resulting from impaired kidney function (1).

Chronic kidney disease (CKD) and osteoarthritis (OA) are among the top thirty largest contributors to the years-lived with a disability (YLD) (2). Chronic kidney disease moved up four places to 24th between 1990 and 2015 and contributed to approximately 8172.8 YLDs (2). CKD is a known complication of other diseases, a comorbid condition, and a side effect of some medications with major impacts on health, healthcare cost and productivity(3). The CKD prevalence is estimated to be 13.4% globally(4). In sub-Saharan Africa, CKD prevalence is 15.8% for stages 1 to 5 and 4.6% for stages 3 to 5 (5). Urban populations have a higher CKD prevalence than rural populations (6). In Kenya, the prevalence of CKD was estimated at 0.41% in Kericho County (7) to a high of 10%-26% based on the global estimates of CKD(8-11).

Osteoarthritis (OA), a painful, upper and lower extremities degenerative joint disease has been on the rise globally(12, 13). Osteoarthritis affects 30 million people in the US resulting in a prevalence of 6% and 3% for symptomatic knee and hip OA respectively(14) while Canada has an overall prevalence of OA of 14.8% (15). In India, the prevalence is estimated at between 21.6–29.7% (16, 17). In Kenya, knee, hip and hand OA prevalence is 15%, 3% and 5% respectively(18).

Non-steroidal anti-inflammatory drugs (NSAIDs) use is a key mechanism linking chronic kidney disease and osteoarthritis. NSAIDs toxic mechanisms to the renal system are two-fold with both functional and inflammatory mechanisms. Approximately, 1–5% or 2.5 million of the patients using NSAIDs are known to experience adverse renal events annually (19-21). All forms of NSAIDs can result in medicine-induced kidney disease, acute kidney injury,

haematuria, proteinuria, flank pain, acute tubular necrosis and interstitial nephritis (21). NSAIDs use contributes to CKD progression (22, 23).

In a retrospective study on young and middle-aged active adults in the United States to assess association between NSAIDs and kidney disease, a modest but statistically significant association was noted between those on high doses of NSAID exposure and kidney disease. A strong association was also noted between CKD and age with a 7-fold increase in hazard ratio in those 50 years and older and CKD and ethnicity with higher levels noted in the African-American participants(18). NSAIDs use is prevalent among CKD and osteoarthritis patients despite their known renal, cardiovascular, and gastrointestinal adverse effects. In Egypt, 65.7% of the patients with CKD were found to use NSAIDs with 36% reporting drug-drug interaction (19). Comorbid CKD has been found among patients with osteoarthritis. In a knee osteoarthritis study, 97% of the CKD group had knee osteoarthritis in comparison to 97.8% knee osteoarthritis prevalence in the control group (24). In an Egyptian CKD study among knee OA and obese patients, 65% of them had CKD (25). The joint risk factors of OA and CKD include old age, being female, hypertension, and diabetes (26, 27). Both diseases independently and jointly impacts patients' quality of life, morbidity and mortality (28).

Hence, the study assessed the prevalence and factors associated with CKD in the osteoarthritis patients given the high rates of association between osteoarthritis and chronic conditions associated with chronic kidney disease (hypertension, diabetes, obesity)(29) and its increased prevalence in the aging population. Our findings will contribute towards management of OA with minimal risk of nephrotoxicity.

1.2 Problem Statement

Chronic kidney disease is a public health problem globally. Its prevalence is on the rise and its debilitating effect on quality of life is undeniable.

Osteoarthritis is also an extremely common cause of medical consultation especially among older adults. The prevalence of risk factors for chronic kidney disease in osteoarthritis patients is high. This has been demonstrated by studies done across the world including Kenya where 51%, 21% and 59.5% of osteoarthritis patients were found to have hypertension, diabetes and overweight or obesity respectively (29). It is also known that OA

patients have chronic, debilitating pain and are on chronic NSAID use. NSAIDs are known to be nephrotoxic and studies have demonstrated chronic NSAID use leads to progression of chronic kidney disease (30). However, no studies have been done in Africa including Kenya to assess the prevalence and the associated risk factors of CKD in this population of patients. Therefore, the study established the burden of CKD in osteoarthritis patients seen at Kenyatta National Hospital and the associated risk factors.

CHAPTER TWO: LITERATURE REVIEW

2.1 Chronic Kidney Disease

Chronic kidney disease (CKD) is a global health problem and contributes to approximately 8172.8 YLDs (1, 2). CKD is a known comorbid condition, complication of other illnesses and side effect of some medications. It has major impacts on health, healthcare cost and productivity (3).

The 2012 KDIGO guidelines define CKD as eGFR <60 mL/min/1.73m^2 and/or kidney damage markers for three or more months. Kidney damage markers include albuminuria, proteinuria, electrolyte imbalances associated with tubular disorders, urine sediment abnormalities, histologically detected abnormalities, and history of kidney transplantation. Table 1 and Figure 1 highlight the five stages of CKD based on kidney function levels (eGFR)(31). Staging of CKD is based on the six categories of GFR (Table 1) and the three categories of albuminuria (A1–A3). These readings used together provide a very useful tool for risk stratification and can be used to not only diagnose but to monitor and predict prognosis. At mild to moderate stages of CKD (3A and 3B), the incidence of cardiovascular mortality is high and exceeds that of kidney failure. However, reduced eGFR and albuminuria are associated with increased risk of hospitalization with acute myocardial infarction, congestive heart failure and peripheral vascular disease (32)

Patients with CKD are mostly asymptomatic, but some may present with symptoms that are kidney-related such as haematuria and flank pain and/or other symptoms like hypertension, uraemia, and oedema. CKD diagnosis and initial management depends on a patient's history, clinical and physical examination, and laboratory tests. An abnormal urinalysis is one of the most common indicators of altered renal function with elevated serum creatinine concentration being indicative of CKD. GFR can be measured or estimated but it is commonly estimated using serum markers such as plasma creatinine(31).

Table 1. Classification of CKD using eGFR according to KDIGO criteria (31, 33)

CKD Stage	GFR, mL/min/1.73 m^2
I	≥90
II	60–89
IIIa	45–59
IIIb	30–44
IV	15–29
V	<15

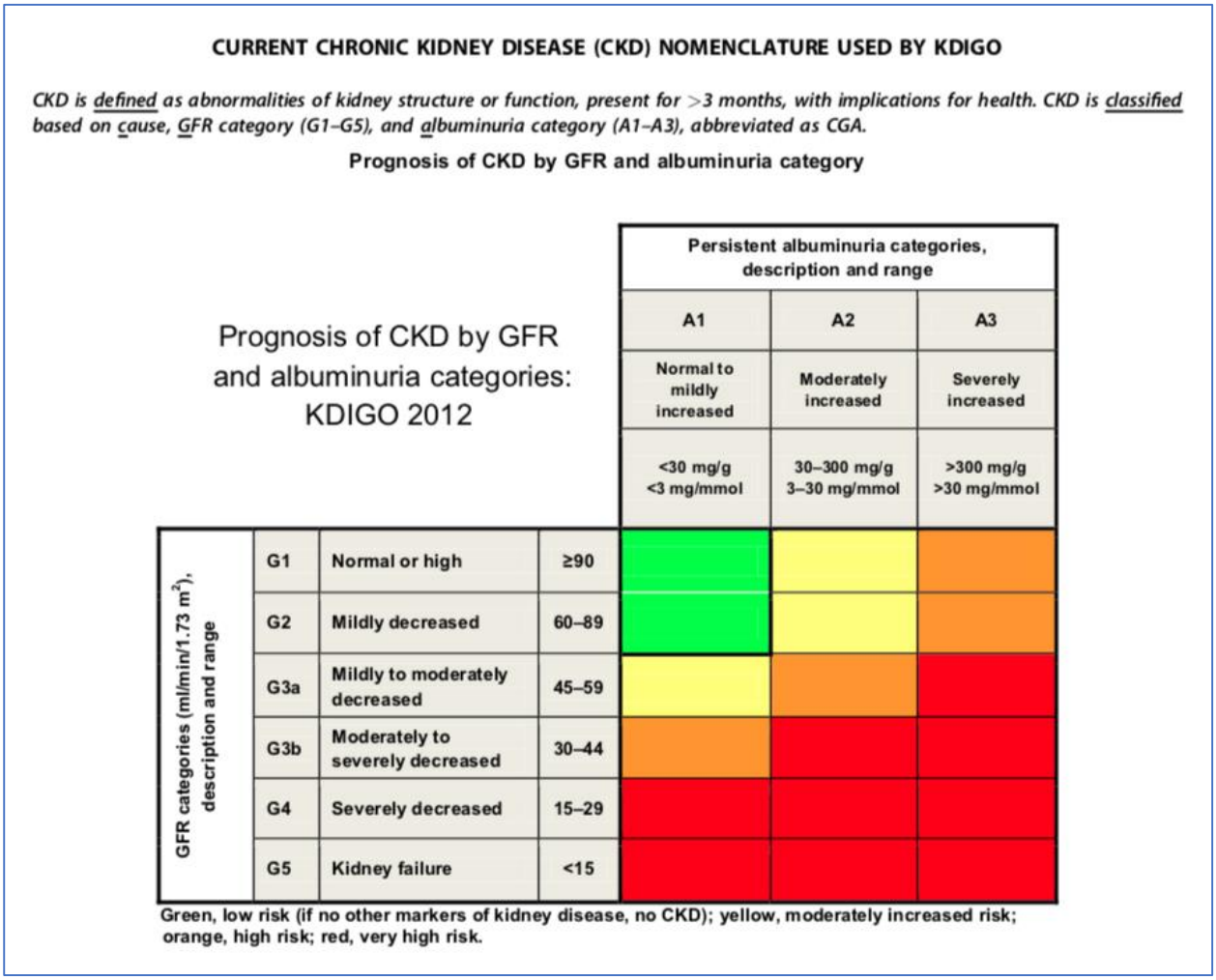

Figure 1. *Current nomenclature used by KDIGO for staging CKD (31, 33)*

2.2 Prevalence of Chronic Kidney Disease

Globally, the CKD prevalence is 13.4% with 10.6% for CKD stages 3–5. Stage 1 and 2 CKD are the most prevalent at 35% and 39% respectively (4). In sub-Saharan Africa (SSA), prevalence for CKD stages 1 to 5 and stages 3 to 5 is 15.8% and 4.6% respectively (5). CKD prevalence is high in SSA compared to the North Africa (17.7% vs. 6.1%) (5), and ranges between 12.4% in urban and 16.5% in rural SSA (6). In Cape Town, South Africa, CKD prevalence was 6.1% and 10% using CKD-EPI and MDRD equation (34) while it was estimated at 1.9% among Nigerians(35). In Ghana, CKD prevalence was 46.9% with 19.1% in stages 1 to 2, 27.8% in stages 3 to 5 and 28.9% with proteinuria (36).

In Tanzania, CKD prevalence is estimated at 13.6% (11–16%) for G3a-G5 eGFR categories and A2-A3 albuminuria categories (3). CKD was most prevalent at 11.2% among patients with moderately increased albuminuria(3). Another study in Tanzania estimated CKD prevalence to be 69.5% (37) while in Uganda, CKD prevalence was 15.2% while the prevalence of stage 1, 2, 3 and 5 was 6.2%, 12.7%, 2.4% and 0.1% respectively (38). In Kenya, a recent study in Kericho county among hospital admissions, CKD prevalence was estimated at 0.31%, 0.39% and 0.46% in 2013, 2014 and 2015 respectively, with an average of 0.41% (41 people per 10,000 populations)(7).

The prevalence of CKD is high among some high-risk groups. In the high-risk populations (hypertension, diabetes and HIV patients), a review found the prevalence of CKD to be 32.3% and 13.3% for stages 1–5 and 3–5 respectively (5) and especially high among hypertensive (35.6%), diabetes (32.6%) and HIV patients (27.3%) (5). In Kinshasa, 36% of the high-risk patients had CKD; eighty-eight per cent of the CKD being undiagnosed. A majority of the patients had stage 3 CKD (18%) while only 4% were in stage 1, 6% stage 2, 6% stage 5 and 2% stage 4 (39).Other factors associated with CKD include high socioeconomic status and use of agrochemicals. A high social economic status was associated with kidney disease in Uganda (38). Moreover, the use of agrochemicals in farming among the majority of agricultural communities contributes to the prevalence of CKD in Kericho, Kenya (7). However, no studies done locally or in Africa have shown an association between prevalence of CKD and NSAID use. This is due to exclusion of drug

history e.g. NSAID use as one of the variables of interest in most of the studies assessing CKD prevalence.

CKD is diagnosed based on either CG, CKD-Epi and MDRD formula and proteinuria or albuminuria(6). Ndosi et. al 2009 demonstrated both Cockcroft-Gault and MDRD methods are comparable to measuring 24-hour creatinine clearance in patients with CKD at KNH (40).

2.3 Osteoarthritis (OA)

OA is a painful, upper and lower extremities degenerative joint disease that has been on the rise globally (12, 13). It was the 13th contributor of the YLDs in 2015 (2) and results in reduced quality of life, increased discomfort, reduced productivity, and increased hospitalization costs (12, 41, 42). It has a significant economic and psychological burden to the patient and their families (12).

2.3.1 Diagnosis and Management of Osteoarthritis

The ACR criterion classifies OA of the hip, knee, and hand while the EULAR diagnostic criterion classifies hand OA. ACR diagnoses knee OA based on: "knee pain and 3 of the following 6 criteria: more than 50 years of age, less than 30 minutes of morning stiffness, crepitus, bony tenderness, no enlargement, or an absence of palpable warmth" (43). According to EULAR, "three symptoms (persistent knee pain, limited morning stiffness, and reduced function) and three signs can be used to correctly diagnose a majority of the OA (crepitus, restricted movement, and bony enlargement)" (44).

The management of OA is dependent upon the clinical presentation of the patients. Management is instituted based on whether the patient has mild, moderate, or severe OA or involvement of one or both joints and presence of comorbidities. It also requires both pharmacological (mostly NSAIDs) and non-pharmacological therapies (physical exercise, aquatic exercise, losing weight, and other strength-based exercises) (45).

2.4 Prevalence of Osteoarthritis

The prevalence of OA varies based on whether the OA is symptomatic, radiographic, self-reported or doctor-diagnosed (12,46, 47). OA can be classified into five levels, 0 to 4 based

on a joint scoring system (43). The prevalence of OA varies widely globally but OA is consistently the most common type of arthritis (14). In the US, more than 30 million people are estimated to be affected by the disease among adults 30 years of age or older (14). Similarly, in Canada, the self-reported prevalence of OA was 14.8%(15) while it was 17% in the Spanish population (48). In Korea, the prevalence is 13.9% among old adults aged 50+ years (49) while it is 21.8% in Germany with it being highest among 80–89 years (31%) and female (23.9%) (50).

In LMICs such as India, the prevalence of knee OA ranges between 21.6% in Punjab (16) to 27.1% in Tamil Nadu (Venkatachalam) and 29.7% in Odisha (17). In Kenya, a national hospital-based study found the prevalence of knee, hip and hand OA to be 15%, 3% and 5% respectively (18).

Consistently, OA is common among women than men. In Korea, the prevalence is 20.1% among women and 5.7% among men making its 3.5 times higher among women than men (49). In a National Health and Wellness Survey, OA prevalence among the employed was 12.3% with moderate OA being the most common at 45.9% followed by mild at 45% and severe at 9.1% (42) with female aged 40-64 years having a higher prevalence than males and those aged ≥65 years (42).

Patients with knee OA in Kenya have comorbidities such as elevated blood pressure and glucose, dyslipidaemia, and overweight and obesity (29, 51). The comorbidities were especially high among patient with a long-standing knee OA which was attributed to advancing age and prolonged use of NSAIDs (29, 51).

2.5 Prevalence and Determinants of CKD among Osteoarthritis

There is paucity of data in this area. A few available studies highlight that CKD is prevalent among OA patients. In an Egyptian CKD prevalence study among patients with knee OA and Obese, 65% of them had CKD (25). The study also found that GFR was correlated with HDL positively and with microalbuminuria and knee OA severity negatively (25). Another study among patients with CKD, 38% experienced musculoskeletal pains, with significantly more female than males experiencing chronic musculoskeletal pain (49% vs. 28%) (52).

In a study among RA patients, 36% of them had CKD. The prevalence was higher among patients with extra-cellular manifestations, elevated ESR, higher radiological stage of diseases and co-existing hypertension (53). A long-standing illness, old age, inappropriate RA treatment and haemoglobin level are associated with CKD among RA patients (53). In another study of CKD, inflammation and CVD risk in rheumatoid arthritis with a high CVD risk sixteen percent of patients had CKD after 89 months of follow-up. (54).

2.6 Factors associated with Chronic Kidney Disease in OA

2.6.1 Age, Gender and Race

Older adults tend to have a high prevalence of CKD, hypertension and diabetes (55, 56). CKD risk factors in a university community was found to be 12.4% for proteinuria, 12.2% obesity, 2.7% glycosuria, 20.8% hypertension and 4.3% hyperglycaemia (35). In Tanzania, older age was identified as a factor associated with impaired kidney function (3). Older adults in Uganda have been shown to have increased odds of CKD (38). In SSA, CKD has been found to affect young adults (57) and female (37).

OA's prevalence also increases with age (14, 58). Both cellular and extracellular matrix aging contributes to OA. There is increased thinning of articular cartilage, accumulation of proteins resulting in increased brittleness causes by altered biomechanical properties due to increased collagen (59). OA is also common among women than men. In Korea, the prevalence is 20.1% among women and 5.7% among men making its 3.5 times higher among women than men (49).In addition, in the Framingham Osteoarthritis Study, 44.2% of women had hand OA compared to 37.7% among men (60).

CKD and ESRD risks are high among the African population (61, 62). The hip and hand OA prevalence is high among the white than among the Chinese and African Americans (14,44). A US study found the 20-year CKD incidence to be higher among African Americans than whites, which was partly attributed to albuminuria(63).

2.6.2 Overweight and Obesity

Obesity and overweight are determinants of hypertension, proteinuria, glycosuria and CKD (35) and misalignment which predicts OA progression(15, 64).Obesity is also a predictor for misalignment which predicts OA progression(15, 64). They increase proteinuria in the body,

and cause hyperfiltration and loss of estimated glomerular filtration rates over time (65). Moreover, high visceral adipose tissue and abdominal obesity have been associated with albuminuria and poorer renal outcomes, respectively (66). In Uganda, overweight and obesity were protective against CKD (38). In Kenya, a fifth and one-tenth of the population are overweight and obesity respectively (67). In a Turkish CKD population-based survey 29.2%of the obese population had CKD compared to 20% among normal weighted population(68). In a Kenyan study among OA patients 59.5% were found to be overweight or obese (29).

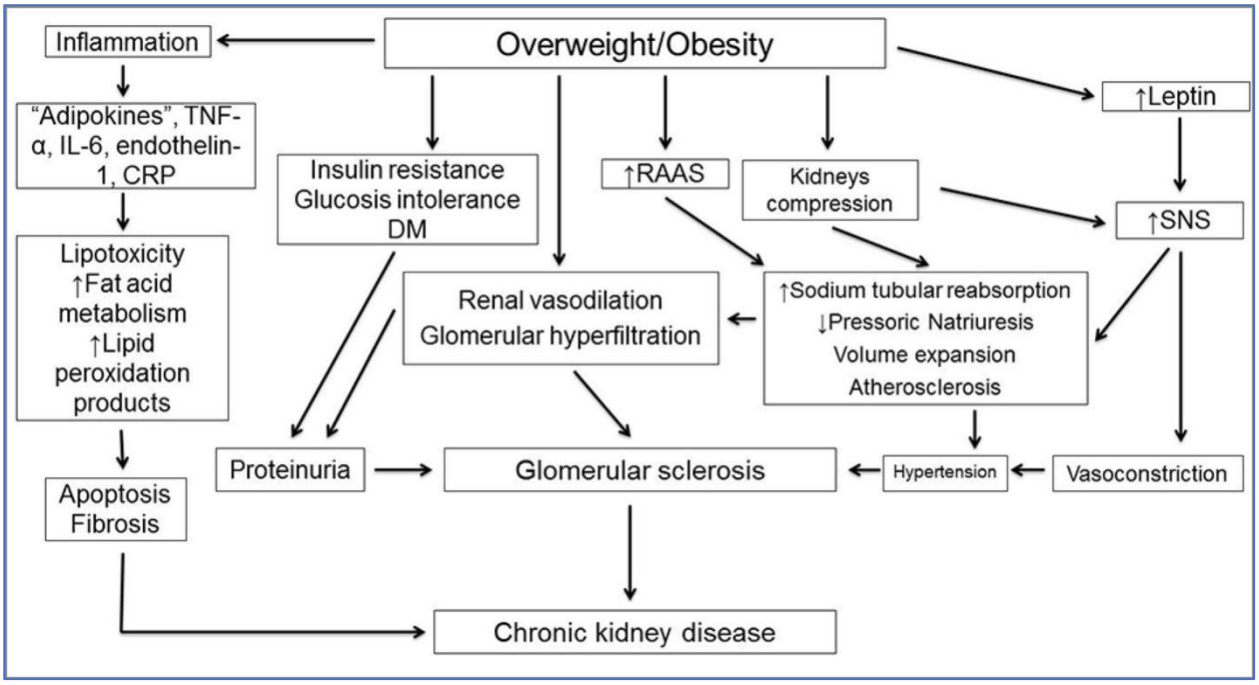

Figure 2*. Obesity and chronic kidney disease pathophysiology (69)*

2.6.3 Hypertension and OA

Elevated and uncontrolled blood pressure increases the risk of CKD. High blood pressure contributes to increased intraglomerular pressure altering glomerular filtration resulting in filtration of proteins. Hypertension is associated with increased damage of blood vessels within the kidney resulting in altered kidney function (poor waste and water removal). In a study among South African teachers, diabetes and hypertension were related to CKD (34). A systematic review of CKD in SSA has showed elevated blood pressure as a leading cause of CKD. Hypertension causes approximately 25–48.7% and 21% of CKD and ESRD in SSA(57). In Kenya, 56% of the population has elevated blood pressure with only 22.3% on

medication for hypertension (70). Approximately 50–60% and 27% of the Kenyan population had high LDL level and overweight and obese respectively, both hypertension risk factors(70). Prevalence of hypertension among OA patients is also high at 51% (29).

2.6.4 Diabetes Mellitus and OA

Diabetes cause 44% of all new CKD cases in the US. Diabetes destroys small blood vessels including those in the kidney resulting in ineffective glomerular filtration. This results in increased fluids and salt retention in the body, proteinuria, increased body weight and ankle swelling. Diabetes also causes elevated blood pressure, hardening of arteries leading to heart disease and nerve injuries. Damage to nerves can cause difficulty in emptying of bladder resulting in stasis causing kidney injury and bacterial infections. The development of diabetes is associated with elevated blood pressure.

Diabetes, proteinuria and hypertension have been found to be significant determinants of CKD in the Democratic Republic of Congo (37, 39). CKD has also been found to be highly prevalent at 14.3% among diabetes patients, with an incidence rate of 2178 cases per 10,000 patients-months and median time to develop of 70.9 months (71). In the US, 38.3% of diabetes patients had CKD over a five-year period (72). In Kenya, CKD prevalence in ambulant diabetics in KNH was 54.5% (73). Comorbid CKD among diabetes patients is associated with old age, diabetic retinopathy, low high-density lipoprotein cholesterol and high body mass index (71).

2.6.5 Non-Steroidal Anti-Inflammatory Drugs and Chronic Kidney Disease

CKD patients can be managed using lifestyle adjustments, blood pressure control and medications. Most medications used by the general population are excreted through the kidney and can thus contribute to altered renal function (21).

NSAIDs, commonly used pain management drugs include aspirin, cyclooxygenase-2 inhibitors and non-selective cyclooxygenase inhibitors such as ibuprofen (74).

NSAIDs toxic mechanisms to the renal system are two-fold with both a functional and inflammatory mechanisms. NSAIDs inhibit cyclooxygenase enzymes resulting in reduced prostaglandin synthesis hence reduced glomerular pressure and glomerular filtration leading

to kidney disease. Prostaglandin synthesis protects the glomerular filtration rate by reducing the preglomerular resistance. NSAIDs causes attenuation of renal vasodilation (74).

NSAIDs not only have renal adverse effect but also cardiovascular. Altered cardiovascular function has a direct association with altered renal function due to the interdependence of the systems (75). NSAIDs have been established to increase blood pressure especially in hypertensive patients through increasing peripheral resistance and blood volume (76). Approximately, 1–5% or 2.5 million of the patients using NSAIDs are known to experience adverse renal events annually (19-21). All forms of NSAIDs can result in medicine-induced kidney disease, acute kidney injury, haematuria, proteinuria, flank pain, acute tubular necrosis and interstitial nephritis (21). NSAIDs use contributes to CKD progression (22, 23).

Despite the known effects of use of the NSAIDs on renal function, there is continued use of NSAIDs among CKD patients and patients with risk of altered renal function. In a study of NSAIDs use among CKD patients in Egypt, 65.7% of the patients were found to use NSAIDs with headache being the most common reason for use. Thirty-six per cent of the NSAIDs users reported drug-drug interaction (19). In Canada, 56.6% of patients with osteoarthritis had received NSAIDs and 33% had received opioid medications for pain management (79). Among patients with symptomatic midfoot OA, paracetamol was used by 36.1%, opioids by 31.9% and NSAIDs by 27.7% (80).

Moreover, in a study assessing kidney disease in RA patients and implication of RA-related drugs (the MATRIX study), dosage adjustment was needed by 83–90% after receiving at least one drug. Approximately 67–70% of patients received a nephrotoxic drug (81). In another study among patients with rheumatoid arthritis, glucocorticoids, NSAIDs, cyclosporine, mycophenolate mofetil, and cyclophosphamide use is linked to an increased CKD, IHD and stroke risk (82).

NSAIDs are also known to worsen hypertension and cardiovascular disease (26) and to interact with various drugs e.g. ACEI, diuretics, calcium channel blockers decreasing their efficacy (21). International recommendations advocate avoidance of these drugs in CKD patients with acetaminophen proposed as the first line. However, an individual risk-benefit assessment should be made as the pain of osteoarthritis can be quite debilitating.

2.6.6 Other Factors

Other factors associated with CKD include race, high socioeconomic status, and use of agrochemicals. A high social economic status was associated with kidney disease in Uganda (38). Moreover, the use of agrochemicals in farming among the majority of agricultural communities contributes to the prevalence of CKD in Kericho, Kenya (7). An occupation requiring cyclic usage of joints such as farming, long-distance running and playing football increases OA risk especially among men (58).Physical inactivity is also an independent determinant of CKD and ESRD (64, 83).Physical activity has been shown to be protective against CKD(84)

2.7 Screening, Progression and Outcome

Screening of CKD is not common. However, screening of CKD is useful in early detection, early interventions, and preventive measures to reduce progression to CKD. Case finding of the populations at risk is the recommended screening strategy compared to mass screening and has been found to be cost-effective (85). Early screening of high-risk populations e.g. diabetics, hypertensive patients or those on nephrotoxic medications is recommended and is the usual standard of care in most health facilities,

CKD patients have a mortality of 24–39% at 5 years and 20–52% at 10.0–12.6 years (86). Mortality also increases with age and with CKD stages (86). In Tanzania, CKD patients had increased odds for in-hospital and 1-month post-discharge mortality (35).OA is associated with reduced quality of life(87) and a high cost of management. In a study among an employed population, the cost of managing OA was estimated at between 9,801 USD for mild and 22,111 for severe compared with 7901 for non-OA (42). The high cost is a result of both direct (consultation, surgery, transport, surgery, and hospitalization) and indirect (loss of productivity and comorbid conditions) costs.

2.8 Conceptual Framework

Patients with osteoarthritis have been found to have a comorbid chronic kidney disease; meaning there is a relationship between osteoarthritis and CKD. The association is influenced by confounders, which are joint risk factors for CKD and OA. Furthermore, the relationship between OA and CKD may be mediated or modified by the use of NSAIDs,

which are useful for patients with OA but have renal adverse effects and are harmful to patients with CKD. Figure 4 illustrates the relationship between OA and CKD and the role of confounders and mediating factors.

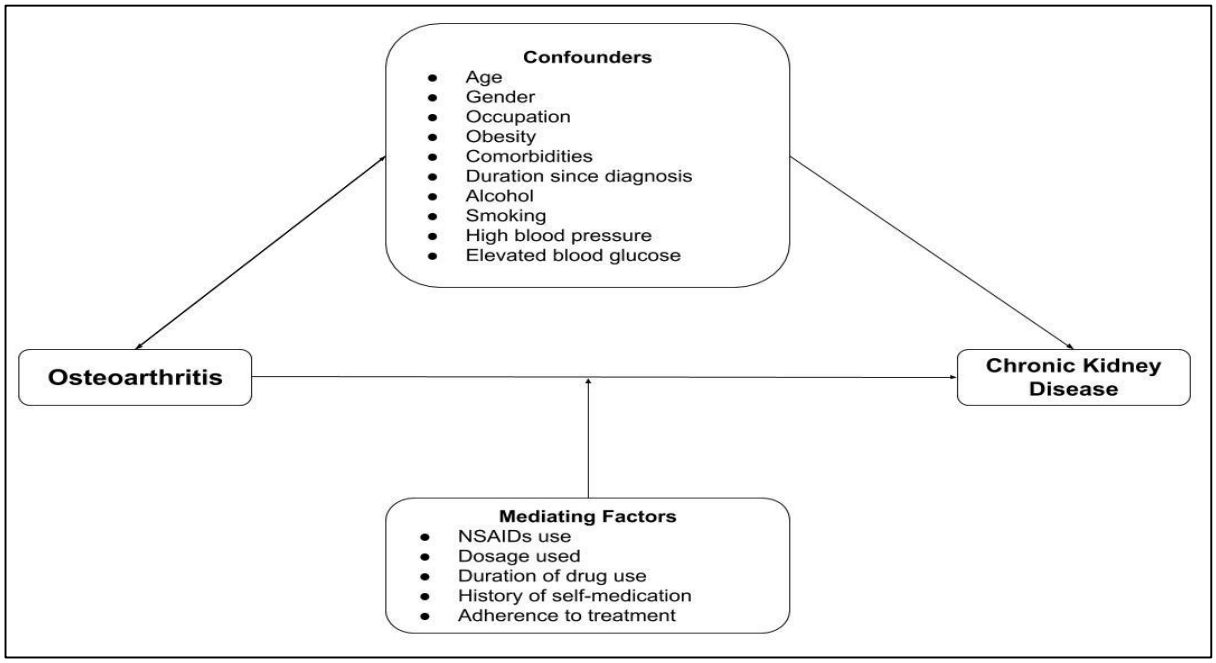

Figure 3. *Conceptual framework*

2.9 Study Justification

The purpose of the study was to determine the prevalence and associated risk factors of chronic kidney disease among osteoarthritis patients attending rheumatology and orthopaedic clinics in Kenyatta National Hospital

Osteoarthritis is a common cause of medical consultation globally. Chronic kidney disease is also of growing concern both globally and locally. Both diseases share similar risk factors e.g. age, hypertension, diabetes and chronic NSAIDs use worsens CKD progression. No studies assessing the prevalence of CKD in OA have been done locally.

This study provides evidence on the burden of kidney dysfunction among OA patients plus the associated risk factors. Knowledge of the risk factors for CKD in Kenya will inform the management of these patients and help in curbing the progression of CKD. It also provides evidence to support screening for CKD among patients with OA. Early detection of CKD

ensures prompt intervention and decreases the rate of CKD progression thus decreasing both morbidity and mortality from CKD.

2.10 Scope of the Study

The study assessed the renal function in OA patients in KNH rheumatology and orthopaedic clinics. It involved the measurement of creatinine levels and calculation of eGFR using validated estimation formulas and urinalysis to check for proteinuria. Sociodemographic and clinical data on factors associated with chronic kidney disease among OA patients were also collected.

2.11 Research Question

What is the burden and associated risk factors of chronic kidney disease in osteoarthritis patients attending rheumatology and orthopaedic clinics in Kenyatta National Hospital?

2.12 Research Objectives

2.12.1 Broad Objective

The broad aim of the study was to determine the prevalence and associated risk factors of chronic kidney disease in osteoarthritis patients attending rheumatology and orthopaedic clinics in Kenyatta National Hospital.

2.12.2 Specific Objectives

1. To determine the prevalence and stages of chronic kidney disease as measured by eGFR and/or proteinuria on urinary dipstick in osteoarthritis patients attending the rheumatology and orthopaedic clinics in Kenyatta National Hospital.
2. To determine the association between chronic kidney disease and selected risk factors namely hypertension, diabetes mellitus, obesity, age, physical inactivity, and drug history e.g. NSAIDs, antihypertensives (ACEI/ARBs) and anti-diabetics in osteoarthritis patients attending the rheumatology and orthopaedic clinics in Kenyatta National Hospital.

CHAPTER THREE: METHODOLOGY

3.1 Study Design

This study adopted a hospital-based analytical cross-sectional study design.

3.2 Study Setting

The study area was the rheumatology and orthopaedic clinics at the Kenyatta National Hospital, Nairobi, Kenya. This is the largest national referral and teaching hospital in Kenya, with 1,800 bed capacity. The rheumatology and orthopaedic clinics are specialised outpatient clinics for patients diagnosed with rheumatic-related and bone-related disorders, respectively. The rheumatology clinic runs every Thursday afternoon from 2.00 pm and approximately 10 osteoarthritis patients are seen during each clinic. The orthopaedic clinic runs on Tuesday, Wednesday, and Friday morning from 8am and approximately 30 osteoarthritis patients are seen during each clinic day.

3.3 Study Population

All patients aged 18 years and older meeting ACR criteria-based diagnosis of osteoarthritis and on follow-up at the rheumatology and orthopaedic outpatient clinics at the Kenyatta National Hospital.

3.4 Eligibility Criteria

3.4.1 Inclusion Criteria

The study included:

- Patients of both sexes aged 18 years and older diagnosed with knee, hip, spine, and hand osteoarthritis according to the ACR criteria and on follow-up at the KNH rheumatology or orthopaedic clinics.
- Patients who provided written informed consent.

3.4.2 Exclusion Criteria

The study excluded:

- Patients with other types of arthritis such as rheumatoid and lupus arthritis, and ankylosing spondylitis.
- Patients with mechanical diseases such as disc-related conditions.

3.5 Sample Size

The sample size was calculated based on the following parameters: prevalence of CKD among osteoarthritis of 32%(53), prevalence of exposure and unknown outcome of 50%, sampling error of 5% and a confidence level of 95% and an expected non-response rate of 10%(88).

$$\mathbf{n = \frac{z^2\, p\, q}{d^2}}$$

Where;

n = minimum sample size

Z= 1.96 standard deviation correspondence to 95% CI

p = Prevalence of CKD among osteoarthritis patients

d = 0.05 (Level of precision at 5%)

n = $(1.96)^2$x 0.32 x (1–0.32) / 0.05^2=**334**

3.5.1 Sample to assess association:

$$n = \frac{r+1}{r(\lambda-1)^2\pi^2}\left[z_\alpha\sqrt{(r+1)p_c(1-p_c)} + z_\beta\sqrt{\lambda\pi(1-\lambda\pi)+r\pi(1-\pi)}\right]^2$$

Where:

$$p_c^* = \frac{P}{r+1}\left(\frac{r\lambda}{1+(\lambda-1)P}+1\right)$$

P = Prevalence of exposure among population (π)

λ=Estimated odds ratio

r = Ratio of exposed to unexposed

Z_α = the desired level of statistical significance, 95%

Z_β = the desired power, where 1-β is 80%.

Table 2. Sample size needed to assess association between CKD and specific risk factors

Risk Factors	Odds Ratio (OR)	Ratio of Exposed / Unexposed	Prevalence of exposure among patients without CKD (%)(89)	Level of Confidence	Power (%)	Sample size
Age	2.7	1	57	1.96	80	**172**
Hypertension	19.0	1	23	1.96	80	**24**
Diabetes	3.6	1	32	1.96	80	**94**
NSAID use	6.0	1	5	1.96	80	**126**
Physical Inactivity	2.0	1	20	1.96	80	**374**
Obesity	3.0	1	39	1.96	80	**122**

Thus, the sample size of **374** was suitable to assess association by all study variables.

3.6 Study Timelines

Approximately 40 patients with OA were seen in both the orthopaedic and rheumatology clinics per week. 30 patients were recruited from the orthopaedic clinic which runs thrice weekly while around 5 patients were recruited from the rheumatology clinic weekly. Patients were recruited over a three-month period between November 2019 and January 2020 until the desired sample size was reached.

3.7 Participant Recruitment / Sampling Techniques

The study participants were recruited using consecutive sampling. Medical files of patients with osteoarthritis at the rheumatology and orthopaedic clinics were reviewed a day before their scheduled clinic visit. Patients meeting inclusion criteria were approached during their clinic visit and informed in detail about the study and allowed to understand the study

through questions and answers. Then, they were provided with a written informed consent form to sign and data collected thereafter.

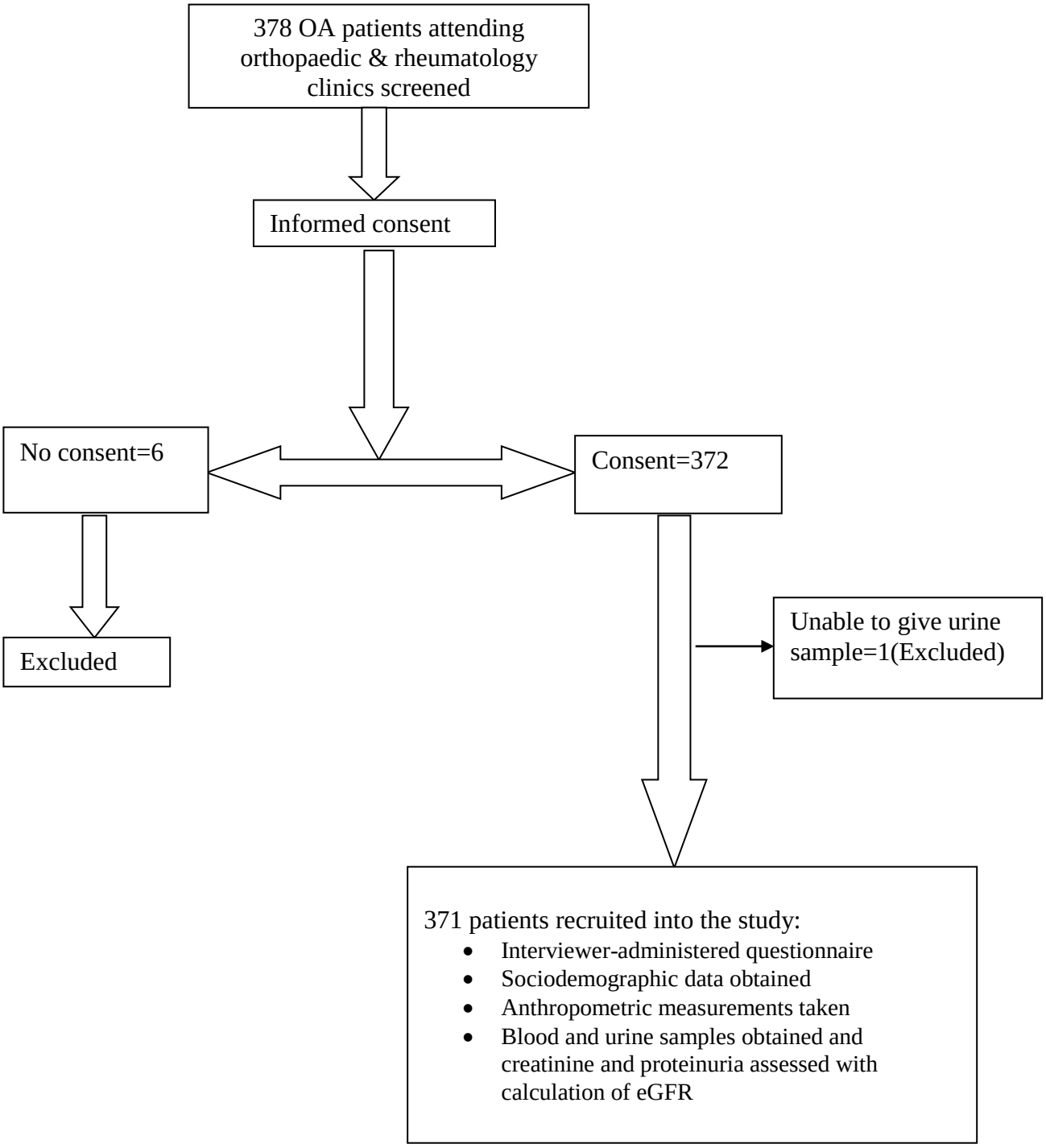

Figure 4. *Flow Chart of Subject Recruitment into the Study*

3.8 Data Collection

3.8.1 Clinical Methods

A researcher-administered questionnaire was used for data collection from among the conveniently sampled patients. The questionnaire had three sections. Section one focused on the sociodemographic data, section two on the clinical and physical examination and section three on anthropometric and laboratory tests (Appendix 3).The questionnaire incorporated the WHO Global Physical Activity Questionnaire (GPAQ) for daily levels of physical activity (90).

3.8.2 Anthropometric Measurements

Blood pressure was measured twice in seated position 15-minutes apart using a calibrated automatic blood pressure machine and appropriate cuff sizes. Weight and height were measured using a calibrated SECA weighing scale in kilograms to the nearest 0.1 kg and SECA stadiometer in centimetres to the nearest 0.1cm in a standing position and on a hard-flat surface, respectively.

3.8.3 Laboratory Methods

The principal investigator and research assistants drew non-fasting blood from the median cubital vein using aseptic techniques. 4 ml sterile plain vacutainers were used to collect the blood sample for creatinine levels. The blood samples were handled as per the hospital standard operating procedures and delivered to the laboratory and tested within four hours using the Mindray BS 400, an automatic biochemistry analyser.

Urine specimens were collected by patients based on instructions on collection of 10mls of midstream urine using a sterile specimen bottle provided for urinalysis. The urine samples were analysed using dipsticks. The dipsticks were used as per the manufacturer's instructions and compared against standardized chart.

3.9 Quality Assurance

The study used the existing hospital standard operating procedures and laboratory protocols and adhered to the manufacturer's instructions on the use of equipment, reagents, and references. An aseptic technique was observed during the general and physical examination and while collecting laboratory samples. Proper sample handling, labelling, processing, storage, and transportation were adhered to. In line with the practices at the hospital laboratory, every 20^{th} sample was sent to an external approved Lancet laboratory for quality control while the daily internal quality control checks were performed per the hospital protocols.

3.10 Case Definition

Osteoarthritis (OA): Any adult patient with a diagnosis of OA meeting the ACR criteria attending KNH orthopaedic and rheumatology clinics during the study period.

Chronic kidney disease: eGFR of less than 60ml/min/1.73m^2 using the Cockcroft Gault formula and/or proteinuria of 30mg/dl detected on urinary dipstick for 3 months or more.

3.11 Study Variables and Operationalization of the Study Variables

3.11.1 Dependent / Outcome Variable

The main outcome of the study was CKD diagnosis among OA patients. CKD diagnosis was based on an eGFR of <60mL/min/1.73m^2calculated using Cockcroft Gault formula and/or proteinuria of ≥30 mg/dl on urinary dipstick for 3 months or more.

3.11.2 Independent / Explanatory Variables

The sociodemographic variables included: age (years), sex (male or female), and education levels (primary and below, secondary, and tertiary), occupation (formal, business, home/farming), and years completed since the first diagnosis.

The behavioural and anthropometric variables included alcohol use (Yes/No), smoking (Yes/No) and body mass index (BMI) (weight in kilogrammes divided by the squared height in meters). BMI was categorised into normal, underweight, overweight, and obese. Waist–

Hip ratio (WHR) was calculated as a ratio of waist circumference and hip circumference. The WHR of ≥0.90 for male and ≥0.85 for females was considered obese.

The clinical variables included hypertension (defined according to the JNC7 classification as either being on treatment or a systolic/ diastolic blood pressure of ≥140/90mmHg) and diabetes (self-reported diabetes and use of antidiabetic drugs).

Other clinical variables included the type (hip, knee, elbow) and number of joints involved, type of medication used (e.g. NSAIDs, ARBs, ACEIs), types of NSAIDs in use, dosage of the drugs in use, duration of use of medication, history of self-medication or over-the-counter medications and total duration of medication use in years.

The laboratory parameters included current kidney function based on eGFR and urine protein levels on dipstick (Present/Absent).

3.12 Data Management

3.12.1 Data Entry, Validation and Handling

All the filled questionnaires and data forms were assessed for completeness and consistency after data collection. Data from the completed questionnaires and data forms were entered into an offline password-protected Microsoft Access database with integrated validation measurement for accuracy of data entry. Delinked data was then exported from the database and shared with the statistician with only the PI having knowledge of the participants' identity. On completion of the study, the electronic delinked data was stored in a password protected server.

3.12.2 Data Analysis

STATA version 13.1 was used to analyse cleaned data. Mean, median, standard deviation and interquartile range were used for continuous variables while frequencies and percentages were used for categorical variables to characterise the participants' and CKD prevalence among osteoarthritis patients. Association between the participants' characteristics and the CKD prevalence was assessed using chi-square test. Determinants of CKD among osteoarthritis patients were assessed using a forward stepwise approach multivariable logistic regression analysis. To find the most parsimonious model, variables with a $p<0.25$ in the

bivariate logistic analysis were included. All the analyses were stratified according to sex. Frequencies, percentages, and odds ratios and 95% confidence interval are reported.

3.13 Ethical Considerations

The Kenyatta National Hospital / University of Nairobi Institutional Research Ethics Committee approved the study. The Helsinki Declaration on the conduct of research on human subjects was adhered to in conduct of the study. The purpose and benefit of the study was shared with the study participants and after demonstrating an understanding of the study through verbalizing the purpose, benefits, risks and having all their questions answered they signed a written informed consent. The participants were free to take part in the study and withdraw at any point in the study without providing reasons.

The study was conducted in strict adherence of the KNH standard operating procedures and as per the approved protocol. There was no interference with the usual patient care and the patients were not exposed to harm or risks. All the blood and urine samples collected were drawn, tested, and discarded after analysis according to the KNH standard operating procedures. All data collected were anonymised, stored in password-protected files and access limited to the research team only. The principal investigator bore all the costs related to the study. Results obtained were shared with the patients, their primary physician and included in their medical records and proper interventions recommended where need arose.

CHAPTER FOUR: RESULTS

4.1 Respondents' Characteristics

The mean age of the participants was 58.3 years (SD: 11.3 years). Many of the respondents had secondary school education (44.7%), were married (82.5%) and rated their health as fair (49.1%). Only 13.7% and 4.6% had ever consumed alcohol or smoked, respectively. A third of them had a low level of physical activity (Table 3).

Fifty-seven per cent and 48% of respondents were obese based on BMI and WHR respectively. The average weight, waist and hip circumferences were 76.9kg (SD: 12.6), 95.8 cm (10.0) and 111 cm (10.2), respectively. Slightly more than half (51.7%) were hypertensive. Most reported pain and stiffness within the past 12 months at 98.4% and 90.3%, respectively. Many of the respondents had one (39.1%) or two (33.7%) joints affected. However, 7.8% of the respondents had more than five joints affected with eight being the highest number of joints affected.

Table 3. Respondents' characteristics

Variables	Characteristics	Total N=371(%)
Age, years	Age, mean (SD)	58.3 (11.3)
	20–34	6 (1.6)
	35–49	75 (20.2)
	51–64	187 (50.4)
	65+	103 (27.8)
Sex	Male	82(22.1)
	Female	289(77.9)
Education levels	Primary and below	148 (39.9)
	Secondary	166 (44.7)
	Tertiary	57 (15.4)
Marital Status	Married	306 (82.5)
	Single	35 (9.4)
	Widowed/Divorced/Separated	30 (8.1)
Employment	Formal employment	117 (31.5)
	Business	104 (28.0)
	Housework/Farming/Others	150 (40.4)
Self-rated Health	Good	123 (33.2)
	Fair	182 (49.1)
	Poor	66 (17.8)
Alcohol	No	320 (86.3)
	Yes	51 (13.7)

Smoking	No	354 (95.4)
	Yes	17 (4.6)
Hypertension	No	179 (48.3)
	Yes	192 (51.7)
SBP	Mean (SD), mmHg	137.2 (17.2)
DBP	Mean (SD), mmHg	81.3 (10.3)
Diabetes	No	337 (90.8)
	Yes	34 (9.2)
Weight	Mean (SD), kg	76.9 (12.6)
Waist-Hip Ratio	Normal	194 (52.3)
	Obesity	177 (47.7)
Body Mass Index	Normal	42 (11.4)
	Overweight	115 (31.3)
	Obesity	210 (57.2)
Physical activity levels	High	120 (32.4)
	Moderate	132 (35.6)
	Low	119 (32.1)
Diagnosis duration	Years	4.7 (4.7)
Pain within 12 months	No	6 (1.6)
	Yes	365 (98.4)
Stiffness within 12 months	No	36 (9.7)
	Yes	335 (90.3)
Number of joints involved	1	145 (39.1)
	2	125 (33.7)
	3–8	101 (27.2)

** Chi-square test of association between gender and respondents' characteristics; † Fishers test; SBP: Systolic blood pressure, DBP: Diastolic blood pressure; SD: standard deviation*

Sixty-two percent of the respondents were using one medication while 7.3% were using 3–4 medications. Four out of every 10 respondent had different medications for treating ailments with 36.7% on antihypertensives, 8.6% on antidiabetics and 99.7% on NSAIDs (Table 4).

Table 4. Medication use

Variables	**Total n (%)**
Number of medications in use	
1(NSAIDs)	229 (61.7)
2(NSAIDs+ AH/AD)	115 (31.0)
3–4(NSAIDs+ AH + AD)	27 (7.3)
Number of NSAIDS used	
0	1 (0.3)
1	261 (70.4)
2	94 (25.3)
3	6 (1.6)
4	9 (2.4)

Antihypertensives	
No	235 (63.3)
Yes	136 (36.7)
Antidiabetics	
No	339 (91.4)
Yes	32 (8.6)
NSAIDs use in 12 months	
No	9 (2.4)
Yes	362 (97.6)
Duration of NSAID use	
Median (IQR)	2.0 (0.5-2.0)

** Chi-square test of association; † Fishers test; IQR: interquartile range; AH Antihypertensives; AD Anti diabetics; AS Anti statins*

4.2 Prevalence of Chronic Kidney Disease (CKD)

The overall prevalence of CKD among patients with osteoarthritis was 61.9% (95% CI: 56.4–66.3) according to CG. CKD prevalence was statistically different among the three CKD formulas. The prevalence of CKD increased by age in all formulas with the prevalence being highest among older adults (65+ years). CKD prevalence was higher among women than men except when using the CG formula. A majority of the respondents had CKD stage 3 (Table 5). Only 12.1% had persistent proteinuria. Many of the patients with persistent proteinuria were female, old, hypertensive, obese and on self-medication.

Table 5. Overall and age- and sex-specific prevalence of CKD based on CKD–CG, CKD–Epi and CKD–MDRD

Characteristic	CKD-CG % (95% CI)	CKD-Epi % (95% CI)	CKD-MDRD % (95% CI)	Proteinuria† % (95% CI)
Overall*	**61.9 (56.4–66.3)**	**77.1 (72.5–81.1)**	**67.9 (63.0–72.5)**	**12.1 (9.2–15.9)**
Age, years				
20–34	33.3 (4.2–85.1)	16.7 (0.9–81.4)	0	33.3 (4.2–85.1)
35–49	17.3 (10.2–27.9)	60.0 (48.3–70.6)	58.7 (47.0–69.4)	6.7 (2.7–15.3)
50–64	63.1 (55.9–69.8)	78.6 (72.1–83.9)	67.9 (60.8–74.3)	12.3 (8.3–17.9)
65+	92.2 (85.1–96.1)	90.3 (82.7–94.8)	78.6 (69.5–85.6)	15.6 (8.9–22.9)
Sex				
Male	65.9 (54.7–75.5)	54.9 (43.8–65.5)	35.4 (25.6–46.5)	11.0 (5.7–20.0)
Female	60.2 (54.4–65.7)	83.4 (78.6–87.3)	77.2 (71.9–81.7)	12.5 (9.1–16.8)
Staging				
MeaneGFR (SD)	**56.3 (13.0)**	**54.4 (9.9)**	**56.8 (9.6)**	
Stage 1	4 (1.1)	2 (0.5)	2 (0.5)	
Stage 2	142 (38.3)	93 (25.1)	118 (31.8)	
Stage 3a	169 (45.6)	221 (59.6)	222 (59.8)	
Stage 3b	51 (13.7)	54 (14.6)	28 (7.6)	
Stage 4/5	5 (1.4)	1 (0.3)	1 (0.3)	

**CG vs. Epi p-value = <0.0001; CG vs. MDRD p-value = <0.0001; MDRD vs. Epi p-value = <0.0001; †Persistent proteinuria (1+, 2++), eGFR: Estimated Glomerular Filtration Rate (mL/ min/1.73m^2); CG: Cockcroft-Gault; MDRD: Modification of Diet in Renal Disease Study; CKD-Epi: Chronic Kidney Disease Epidemiology Collaboration * The 1 person had a urine protein of 3+.*

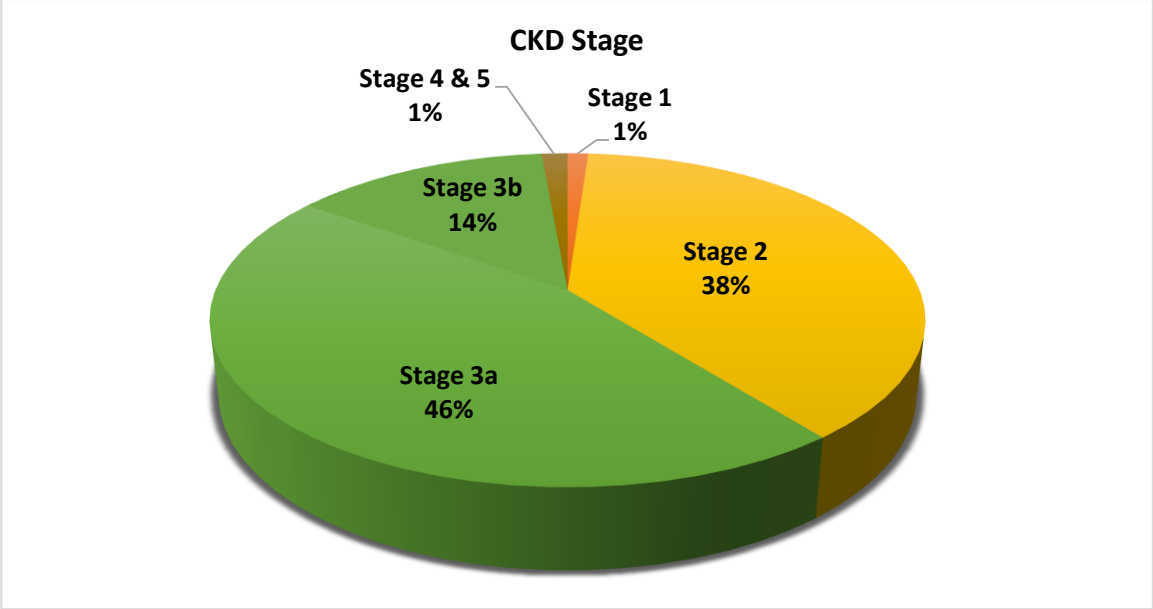

***Figure 5**. Prevalence of CKD by stages*

Table 6 outlines the proportion of respondents with or without CKD based on CG according to their characteristics. Among those with CKD, the mean age was 63 years compared to 50.7 years in the no CKD group. Majority were aged 50–64years (51.8%), female (76.3%), with primary level of education (50.4%), rated their health as fair (61%), self-medicated (90.4%), were hypertensive (69.7%) and on prescribed medication (NSAIDs) for at least two years. Those in the no CKD group had better socioeconomic status (higher level of education, employment and good health) compared to the CKD group. Many of the respondents in our study were in low and moderate KDIGO risk categories at 38% and 38.3% respectively. Only 12% and 11.6% were in high and very high-risk categories. Thus, while the prevalence of CKD was high, most of our respondents (76%) had low risk of CKD progression and therefore a concomitant low risk of cardiovascular disease (Table 7).

Table 6. Proportion of respondents with or without CKD based on CG according to their characteristics

Variables	Characteristic	No CKD n (%)	CKD n (%)	p-value*
Age, years	Average age (SD)	50.7 (8.9)	63.0 (10.0)	**<0.001§**
	20–34	4 (2.8)	2 (0.9)	
	35–49	66 (46.2)	15 (6.6)	
	50–64	69 (48.3)	118 (51.8)	**<0.001**
	65+	8 (5.6)	95 (41.7)	
Sex	Male	28 (19.6)	54 (23.7)	0.354
	Female	115 (80.4)	174 (76.3)	
Education levels	Primary and below	33 (23.1)	115 (50.4)	
	Secondary	76 (53.2)	90 (39.5)	**<0.001**
	Tertiary	34 (23.8)	23 (10.1)	
Employment	Formal employment	62 (43.4)	55 (24.2)	
	Business	45 (31.5)	59 (25.9)	**<0.001**
	Housework/Farming/Others	36 (25.2)	114 (50.0)	
Self-rated Health	Good	86 (60.1)	37 (16.2)	
	Fair	43 (30.1)	139 (61.0)	**<0.001**
	Poor	14 (9.8)	52 (22.8)	
Alcohol	No	122 (85.3)	198 (86.8)	0.678
	Yes	21 (14.7)	30 (13.2)	
Smoking	No	140 (97.9)	214 (93.9)	0.070†
	Yes	3 (2.1)	14 (6.1)	
Physical Activity	High	39 (27.3)	81 (35.5)	
	Moderate	52 (36.4)	80 (35.1)	0.199
	Low	52 (36.4)	67 (29.4)	
WHR	Normal	82 (57.3)	112 (49.1)	0.123
	Obese	61 (42.7)	116 (50.9)	
BMI	Normal	9 (6.4)	33 (14.5)	
	Overweight	38 (27.1)	77 (33.9)	**0.008**
	Obese	93 (66.4)	117 (51.5)	
Hypertension	Non-hypertensive	110 (76.9)	69 (30.3)	**<0.001**
	Hypertensive	33 (23.1)	159 (69.7)	
Diabetes	No	137 (95.8)	200 (87.7)	**0.009**
	Yes	6 (4.2)	28 (12.3)	
All medications	1	117 (81.8)	112 (49.1)	
	2	22 (15.4)	93 (40.8)	**<0.001**
	3–4	4 (2.8)	23 (10.1)	
Duration of NSAID use, years	Median (IQR)	1.0 (0.4–2.0)	2.0 (0.6–3.0)	**0.0003**
Joints Involved	Median, IQR	1 (1–2)	2 (1–3)	**0.001**
Self-medication	No	10 (7.0)	22 (9.7)	0.375
	Yes	133 (93.0)	206 (90.4)	

** Chi-square test of association; † Fishers test; § Student's t-test; IQR: Interquartile Range; CKD: Chronic Kidney Disease; BMI: Body Mass Index; WHR: Waist-Hip Circumference; AD: Antidiabetics; AH: antihypertensives;*

Table7.KDIGO current chronic kidney disease nomenclature (31)

CKD stage ($eGFR_{CG}$ mL/min/1.73)	Nil	Persistent Proteinuria	Total
G1(>90)	4(1.1%)	0	4(1.1%)
G2(60-89)	137(36.9%)	5(1.3%)	142(38.3%)
G3a (45-59)	142(38.3%)	27(7.3%)	169(45.6%)
G3b (30-44)	40(10.8%)	11(3%)	51(13.7%)
G4(15-29)	3(0.8%)	1(0.3%)	4(1.1%)
G5(<15)	0	1(0.3%)	1(0.3%)
Total	326	45	371

Note: Green= low risk, Yellow= moderate risk, Orange= high risk, Red= very high risk

4.3 Factors Associated with CKD in Patients with Osteoarthritis

Table 8 highlights the association between the respondent's characteristics and chronic kidney disease. In the bivariate analysis, older age, higher education levels, household/farming work, fair and poor self-rated health, number of joints involved, number of medications in use, duration of NSAID use, diabetes and hypertension were independently associated with chronic kidney disease. After adjusting for all confounders in the multivariable logistic regression, old age, poor and fair self-rated health, use of more than one medication namely an NSAID plus an antihypertensive and antidiabetic and hypertension increased the odds of CKD among patients with osteoarthritis. The odds of CKD increased 120 times among participants aged 65 years and above compared to those aged 20–49 years. Participants who rated their health as being poor had 12 times increased odds of CKD compared to those who rated their health as good. Hypertensive participants had 22 times increased odd of CKD compared to non-hypertensive participants. Those on multiple drugs namely NSAIDs plus ARB/ACEIs and antidiabetics had 2 times increased odds of CKD compared to those on NSAIDs alone. In contrast, moderate levels of physical activity, overweight and obesity were protective of CKD. Participants with moderate level of physical activity, overweight and obesity had 76%, 81%, 98% reduced odds of CKD compared to those with high levels of physical activity and normal BMI, respectively.

Table 8. Association between respondents' characteristics and prevalence of chronic kidney disease

Variables	Characteristics	Bivariate		Multivariable	
		COR (95% CI)	p-value	AOR (95% CI)	p-value
Age, years	20–49	Ref		Ref	
	50–64	7.52 (3.99–14.2)	<0.001	21.4 (7.00–65.9)	**<0.001**
	65+	52.2 (21.0–130.1)	<0.001	119.7 (26.6–538.4)	**<0.001**
Sex	Male	Ref		Ref	
	Female	0.78 (0.47–1.31)	0.354	2.58 (0.94–7.12)	0.067
Education levels	Primary and below	Ref		Ref	
	Secondary	0.34 (0.21–0.56)	<0.001	0.89 (0.39–2.06)	0.803
	Tertiary	0.19 (0.10–0.37)	<0.001	0.45 (0.13–1.55)	0.208
Employment	Formal employment	Ref		Ref	
	Business	1.48 (0.87–2.51)	0.15	1.32 (0.52–3.37)	0.564
	Housework/Farming	3.57 (2.12–6.01)	<0.001	0.75 (0.29–1.96)	0.557
Self-rated Health	Good	Ref		Ref	
	Fair	7.51 (4.49–12.6)	<0.001	7.08 (2.67–18.7)	**<0.001**
	Poor	8.63 (4.23–17.5)	<0.001	11.9 (3.36–42.7)	**<0.001**
Alcohol	No	Ref			
	Yes	0.88 (0.48–1.61)	0.678	1.08 (0.32–3.60)	0.900
Smoking	No	Ref		Ref	
	Yes	3.05 (0.86–10.8)	0.084	1.18 (0.13–11.0)	0.884
Physical Activity Levels	High	Ref		Ref	
	Moderate	0.74 (0.44–1.24)	0.256	0.24 (0.10–0.58)	**0.002**
	Low	0.62 (0.37–1.05)	0.075	0.51 (0.21–1.26)	0.145
Diabetes	No	Ref		1.02 (0.97–1.06)	0.417
	Yes	3.20 (1.29–7.93)	0.012	8.88 (0.58–137.0)	0.118
Hypertension	No	Ref			
	Yes	7.68 (4.75–12.4)	<0.001	22.6 (6.18–83.0)	**<0.001**
Number of Affected Joints	1	Ref		Ref	
	2	6.65 (3.79–11.7)	<0.001	2.38 (0.99–5.74)	0.053
	3-8	3.09 (1.81–5.26)	<0.001	0.79 (0.27–2.25)	0.653
All medications	1 (NSAIDs)	Ref		Ref	
	2 (NSAIDs + AH/AD)	4.42 (2.59–7.52)	<0.001	0.37 (0.10–1.36)	0.134
	3-4 (NSAIDs, AH, AD)	6.01 (2.01–17.9)	0.001	2.11 (0.00–0.47)	**0.019**
Duration of NSAID use		2.00 (0.6–3.0)	<0.001	1.00 (1.00–1.00)	0.491
BMI	Normal	Ref			
	Overweight	0.55 (0.24–1.27)	0.163	0.19 (0.04–0.80)	**0.023**
	Obese	0.34 (0.16–0.75)		0.02 (0.004–0.10)	**<0.001**
WHR	Normal	Ref			
	Obese	1.39 (0.91–2.12)	0.123	0.69 (0.32–1.51)	0.358

Note: Ref: Reference category; COR: Crude Odds Ratio; AOR: Adjusted Odds Ratio; CI: Confidence Interval

CHAPTER FIVE: DISCUSSION

Most of the respondents were recruited from the orthopaedic clinic and were females (77.9%) and this is similar to other studies where prevalence of osteoarthritis is higher in women (14, 42). The mean age of the respondents was 58.3 years (SD: 11.3 years). Fifty-seven per cent of respondents were obese based on BMI and slightly more than half (51.7%) were hypertensive. This confirms previous findings in Kenya that have shown that patients with knee OA tend to have comorbidities such as hypertension, diabetes, dyslipidaemia and are overweight and obese (18,29,51).

The overall prevalence of CKD among patients with osteoarthritis was 61.9%. The prevalence was higher among males than females and most of the respondents had CKD stage 3. The CKD prevalence in this study is similar to the 65% found in Egypt among patients with knee OA and obesity where absolute GFR was used to assess for CKD (25). Our CKD prevalence was higher than the 28.7% among rheumatoid arthritis patients at KNH (91). Most of our respondents were obese, hypertensive, and physically inactive which could explain the high prevalence of CKD. Studies have shown that the prevalence of CKD is high among patients diagnosed with hypertension and diabetes (5). Also, Kibe (2018) found 51%, 21% and 59.5% of knee osteoarthritis patients had comorbid hypertension, diabetes and overweight or obesity respectively (29) which are known risk factors for CKD. The high prevalence highlights a need to screen OA patients for CKD for early diagnosis and management especially since most of our patients did not have persistent proteinuria, an indicator of CKD progression.

The prevalence of CKD based on proteinuria was lower compared to the prevalence of CKD based on CG, CKD-Epi and MDRD. This finding is similar to Ghana where the prevalence was 46.9% using CKD-Epi and 28.9% with proteinuria (36). Also, the findings mirrors that done among RA patients where none had proteinuria (91). Persistent proteinuria usually depicts advanced progression of CKD. However, in our population, few respondents had persistent proteinuria; most were female, old, hypertensive, obese and on self-medication.

The low prevalence of persistent proteinuria is a good indicator for our patients as most of our patients were in low and moderate risk categories highlighting that the CKD is still reversible because it has not progressed to major kidney damage (32). Hence, with the right measures to control hypertension, diabetes and reduced exposure to nephrotoxic drugs, CKD progression can be slowed down. CKD staging can also be used to assess cardiovascular (CVD) risk. Studies have shown, cardiovascular risk increases with disease progression as depicted by increased staging and subsequently increased risk stratification (92). Given our population were mostly in CKD stage 2 and 3 and at low/moderate risk stratification, we have an opportunity to control the modifiable risk factors and slow the progression of CKD and therefore reduce their CVD risk. These findings show that eGFR can be used for initial screening while proteinuria is used to assess progression in our setting.

The study found that old age is associated with the CKD among OA patients. Adults aged 65 years and more had the highest age-specific prevalence and increased odds of CKD. Older adults tend to have a high prevalence of OA (14, 58) and CKD, hypertension and diabetes (55, 56). In Tanzania, older age was identified as a factor associated with impaired kidney function (3) while in Uganda it has been shown to increase odds of CKD (38).

More women with OA had CKD compared to men. Similarly, studies have shown that CKD prevalence is higher among females than males (37) and that females also have a high incidence of OA (14, 42). However, female gender was not a statistically significant factor associated with CKD based CG. CG equation over-estimates GFR in overweight/obese and might have resulted in potential under-estimation of prevalence of CKD hence the non-significance. Female gender was found as a factor associated with CKD based on CKD-Epi and MDRD. Using the concept of biologic plausibility, we could also postulate that the positive association between CKD and housework/farming and lower level of education on bivariate analysis could be due to this population being predominantly female. However, this association was not significant after adjusting for confounders on multivariable regression.

Hypertension is known to increases the risk of CKD (34,57, 70). Hypertension is associated with increased damage of blood vessels within the kidney resulting in altered kidney function (poor waste and water removal). Hypertension causes approximately 25–48.7% of CKD in

SSA (57). In our study, hypertension increased the odds of CKD by twenty-two times. Also, more than half of our respondents were hypertensive which confirms previous findings that also found patients with knee OA in Kenya had comorbidities such as elevated blood pressure and glucose, dyslipidaemia, and overweight and obesity which were attributed to advancing age and prolonged use of NSAIDs (18, 51). However, while diabetes was significantly associated with CKD in the bivariate analysis, the effect disappeared after adjusting for confounders. This could be attributed to the small number of osteoarthritis patients living with diabetes in our sample.

Obesity and overweight are determinants of hypertension, proteinuria, glycosuria and CKD (35). They increase proteinuria in the body, and cause hyperfiltration and loss of estimated glomerular filtration rates over time (65). However, based on CG and similar to studies in Uganda (38) and Kenya (93), overweight and obesity were protective against CKD. The difference in the effect of overweight and obesity may be explained by the CG equation which over-estimates GFR in overweight/obese resulting in potential under-estimation of prevalence of CKD though the exact mechanism of how they are protective of CKD is unclear. This could also be paradoxical as those who are overweight/obese have improved socioeconomic status which has been linked to better kidney function (94).

Self-rated health reflects a person's perception of their health and acts as a proxy to their quality of life. Thus, respondents who rated their health as being fair/poor had increased odds for CKD. This could highlight existing health problems and complications related to the health problems. CKD is a known comorbid condition, complication of other illnesses and diseases and side effect of some medications. CKD has major impacts on health, healthcare cost and productivity (3). Both OA and CKD independently and jointly impacts patients' quality of life, morbidity and mortality (28) hence the fair/poor self-rated health.

In addition, the study found that moderate levels of physical activity were protective of CKD. The findings highlight the importance of physical activity among patients with OA especially noting that physical inactivity is an independent determinant of CKD and ESRD (83).

Lastly, the use of multiple classes of medications i.e. NSAIDs, ARBs/ACEI and antidiabetics increased the odds of CKD. This could be resulting from multiple comorbidities in this group of patients. Proper management of comorbidities is key in managing OA and reducing the likelihood of developing complications such as CKD.

5.1 Study Limitations

First, the study used a single measurement of serum creatinine and GFR to determine CKD prevalence resulting in a potential under- or over-estimation of the prevalence. Also, urine dipstick assay for proteinuria was used. This could result in under-estimation of proteinuria as microalbuminuria was not assessed. Second, the study is cross-sectional in nature thus no causation can be inferred. Third, the study relied on patients recall for some information such as the history of the diseases or behavioural risk factors. Patients may be unable to correctly recall some of the information and may supply inaccurate information. However, information provided by patient was counterchecked against their medical records for verification. Fourth, while we found statistically significant associations between CKD and various variables e.g. age, hypertension etc. the confidence intervals are wide, indicating that our sample size may not be adequate, therefore a study with a larger sample size should be attempted from whence clearer conclusions can be drawn.

CHAPTER SIX: CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

The prevalence of CKD is high among patients with OA with at least 6 out of every 10 OA patients being diagnosed with CKD. The prevalence is higher among males than females. However, most of our respondents have low and moderate risk classification based on the KDIGO nomenclature and thus don't have progressive disease with kidney damage despite the high prevalence. Old age, hypertension, poor and fair self-rated health and use of more than one medication i.e. NSAIDs plus ARB/ACEI and antidiabetics increased the odds of CKD while moderate levels of physical activity and overweight and obesity decreased the odds of CKD among patients with osteoarthritis.

6.2 Recommendations

The following are recommended based on the study findings:

a) OA patients should be included among the high-risk population for CKD and should be screened routinely for CKD using serum creatinine-based formulas to estimate GFR and urinalysis for proteinuria.
b) As age has been linked as a non-modifiable risk factor for CKD, proper attention should be employed when managing these patients as they tend to have comorbidities and are on multiple drugs. Best clinical practice methods on pain management should be employed to minimise exposure to nephrotoxic drugs.
c) Proper management of comorbidities e.g. HTN, DM etc is key as this has been shown to reduce the risk of CKD.
d) Longitudinal studies are needed to look at outcomes with respect to kidney function in the osteoarthritis population.

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APPENDICES

Appendix 1: Patient Information Sheet and Consent Form

Title of Study: Prevalence of and factors associated with Chronic Kidney Disease in Osteoarthritis Patients at Kenyatta National Hospital

Principal Investigator\and institutional affiliation: Dr Maureen Muyodi\University of Nairobi

Introduction

My name is Dr. Maureen Muyodi. I am a postgraduate student of Internal Medicine at the University of Nairobi. The purpose of this statement is to inform you about a research study I am carrying out. I am doing a study on the prevalence of and factors associated with chronic kidney disease (CKD) in osteoarthritis' patients attending adult outpatient clinics at Kenyatta National Hospital. The purpose of this study is to determine how many osteoarthritis patients have renal dysfunction (chronic kidney disease).

Procedures to be followed in the study

Participation in the study is voluntary. Should you accept to participate, the following is a summary of what the study involves:

1. Obtaining your personal information and information on osteoarthritis and any other medical condition you have.
2. Blood pressure and anthropometric measurements will be recorded.
3. A blood sample, approximately 4mls (equivalent to teaspoon) for creatinine levels will be collected.
4. A urine sample approximately 10mls for urinalysis to assess levels of proteinuria will be collected.

This will take 30 minutes of your time.

Risks and costs incurred: There will be no or minimal interference with the usual patient care and the patients will be exposed to no harm or risks. However, there will be minimal pain sustained during the prick while withdrawing the blood sample for the laboratory test. No costs will be incurred.

Your rights as a participant: Your participation in this research is voluntary and if you refuse to participate your treatment will not be affected. If you choose to participate and not to answer certain questions you are free to do so. You are free to terminate the interview and

withdraw from the study at any time. You are free to ask questions before signing the consent form.

Assurance of confidentiality: All your responses as well as results will remain confidential. Your individual responses will be stored in a locked place under my control and will be seen by the statistician and me, the principal investigator.

Benefits: All the above examination and procedures shall be done free of charge (the principal investigator shall bear the cost of the laboratory investigations). The results of the creatinine levels and urinalysis will be put in your file, and if found to have renal dysfunction your primary health physician will be informed and you will be referred to a nephrologist for further management.

Compensation

Participants will not receive any monetary compensation for participating in this study.

Contacts

If you have any questions, please do not hesitate to ask. Clarifications may be sought from:

Dr. Maureen Muyodi,
Principle Investigator
P.O.BOX 81464-80100
Mombasa
Tel: 0726719886

Prof. Kirana M. Bhatt,
Lead Supervisor
Department of Clinical Medicine & Therapeutics,
College of Health Sciences,
University of Nairobi
P.O. BOX 19676
Nairobi
Tel: 0722771603

The Secretary
KNH/UON Ethics and Review Committee
Tel: 2726300 Ext: 44102

CONSENT FORM (STATEMENT OF CONSENT)

Participant's statement

I have read this consent form or had the information read to me. I have had my questions answered in a language that I understand. The risks and benefits have been explained to me.

I understand that my participation in this study is voluntary and that I may choose to withdraw any time. I freely agree to participate in this research study.

I understand that all efforts will be made to keep information regarding my personal identity confidential.

By signing this consent form, I have not given up any of the legal rights that I have as a participant in a research study.

I agree to participate in this research study:	**Yes**	**No**
I agree to have my specimens preserved for later study:	Yes	No
I agree to provide contact information for follow-up:	Yes	No

Participant printed name:

_____

Participant signature / Thumb stamp _____ **Date**

_____

Researcher's statement

I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has willingly and freely given his/her consent.

Researcher 's Name: _____ **Date**:

_____

Signature

_____

Role in the study: _____ *[i.e. study staff who explained informed consent form.]*

For more information contact _____ at _____ from

_____ to _____

Witness Printed Name (*If witness is necessary, a witness is a person mutually acceptable to both the researcher and participant*)

Name _____**Contact information**_____

Signature /Thumb stamp: _____ **Date**;

_____

Appendix 2: Fomu ya Ridhaa ya Utafiti na Fomu ya Idhini

Jina la Utafiti: Prevalence of and factors associated with Chronic Kidney Disease in Osteoarthritis Patients at Kenyatta National Hospital

Mpelelezi Mkuu: Dr Maureen Muyodi wa Chuo Kikuu cha Nairobi

Utangulizi

Jina langu ni Dr. Maureen Muyodi. Mwanafunzi wa uzamili, idara ya Internal Medicine katika chuo kikuu cha Nairobi. Ninataka kukueleza madhumuni ya utafiti ninayofanya. Madhumuni ni kujua mzigo wa ugonjwa wa figo na uwiano wake na vitu vinavyo changia ugonjwa huo baina ya watu walio na osteoarthritis wanaohudumiwa katika kliniki ya nje katika hospitali ya Taifa ya Kenyatta.

Taratibu za kufuatwa katika utafiti

Ushiriki wako katika utafiti ni kwa hiari yako. Iwapo utakubali kushiriki yanayofuata ni muhtasari ya kile utafiti unahusisha:

1) Maelezo yako ya kibinafsi na maelezo kuhusu ugonjwa wa figo, osteoarthritis na ugonjwa yoyote mwingine ulio nao utachukuliwa.

2) Kipimo cha shinikizo la damu, urefu na uzito wako utachukuliwa

3) Damu kama mililita tano (kama kijiko kidogo cha chai) ya kupima kiwango cha creatinine itachukuliwa kwa njia stadi.

4) Kipimo cha mkojo, kuangulia kiwango cha protini itachukuliwa.

Utafiti utachukua dakika 30 ya muda wako

Hatari na gharama: Wagonjwa watahudumiwa kama kawaida na hakuna madhara au hatari. Kuta kuwepo na maumivu kidogo utakapo dungwa sindano wakati wa kutoa damu. Hakuna gharama yoyote kwa mgonjwa.

Haki yako kama mgonjwa: Ushiriki wako katika utafiti ni kwa hiari, na iwapo utakataa kushiriki matibabu yako haitakatizwa. Ukiamua kushiriki na kutojibu maswali fulani uko na uhuru wa kusimamisha mahojiano na kujiondoa kutoka kwa utafiti wakati wowote. Uko na haki ya kuuliza maswali kabla ya kutia saini fomu hii.

Usiri: Habari unayotoa na majibu yako yatashughulikiwa kisiri. Habari yako itafungiwa mahali salama na itadhibitiwa na mimi mchunguzi mkuu.

Faida: Uchunguzi na taratibu zote zinafanywa bila malipo yoyote kwa mgonjwa (mchunguzi mkuu ata gharamia). Majibu yako ya kipimo cha damu na mkojo yata wekwa katika faili na anayepatikana na shida ya figo, daktari wake katika kliniki atajulishwa na atatumwa kwa daktari mtaalamu apate matibabu.

Malipo: Hakuna malipo yakushiriki katika utafiti huu.

Anwani:

Ukiwa na swali yoyote usiogope kuuliza. Utapata ufafanuzi kutoka kwa:

Dr. Maureen Muyodi,
Mpelelezi Mkuu
P.O.BOX 81464-80100
Mombasa
Tel: 0726719886

Prof. Kirana M. Bhatt,
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Katibu
KNH/UON Ethics and Review Committee
Tel: 2726300 Ext: 44102

FOMU YA IDHINI

Taarifa ya Mshiriki

Nimesoma fomu hii ya idhini. Nimepata maswali yangu kujibiwa kwa lugha ambayo naelewa. Hatari na faida zimeelezwa kwangu. Ninaelewa kuwa ushiriki wangu katika utafiti huu ni wa hiari na kwamba naweza kuchagua kujiondoa wakati wowote. Nakubali kwa bure kushiriki katika utafiti huu. Ninaelewa kuwa juhudi zote zitafanywa kuweka habari kuhusu siri yangu yaki binafsi.

Kwa kusaini fomu hii ya idhini, sijapeana haki yoyote ya kisheria ambayo mimi ninayo kama mshiriki wa utafiti.

Ninakubali kushiriki katika utafiti huu**: Ndio.....Hapana.....**
Ninakubali kuhifadhiwa kwa damu kwa masomo ya baadaye: **Ndio.....Hapana.....**
Ninakubali kutoa habari ya mawasiliano kwa ufuatiliaji: **Ndio.....Hapana.....**

Jina ya Mshiriki: _____

Saini ya mshiriki / muhuri wa kidole gumba _____

Tarehe _____

Taarifa ya mtafiti

Mimi, nimeelezea kikamilifu maelezo muhimu ya utafiti huu kwa mshiriki aliyetajwa hapo juu na ninaamini kwamba mshiriki ameelewa na ametoa ridhaa yake kwa hiari yake.

Jina la Mtafiti: _____ Tarehe: _____

Sahihi_____

Jukumu katika utafiti: _____ [i.e. wafanyikazi wa utafiti ambao walielezea fomu ya ridhaa yenye habari.]

Kwa habari zaidi wasiliana na _____

kutoka_____ kwa _____

Jina lililochapishwa la shahidi (Ikiwa shahidi anahitajika, shahidi ni mtu anayekubalika kwa mtafiti na mshiriki)_____

Maelezo ya mawasiliano _____

Saini/muhuri wa kidole gumba:_____

Tarehe; _____

Appendix 3: Data Collection Tool

SECTION I: Sociodemographic and Behavioural Data

1. How old are you now?
2. Record sex of the respondent
3. What is the highest level of education that you have completed?
4. What is your current marital status?
5. What is/was his/her main occupation?
6. In general, how would you rate your health today?
7. Have you ever consumed a drink that contains alcohol (such as beer, wine, spirits, etc.)?
    a. Yes
    b. No
    c. Never
8. Have you consumed alcohol in the last 30 days?
    a. Yes
    b. No
9. In the last 12 months, how frequently [on how many days] on average have you had at least one alcoholic drink?
    a. No Days.
    b. Less Than Once A Month
    c. One to Three Days Per Month
    d. One to Four Days Per Week
    e. Five Or More Days Per Week
10. Have you ever smoked tobacco or used smokeless tobacco?
    a. Yes
    b. No
11. Do you currently use (smoke, sniff or chew) any tobacco products such as cigarettes, cigars, pipes, chewing tobacco or snuff?
    a. Yes, Daily
    b. Yes, But Not Daily
    c. No, Not at All
12. In the past, did you ever smoke tobacco or use smokeless tobacco daily?
    a. Yes
    b. No

SECTION II: Clinical and Physical Examination

13. Have you ever been diagnosed with/told you have arthritis (a disease of the joints, or by other names rheumatism or osteoarthritis)?
    a. YES
    b. NO
14. When were you told or diagnosed? …….....
15. Have you been taking medications or other treatment for it?

…During the last 2 weeks?

    a. YES
    b. NO

…During the last 12 months?

c. YES
d. NO

16. During the last 12 months, have you experienced, pain, aching, stiffness or swelling in or around the joints (like arms, hands, legs or feet) which were not related to an injury and lasted for more than a month?
    a. YES
    b. NO
17. During the last 12 months, have you experienced stiffness in the joint in the morning after getting up from bed, or after a long rest of the joint without movement?
    a. YES
    b. NO
18. Have you ever been diagnosed with diabetes (high blood sugar)? (Not including diabetes associated with a pregnancy)
    a. YES
    b. NO
19. Have you been taking insulin or other blood sugar lowering medications?
    ….in the last 2 weeks?
    a. YES
    b. NO
    ….in the last 12 months?
    c. YES
    d. NO
20. Have you ever been diagnosed with high blood pressure (hypertension)?
    a. YES
    b. NO
21. Have you been taking any medications or other treatment for it during …
    ….the last 2 weeks?
    a. YES
    b. NO
    ….the last 12 months?
    c. YES
    d. NO
22. In the last 12 months, have you been involved in an accident where you suffered from bodily injury?
    a. YES
    b. NO
23. How did the injury happen? Was it an accident, did someone else do this to you, or did you do this to yourself?
    a. It Was an Accident (Unintentional)
    b. Someone Else Did It to Me Deliberately (Intentional)
    c. I Did It to Myself Deliberately (Self-Inflicted)
    d. Don't Know
24. Did you receive any medical care or treatment for your injuries?
    a. YES
    b. NO
25. Did you suffer a physical disability as a result of being injured?
    a. YES
    b. NO

26. OSTEOARTHRITIS

a) Type of joints involved …….

b) Number of joints involved …….

c) Type of medication used (e.g. NSAIDs) …….

d) Types of NSAIDs in use …….

e) Dosage of the drugs in use ……

f) Duration of use of medication……

g) History of self-medication or over-the-counter medications ……

h) Adherence to medication ……

SECTION III: Anthropometric and Laboratory Tests

1. Blood pressure
    a. Systolic (mmHg) …….
    b. Diastolic (mmHg) ……
2. Weight (kg) …….
3. Height (cm) …….
4. Waist circumference (cm) ……...
5. Hip circumference (cm) …….
6. Current kidney function (eGFR) …….
7. Urine protein level ……

Appendix 4: WHO Global Physical Activity Questionnaire (GPAQ)

Physical Activity

Next, I am going to ask you about the time you spend doing different types of physical activity in a typical week. Please answer these questions even if you do not consider yourself to be a physically active person.

Think first about the time you spend doing work. Think of work as the things that you have to do such as paid or unpaid work, study/training, household chores, harvesting food/crops, fishing or hunting for food, seeking employment. [Insert other examples if needed]. In answering the following questions 'vigorous-intensity activities' are activities that require hard physical effort and cause large increases in breathing or heart rate, 'moderate-intensity activities' are activities that require moderate physical effort and cause small increases in breathing or heart rate.

Question	Response	Code
Work		
Does your work involve vigorous-intensity activity that causes large increases in breathing or heart rate like [carrying or lifting heavy loads, digging or construction work] for at least 10 minutes continuously? [INSERT EXAMPLES] (USE SHOWCARD)	Yes 1 No 2If No, go to P 4	P1
In a typical week, on how many days do you do vigorous-intensity activities as part of your work?	Number of days . /0	P2
How much time do you spend doing vigorous-intensity activities at work on a typical day?	Hours: minutes . /3/0: /3/0 hrs Mins	P3 (a-b)
Does your work involve moderate-intensity activity, that causes small increases in breathing or heart rate such as brisk walking [or carrying light loads] for at least 10 minutes continuously? [INSERT EXAMPLES] (USE SHOWCARD)	Yes 1 No 2If No, go to P 7	P4
In a typical week, on how many days do you do moderate-intensity activities as part of your work?	Number of days . /0	P5
How much time do you spend doing moderate-intensity activities at work on a typical day?	Hours: minutes . /3/0: /3/0 hrs Mins	P6 (a-b)
Travel to and from places		
The next questions exclude the physical activities at work that you have already mentioned. Now I would like to ask you about the usual way you travel to and from places. For example, to work, for shopping, to market, to place of worship. [Insert other examples if needed]		
Do you walk or use a bicycle (pedal cycle) for at least 10 minutes continuously to get to and from places?	Yes 1 No 2If No, go to P 10	P7
In a typical week, on how many days do you walk or bicycle for at least 10 minutes continuously to get to and from places?	Number of days . /0	P8

How much time do you spend walking or bicycling for travel on a typical day?	Hours: minutes . /3/0: /3/0 hrs Mins	P9 (a-b)
Question	Response	Code
Recreational activities		
The next questions exclude the work and transport activities that you have already mentioned. Now I would like to ask you about sports, fitness, and recreational activities (leisure), [Insert relevant terms].		
Do you do any vigorous-intensity sports, fitness or recreational (leisure) activities that cause large increases in breathing or heart rate like [running or football] for at least 10 minutes continuously? [INSERT EXAMPLES] (USE SHOWCARD)	Yes 1 No 2If No, go to P 13	P10
In a typical week, on how many days do you do vigorous-intensity sports, fitness or recreational (leisure) activities?	Number of days . /0	P11
How much time do you spend doing vigorous-intensity sports? fitness or recreational activities on a typical day?	Hours: minutes . /3/0: /3/0 Hrs Mins	P12 (a-b)
Do you do any moderate-intensity sports, fitness or recreational (leisure) activities that cause a small increase in breathing or heart rate such as brisk walking, [cycling, swimming, volleyball] for at least 10 minutes continuously? [INSERT EXAMPLES] (USE SHOWCARD)	Yes 1 No 2If No, go to P16	P13
In a typical week, on how many days do you do moderate-intensity sports, fitness or recreational (leisure) activities?	Number of days . /0	P14
How much time do you spend doing moderate-intensity sports? fitness or recreational (leisure) activities on a typical day?	Hours: minutes . /3/0: /3/0 Hrs Mins	P15 (a-b)
Sedentary behaviour		
The following question is about sitting or reclining at work, at home, getting to and from places, or with friends including time spent sitting at a desk, sitting with friends, travelling in car, bus, train, reading, playing cards or watching television, but do not include time spent sleeping. [INSERT EXAMPLES] (USE SHOWCARD)		
How much time do you usually spend sitting or reclining on a typical day?	Hours: minutes. /3/0: /3/0 hrs Mins	P16 (a-b)

Appendix 5: Supplementary Tables

Table 9: Joints Involved by gender and sides of the body

Joint Involved	Gender [n (%)]		Side of the affected Joint [n (%)]				Total n (%)
	Male	Female	Left	Right	Both	Unspecified	
Knee	44 (17.9)	202 (82.1)	85 (34.5)	59 (24.0)	102 (41.5)	0	246 (41.1)
Spine	41 (23.2)	136 (76.8)					177 (29.5)
Hip	23 (25.3)	68 (74.7)	35 (38.5)	35 (38.5)	20 (22.0)	0	91 (15.2)
Shoulder	3 (10.3)	25 (89.7)	11 (39.3)	13 (46.4)	4 (14.3)	1 (3.6)	28 (4.8)
Ankle	6 (28.6)	15 (71.4)	4 (19.0)	4 (19.0)	13 (61.9)	0	21 (3.5)
Wrist	0	18 (100)	0	4 (22.2)	5 (27.8)	9 (50.0)	18 (3.0)
Hand	0	7 (100)	1 (14.2)	2 (28.6)	2 (28.6)	2 (28.6)	7 (1.2)
Metacarpals	1 (16.7)	5 (83.3)	0	4 (66.7)	2 (33.3)	0	6 (1.0)
Elbow	0	3 (100)	2 (66.7)	1 (33.3)	0	0	3 (0.5)
Fingers	0	1 (100)	0	0	0	1 (100)	1 (0.2)
Total	118	481	115	122	148	13	599

Table 10. NSAIDs used

NSAIDS	First Choice	Second Choice	Third+ Choice	Total
Meloxicam	141 (38.1)	16 (14.7)	2 (13.3)	159 (31.7)
Aceclofenac	87 (25.5)	10 (9.2)	9 (60.0)	106 (21.2)
Celecoxib	43 (11.6)	42 (39.5)	11 (26.7)	99 (19.8)
Diclofenac	54 (14.6)	33 (30.3)		86 (17.2)
Lornoxicam	26 (7.0)			26 (5.2)
Etoricoxib	14 (3.8)	5 (4.6)		18 (3.6)
Ibuprofen	4 (1.1)	1 (0.9)		5 (1.0)
Indomethacin	1 (0.3)			1 (0.2)
Tramcetal		1 (0.9)		1 (0.2)

Table 11. *Proportion of respondents with or without CKD based on CKD–MDRD according to their characteristics*

Variables	Characteristic	No CKD n (%)	CKD n (%)	p-value*
Age, years	Average age	55.5 (11.4)	59.6 (11.0)	**<0.001§**
	20–34	6 (5.0)	0 (0.0)	
	35–49	31 (26.1)	44 (17.5)	
	50–64	60 (50.4)	127 (50.4)	**<0.001**
	65+	22 (18.5)	81 (32.1)	
Sex	Male	53 (44.5)	29 (11.5)	0.354
	Female	66 (55.5)	223 (88.5)	
Education levels	Primary and below	39 (32.8)	109 (43.3)	
	Secondary	57 (47.9)	109 (43.3)	**<0.001**
	Tertiary	23 (19.3)	34 (13.5)	
Employment	Formal employment	53 (44.5)	64 (25.4)	
	Business	31 (26.1)	73 (29.0)	**<0.001**
	Housework/Farming/Others	35 (29.4)	115 (45.6)	
Self-rated Health	Good	43 (36.1)	80 (31.7)	
	Fair	53 (44.5)	129 (51.2)	0.489
	Poor	23 (19.3)	43 (17.1)	
Alcohol	No	90 (75.6)	230 (91.3)	**<0.001**
	Yes	29 (24.4)	22 (8.7)	
Smoking	No	112 (94.1)	242 (96.0)	0.411
	Yes	7 (5.9)	10 (4.0)	
Physical Activity	High	43 (36.1)	77 (30.6)	
	Moderate	47 (39.5)	85 (33.7)	0.092
	Low	29 (24.4)	90 (35.7)	
WHR	Normal	51 (42.9)	143 (56.8)	**0.012**
	Obese	68 (57.1)	109 (43.2)	
BMI	Normal	24 (20.3)	18 (7.2)	
	Overweight	39 (33.1)	76 (30.5)	**<0.001**
	Obese	55 (46.6)	155 (62.3)	
Hypertension	Non-hypertensive	75 (63.0)	104 (41.3)	**<0.001**
	Hypertensive	44 (37.0)	148 (58.7)	
Diabetes	No	111 (93.3)	226 (89.7)	0.263
	Yes	8 (6.7)	26 (10.3)	
All medications	1	93 (78.2)	136 (54.0)	
	2	20 (16.8)	95 (37.7)	**<0.001**
	3–4	6 (5.0)	21 (8.3)	
NSAID use duration	Median (IQR)	0.8 (0.5–2.0)	2.0 (0.4–2.2)	**0.003**
Joints Involved	Median, IQR	1 (1–2)	2 (1–3)	**0.001**
Self-medication	No	10 (8.4)	22 (8.7)	0.917
	Yes	109 (91.6)	230 (91.3)	

** Chi-square test of association; † Fishers test; § Student's t-test; IQR: Interquartile Range; CKD: Chronic Kidney Disease; BMI: Body Mass Index; WHR: Waist-Hip Circumference; AD: Antidiabetics; AH: antihypertensives.*

Table 12. *Proportion of respondents with or without CKD based on CKD–Epi according to their characteristics*

Variables	Characteristic	No CKD n (%)	CKD n (%)	p-value*
Age, years	Average age	52.7 (11.0)	59.9 (10.8)	**<0.001§**
	20–34	5 (5.9)	1 (0.4)	
	35–49	30 (35.3)	45 (15.7)	
	50–64	40 (47.1)	147 (51.4)	**<0.001**
	65+	10 (11.8)	93 (32.5)	
Sex	Male	37 (43.5)	45 (15.7)	**<0.001**
	Female	48 (56.5)	241 (84.3)	
Education levels	Primary and below	22 (25.9)	126 (44.1)	
	Secondary	46 (54.1)	120 (42.0)	**0.010**
	Tertiary	17 (20.0)	40 (14.0)	
Employment	Formal employment	46 (54.1)	71 (24.8)	
	Business	20 (23.5)	84 (29.4)	**<0.001**
	Housework/Farming/Others	19 (22.4)	131 (45.8)	
Self-rated Health	Good	33 (38.8)	90 (31.5)	
	Fair	34 (40.0)	148 (51.8)	0.163
	Poor	18 (21.2)	48 (16.8)	
Alcohol	No	70 (82.4)	250 (87.4)	0.234
	Yes	15 (17.6)	36 (12.6)	
Smoking	No	80 (94.1)	274 (95.8)	0.514
	Yes	5 (5.9)	12 (4.2)	
Physical Activity	High	29 (34.1)	91 (31.8)	
	Moderate	34 (40.0)	98 (34.3)	0.362
	Low	22 (25.9)	97 (33.9)	
WHR	Normal	30 (35.3)	164 (57.3)	**<0.001**
	Obese	55 (64.7)	122 (42.7)	
BMI	Normal	15 (17.9)	27 (9.5)	
	Overweight	34 (40.5)	81 (28.6)	**0.003**
	Obese	35 (41.7)	175 (61.8)	
Hypertension	Non-hypertensive	59 (69.4)	120 (42.0)	**<0.001**
	Hypertensive	26 (30.6)	166 (58.0)	
Diabetes	No	81 (95.3)	256 (89.5)	0.134
	Yes	4 (4.7)	30 (10.5)	
All medications	1	69 (81.2)	160 (55.9)	
	2	12 (14.1)	103 (36.0)	**<0.001**
	3–4	4 (4.7)	23 (8.0)	
NSAID use Duration	Median (IQR)	0.8 (0.4–2.0)	2.0 (0.5–2.2)	**0.003**
Joints Involved	Median, IQR	1 (1–2)	2 (1–3)	**0.001**
Self-medication	No	9 (10.6)	23 (8.0)	0.463
	Yes	76 (89.4)	263 (92.0)	

** Chi-square test of association; † Fishers test; § Student's t-test; IQR: Interquartile Range; CKD: Chronic Kidney Disease; BMI: Body Mass Index; WHR: Waist-Hip Circumference; AD: Antidiabetics; AH: antihypertensives.*

Table 13. *Proportion of respondents with or without CKD based on proteinuria according to their characteristics*

Variables	Characteristic	Nil	1+	2++	p-value
Age, years	Average age	58.2 (11.4)	58.4 (11.1)	59.8 (7.5)	0.803
	20–34	4 (1.3)	2 (5.0)	0	
	35–49	70 (21.5)	5 (12.5)	0	
	50–64	164 (50.3)	19 (47.5)	4 (80.0)	0.249
	65+	88 (27.0)	14 (35.0)	1 (20.0)	
Sex	Male	73 (22.4)	7 (17.5)	2 (40.0)	0.904
	Female	253 (77.6)	33 (82.5)	3 (60.0)	
Education levels	Primary and below	136 (41.7)	11 (27.5)	1 (20.0)	
	Secondary	141 (43.3)	22 (55.0)	3 (60.0)	0.153
	Tertiary	49 (15.0)	7 (17.5)	1 (20.0)	
Employment	Formal employment	105 (32.2)	10 (25.0)	2 (40.0)	
	Business	88 (27.0)	15 (37.5)	1 (20.0)	0.118
	Housework/Farming	133 (40.8)	15 (37.5)	2 (40.0)	
Self-rated Health	Good	104 (31.9)	18 (45.0)	1 (20.0)	
	Fair	162 (49.7)	18 (45.0)	2 (40.0)	**0.023**
	Poor	60 (18.4)	4 (10.0)	2 (40.0)	
Alcohol	No	276 (84.7)	39 (97.5)	5 (100)	**0.049**
	Yes	50 (15.3)	1 (2.5)	0	
Smoking	No	309 (94.8)	40 (100)	5 (100)	0.327
	Yes	17 (5.2)	0	0	
Physical Activity	High	108 (33.1)	10 (25.0)	2 (40.0)	
	Moderate	116 (35.6)	16 (40.0)	0	0.455
	Low	102 (31.3)	14 (35.0)	3 (60.0)	
WHR	Normal	171 (52.5)	21 (52.5)	2 (40.0)	0.787
	Obese	155 (47.5)	19 (47.5)	3 (60.0)	
BMI	Normal	38 (11.8)	3 (7.5)	1 (20.0)	
	Overweight	109 (33.9)	5 (12.5)	1 (20.0)	0.096
	Obese	175 (54.3)	32 (80.0)	3 (60.0)	
Hypertension	Non-hypertensive	164 (50.3)	12 (30.0)	3 (60.0)	0.082
	Hypertensive	162 (49.7)	28 (70.0)	2 (40.0)	
Diabetes	No	296 (90.8)	36 (90.0)	5 (100)	0.651
	Yes	30 (9.2)	4 (10.0)	0	
All medications	1	198 (60.7)	26 (65.0)	5 (100)	
	2	104 (31.9)	11 (27.5)	0	0.154
	3-4	24 (7.4)	3 (7.5)	0	
NSAID use Duration	Median (IQR)	1.5 (0.5–2.0)	2.0 (0.7–2.0)	0.8 (0.2–1.0)	0.970
Joints Involved	Median, IQR	2 (1–3)	2 (1–2)	1 (1–3)	0.453
Self-medication	No	32 (9.8)	0 (0.0)	0 (0.0)	**0.003**
	Yes	294 (90.2)	40 (100.0)	5 (100.0)	

* Chi-square test of association; † Fishers test; § Student's t-test; IQR: Interquartile Range; CKD: Chronic Kidney Disease; BMI: Body Mass Index; WHR: Waist-Hip Ratio; AD: Antidiabetics; AH: antihypertensives.

Table 14. Association between respondents' characteristics and prevalence of chronic kidney disease

Variables	Characteristics	CKD-CG		CKD-Epi		CKD-MDRD		Proteinuria	
		AOR (95% CI)	p-value	AOR (95% CI)	p-value	AOR (95% CI)	p-value	AOR (95% CI)	p-value
Age (Ref: 20–49 years)	50–64	21.4 (7.00–65.9)	**<0.001**	3.17 (1.35–7.44)	**0.008**	2.14 (1.02–4.52)	**0.045**	1.35 (0.45–4.04)	0.595
	65+	119.7 (26.6–538)	**<0.001**	18.9 (5.38–66.2)	**<0.001**	5.16 (1.90–14.0)	**<0.001**	3.84 (1.09–13.6)	**0.037**
Sex (*Ref: Male*)	Female	2.58 (0.94–7.12)	0.067	12.9 (5.28–31.3)	**<0.001**	9.06 (4.23–19.4)	**<0.001**	0.74 (0.27–2.07)	0.572
Education levels (*Ref: Primary and below*)	Secondary	0.89 (0.39–2.06)	0.803	0.42 (0.18–0.96)	**0.040**	0.79 (0.40–1.56)	0.499	2.30 (0.94–5.62)	0.067
	Tertiary	0.45 (0.13–1.55)	0.208	0.82 (0.27–2.51)	0.734	1.14 (0.45–2.89)	0.785	3.52 (0.13–1.55)	0.208
Employment (*Ref: Formal employment*)	Business	1.32 (0.52–3.37)	0.564	1.92 (0.83–4.47)	0.129	1.81 (0.86–3.83)	0.121	1.51 (0.54–4.26)	0.433
	Housework/Farming	0.75 (0.29–1.96)	0.557	1.25 (0.50–3.39)	0.629	1.00 (0.46–2.15)	0.998	1.19 (0.44–3.20)	0.736
Self-rated Health (*Ref: Good)*	Fair	7.08 (2.67–18.7)	**<0.001**	2.11 (0.93–4.79)	0.073	1.42 (0.71–18.7)	0.326	0.72 (0.27–1.90)	0.503
	Poor	11.9 (3.36–42.7)	**<0.001**	1.21 (0.44–3.39)	0.710	0.87 (0.35–2.16)	0.769	0.51 (0.14–1.83)	0.303
Alcohol (*Ref: No*)	Yes	1.08 (0.32–3.60)	0.900	1.10 (0.37–3.30)	0.865	0.29 (0.11–0.78)	**0.014**	0.07 (0.01–0.83)	**0.035**
Smoking (*Ref: No*)	Yes	1.18 (0.13–11.0)	0.884	1.40 (0.25–8.01)	0.704	4.75 (1.03–21.9)	**0.046**	1.00	
Physical Activity Levels (*Ref: High*)	Moderate	0.24 (0.10–0.58)	**0.002**	0.59 (0.28–1.26)	0.172	0.63 (0.33–1.21)	0.164	1.40 (0.57–3.44)	0.457
	Low	0.51 (0.21–1.26)	0.145	1.75 (0.77–3.93)	0.179	1.74 (0.85–3.53)	0.128	1.01 (0.42–2.45)	0.981
Diabetes (*Ref: No*)	Yes	8.88 (0.58–137.0)	0.118	0.00 (0.00–0.00)	0.994	1.10 (0.13–9.13)	0.928	3.73 (0.29–48.1)	0.313
Hypertension (*Ref: No*)	Yes	22.6 (6.18–83.0)	**<0.001**	3.01 (1.03–8.79)	**0.044**	1.35 (0.58–3.12)	0.482	4.80 (1.80–12.8)	**0.002**
Number of Affected Joints (*Ref: 1*)	2	2.38 (0.99–5.74)	0.053	0.61 (0.25–1.47)	0.273	1.25 (0.61–2.58)	0.545	0.91 (0.36–2.29)	0.837
	3	0.79 (0.27–2.25)	0.653	0.18 (0.07–0.46)	0.001	0.67 (0.31–1.43)	0.295	0.66 (0.24–1.84)	0.428
All medications (*Ref: 1*)	2 (NSAIDs + AH/AD)	0.37 (0.10–1.36)	0.134	0.75 (0.21–2.57)	0.645	1.92 (0.75–4.91)	0.176	0.20 (0.07–0.56)	**0.002**
	3-4 (NSAIDs, AH, AD)	2.11 (0.00–0.47)	**0.019**	0.00 (0.00–0.00)	0.993	1.51 (0.12–18.9)	0.749	0.07 (0.00–1.33)	0.076
Duration of NSAID use		1.00 (1.00–1.00)	0.491	1.00 (1.00–1.00)	0.867	1.00 (1.00–1.00)	0.988	1.00 (1.00–1.00)	0.491
BMI (*Ref: Normal*)	Overweight	0.19 (0.04–0.80)	**0.023**	2.35 (0.87–6.30)	0.090	4.37 (1.80–10.6)	**0.001**	0.58 (0.14–2.37)	0.450
	Obese	0.02 (0.004–0.10)	**<0.001**	4.75 (1.70–13.2)	**0.003**	4.44 (1.85–10.7)	**0.001**	1.48 (0.43–5.07)	0.432
WHR (*Ref: Normal*)	Obese	0.69 (0.32–1.51)	0.358	0.26 (0.13–0.55)	**<0.001**	0.45 (0.25–0.83)	**0.010**	1.00 (0.47–2.12)	0.999

Note: Ref: Reference category; COR: Crude Odds Ratio; AOR: Adjusted Odds Ratio; CI: Confidence Interval