KIDNEY FUNCTION STATUS OF PATIENTS ATTENDING NATIONAL ORTHOPAEDIC HOSPITAL DALA-KANO, NIGERIA

BY

SHEHU MUSA ADAMU B.Sc., PGDC, AMLSCN

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DECLARATION

I hereby declare that this work is the product of my research efforts undertaken under the supervision of Prof. A. M. WUDIL and has not been presented anywhere for the award of a degree or certificate. All sources have been duly acknowledged.

SHEHU MUSA ADAMU
SPS/13/MBC/00007

CERTIFICATION

This is to certify that the research work for this dissertation and the subsequent write by (SHEHU MUSA ADAMU SPS/13/MBC/00007) were carried out under my supervision.

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Prof. A. M. Wudil Sign/Date
(Supervisor)

APPROVAL

This Dissertation has been examined and approved for the award of Masters of Science in BIOCHEMISTRY.

…….. ……
Dr. A.B. Sallau Sign/Date
External Examiner

…….. ……
Mallam Aminu Ibrahim Sign/Date
Internal Examiner

…….. ……
Prof. Alhassan M. Wudil Sign/Date
Supervisor

…….. ……
Dr. Mukhtar Bala Sign/Date
Head of Department

…….. ……
Dr. Y.Y. Muhammad Sign/Date
SPS Representative

DEDICATION

This research work is dedicated to **DR. MUHAMMED NUHU SALIHU** MBBS, FWACS, FAOI, MNIM, for his contributions to the development of training and research in National Orthopaedic Hospital Dala-Kano.

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ABSTRACT

Kidney dysfunction in orthopaedic cases may be as a result of kidney injury due to fracture, burns, osteomyelitis, spinal injury, spinal tuberculosis, sickle cell disease and various forms of arthritis among others. This study was aimed at assessing the biomarkers kidney of dysfunction among patients attending National Othropeadic Hospital, Dala Kano. It is prospective randomized study conducted on total of one hundred (100) subjects; sixty (60) patients and forty (40) apparently healthy individuals between the ages of 20-80 years among both sexes. Serum urea, creatinine, malondialdehyde, uric acid, calcium, phosphate and chloride concentrations were estimated by spectrophotometric methods; sodium and potassium concentration by flame photometric method; bicarbonate by titrimetric method while eGFR and BMI were calculated. The number of males 43(71.7%) were more than females 17(28.3%) among which students were 18(30%), civil servants 12(20%), business 11(18.3%), housewives 9(15%), engineers 1(1.7%) while the rest of occupations were 9(15%) among the patients respectively. Overall prevalence of kidney disease in this study was 1.7% which is higher in males (2.3%) than their female counterparts (0%). Kidney disease was found among gouty arthritis patients within the age group 61-80 years, however none was found among 20-40 and 41-60 years. There was significant difference ($p<0.05$) in mean serum potassium (4.0±04 and 3.8±0.4 mmol/l), eGFR (188±54 and 152±33 ml/min/1.73m^2) and BMI (21.28±4.4 and 25.48±5.6 kg/m^2) between males and females respectively. The prevalence of kidney dysfunction in orthopaedic patients was higher in males than females and increasing with age and related to underweight. However, most of the biomarkers of kidney function are irrespective of gender.

CHAPTER ONE

1.0 INTRODUCTION

Kidney injury (KI) has traditionally been defined as a loss of kidney function with resultant accumulation of nitrogenous waste and dysregulation of electrolytes and blood volume (Sehgal *et al*., 2014). In most cases, renal disease does not show symptoms until in its clinical cause. Laboratory tests are often employed to evaluate glomerular and tubular functions (Durfour, 2001; Gowda *et al*., 2010). As Glomerular filtration rate (GFR) declines, a wide range of disorders develop, including fluid and electrolyte imbalance such as hyperkalemia, metabolic acidosis, volume over load and hypophosphatemia (Wallia *et al.*,1986). As glomerular function deteriorates, substances that are normally cleared by the kidneys accumulate in the plasma. The biochemical investigations of renal function can be used to diagnose the presence of renal dysfunction or the severity of the disorder and response to treatments (Mayne, 1994).

Orthopaedics is the branch of medicine that deals with the treatment of deformities, diseases and injuries of bones, joints, muscles, tendons and nerves (Solomon *et al.,* 2001; Webster's 2010). The overall incidence of kidney dysfunction (KD) after elective or emergency orthopedic surgical procedures is reported to reach 9.1%. The risk of acute kidney injury (AKI) in surgical patients has been estimated to be approximately 1% of

all hospitalized patients. It is known to be an independent predictor of poor in-hospital outcome (Konstantinos *et al.*, 2012). Biochemical markers play an important role in accurate diagnosis and also for assessing risk and adopting therapy that improves clinical outcome. Over the decades, research and utilization of biomarkers has evolved substantially. As markers of renal function, creatinine, urea, uric acid and electrolytes are for routine analysis (Gowda *et al.,* 2010).

Patients that undergo major orthopaedic procedures are also at high risk for kidney disease (KD) due to severe electrolyte disturbances, development of perioperative infection or sepsis, and presence of several co morbidities that may impair renal function (i.e. diabetes, heart failure, severe arrhythmias, pulmonary embolism etc). In addition, pre- or post-operative KD is a risk factor for postoperative complications, including acute renal failure and cardiovascular disease, leading to increased mortality and morbidity (Konstantinos *et al.*, 2012).

1.1 Statement of the Problem

Most patients with orthopaedic problems are known to have kidney dysfunction but there is no reliable data about its prevalence and the disease condition more associated with the disease in National Orthopaedic Hospital Dala. Any association between the body mass index (BMI) and kidney disease has so far proved inconclusive.

1.2 Justification

Even though physicians are requesting patients especially above 40 years to carry out kidney function test before undergoing surgical procedures in the National Orthopaedic Hospital Dala, Kano which may not be unconnected with the bone healing and pre operative procedures but they do not usually request in other disease conditions that do not involve surgical procedures. In addition, similar work has not been done in this hospital before; therefore additional information is needed for better diagnosis and patient's management. Researchers also need to know the prevalence of kidney disease among orthopaedic patients in the study area.

1.3 Aim and Objectives

1.3.1 Aim

This work was aimed at assessing the kidney function status among in and out- patients attending National Orthopaedic Hospital Dala, Kano.

1.3.2 Specific objectives are to:

- Estimate the level of kidney function indices (serum urea, sodium, potassium, chloride, bicarbonate, creatinine, uric acid, calcium, phosphate, Malondialdehyde and vitamin D concentrations and eGFR) among orthopaedic patients.
- Measure the body mass index and compare it with kidney profile of the patients.

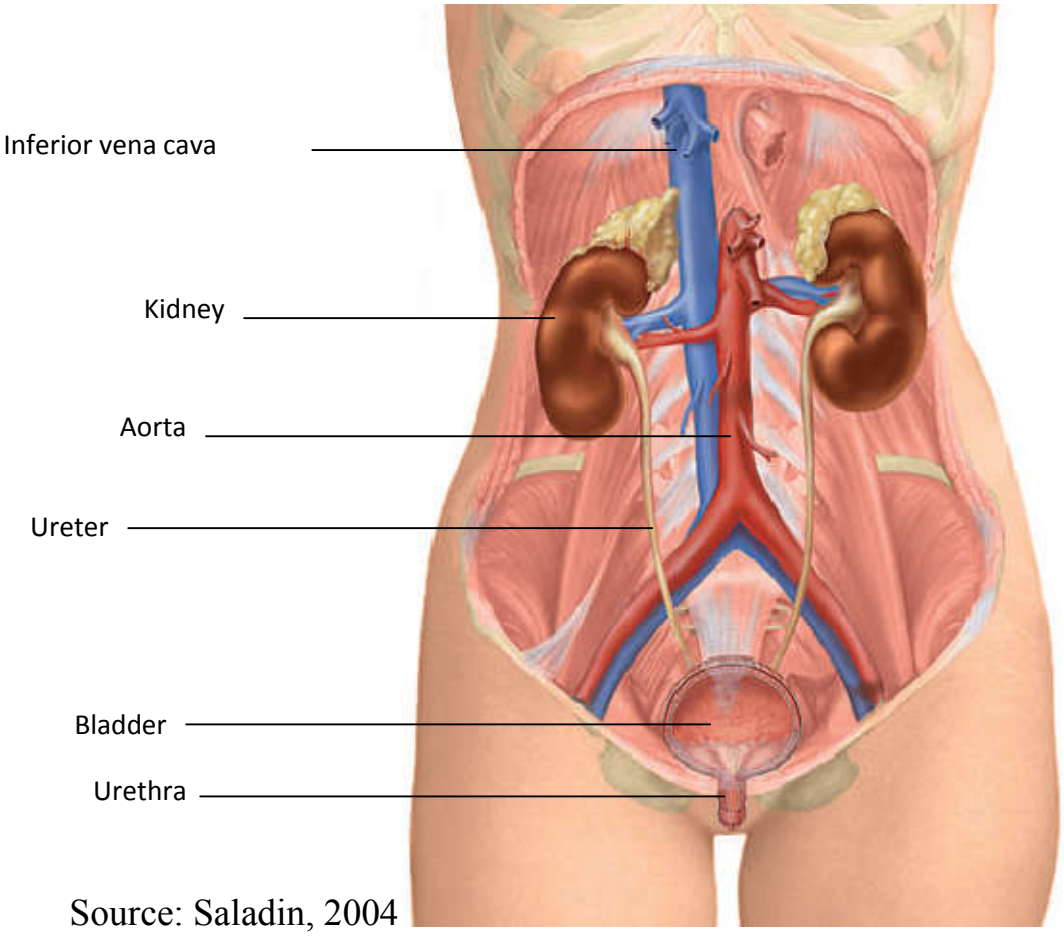
- To compare the Kidney function indices and BMI between females and males patients.
- To determine the socio-demographic factors of the patients attending National Orthopaedic Hospital Dala Kano.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 The kidney

The kidney lies against the posterior abdominal wall at the level of vertebrae TI2 to L3. The right kidney is slightly lower than the left because of the space occupied by the liver above it. Both kidneys also lie adjacent to the suprarenal glands, which, as their name implies, are found perched atop and alongside the superior pole of each kidney, the two structures are related spatially but are mostly independent functionally. Each kidney weighs about 160g and measure about 12cm long, 5cm wide and 2.5cm thick. The kidney has characteristic shape through which passes the vessels, nerves and ureter in which the lateral surface is convex while the medial surface is concave and has a slit called hilium where it receives the renal nerves, blood vessels, lymphatic vessels and ureter (Saladin, 2004; Burtis *et al*, 2008).



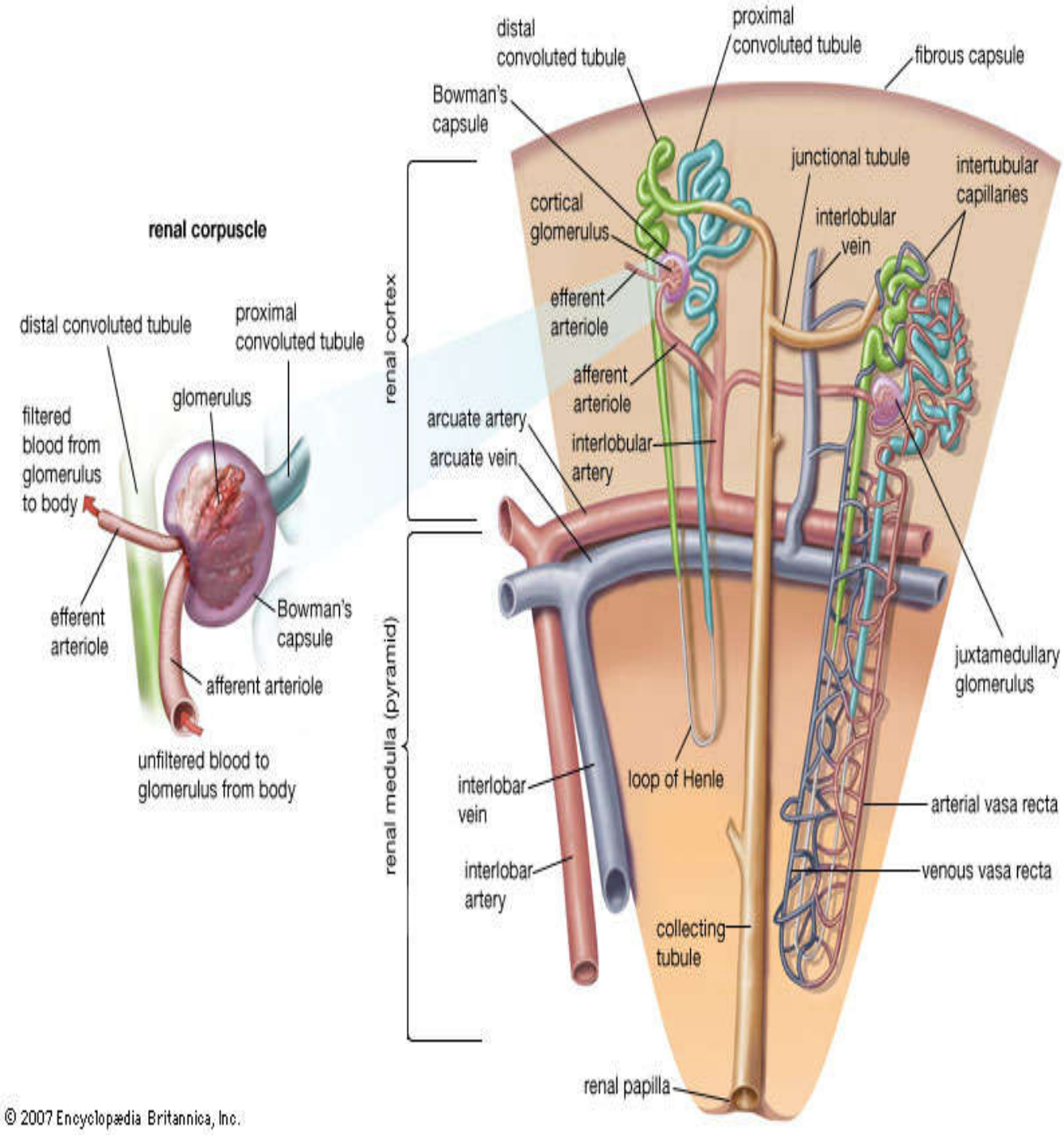
Source: Saladin, 2004

Renal system

2.2 Nephron as a Functional Unit of the Kidney

Nephron is the functional unit of the kidney; it produces urine in the process of removing waste and excess substances from the blood (National Kidney Foundation (NKF), 2015a). Each kidney contains about 1.2 million nephrons. Understanding the function of one nephron, nearly understands everything about the function of the kidney. A nephron consists of two principal parts: a *renal corpuscle* where the blood plasma is filtered and a long *renal tubule* that processes this filtrate into urine (Saladin, 2004).

The glomerulus is a high-pressure filtration system; composed of a specialized capillary network. It generates an ultra filtrate that is free of blood and significant amounts of blood proteins (Nankivell, 2001).



The glomerulus

2.3 Biochemical Functions of the Kidney

Kidney is a structurally complex organ, its functions of which encompass a multitude of secretary, metabolic and reabsoptive functions (Rogers and Hammerman, 2004). The kidney is important for maintaining the stability of internal environment, regulation of osmolarity including acid base balance, excretion of metabolic wastes and removal of toxins (Mayne, 1994).

The kidneys are source of several hormones and are target organ for several hormones. They also have an influence on circulation, bone, intermediary metabolism and erythropoesis by secreting hormone erythropoietin. The *Zona fasciculata* of the adrenal cortex synthesize and secrete hormone cortisol that plays very important role in Gluconeogenesis; *Zona reticularis* of the adrenal cortex produce small quantities of androgens and minute quantity of oestrogens. They also control the arterial pressure by producing the hormone renin that acts on angiotensinogen to produce angiotensin I and subsequently angiotensin II and also aldosterone which is produced by *Zona glomerulosa* of the adrenal cortex (Mayne, 1994; Greger and Windhorst, 1996). The second step in Vitamin D bioactivation; the formation of 1, 25-dihydroxyvitaminD from 25-hydroxyvitaminD also occurs in the kidney (Dusso *et al*., 2005).

2.4 Renal Function and Glomeruler Filtration Rate (GFR)

Renal function can be evaluated by measuring the GFR. Renal damage or alterations in glomerular function affect the kidneys' ability to remove metabolic substances from the blood into the urine (Nankivell, 2001).

Glomerular filtration rate (GFR) is the rate (volume per unit of time) at which ultra filtrate is formed by the glomerulus. Approximately 120 mL are formed per minute. The GFR is a direct measure of renal function. It is reduced before the onset of symptoms of renal failure and is related to the severity of the structural abnormalities in chronic renal disease. The GFR can predict the signs and symptoms of ureamia, especially when it falls to below 10-15 mL/min. Unfortunately it is not an ideal index, being difficult to measure directly and is sometimes insensitive for detecting renal disease. Directly, the serum creatinine concentration is often used to assess renal function. GFR can be calculated from the serum creatinine or more exactly from the results of a 24-hour urine collection. Isotopic methods can be used if a very accurate measurement of the GFR is required (Nankivell, 2001).

As glomeruler filtration rate (GFR) declines, a wide range of disorders develops including fluid and electrolyte imbalance such as hyperkalemia, metabolic acidosis, volume over load and hypophosphatemia (Wallia *et al.*,1986).

Although creatinine clearances can be calculated from urine creatinine concentration measured in a 24 hour urine collection and a concomitant serum Creatinine concentration, a more practical approach in the office is to estimate GFR (estimated GFR or eGFR) from the serum creatinine concentration, using either the Cockcroft-Gault or the Modification of Diet in Renal Disease (MDRD) Study estimating equations (Robert *et al*., 2008).

2.5 Kidney Injury

Kidney injury has traditionally been defined as a loss of kidney function with resultant accumulation of nitrogenous waste and dysregulation of electrolytes and blood volume (Sehgal *et al*., 2014). Nephrons are lost via toxic, anoxic, or immunological injury that may initially injure glomerulus, tubule or both. The kidneys have considerable ability to increase their functional capacity in response to injury. Thus a significant reduction in renal mass (50%-60%) may occur before the onset of any significant symptoms or even before any major biochemical alterations appear. The GFR (glomeruler filtration rate) is reduced even before the minor signs and symptoms are observed. This increase in workload per nephron is thought to be an important cause of progressive renal injury itself (Burtis *et al*, 2008). As the kidney functions deteriorate, a progressive disruption of mineral homeostasis leads to skeletal and

extraskeletal complications which impact with on the quality of life and survival of patients (Thibedi *et al.,* 2014).

2.6 Acute Kidney Failure

Renal failure is also defined as the acute or chronic decline of the renal function (Burtis *et al.*, 2008).

Acute kidney injury (AKI) has been defined as an abrupt loss of kidney function with resultant accumulation of nitrogenous waste and dysregulation of electrolytes and blood volume (Sehgal *et al*., 2014). It most commonly occurs in a hospital setting frequently as a result of ischemic or nephrotoxic insult (Burtis *et al.*, 2008). The risk of acute kidney injury in surgical patients has been estimated to be approximately 1% of all hospitalized patients. It is known to be an independent predictor of poor in-hospital outcome (Konstantinos *et al.*, 2012) and also AKI occurs commonly in hospitalized patients and carries a high mortality (Nash *et al*., 2002); being a common complication of varieties of critical illness and independent risk factor for hospital mortality and is associated with longer intensive care unit (ICU) stay, increased morbidity, utilization of resources, and higher mortality at six-month follow-up (Zhang, *et al.,* 2013; Sehgal *et al*., 2014). It is also an important prognostic marker for complications during hospitalization in the elderly (Sehgal *et al*., 2014).

Efforts have been made to elucidate the underlying mechanisms of the development of AKI based on which preventive or therapeutic strategies can be developed to control this devastating complication. Although there are numerous strategies for the prevention and treatment of AKI including optimization of hemodynamic status, use of vasodilators (e.g. dopamine and fenoldopam), early initiation of continuous renal replacement therapy and use of natriuretic peptides, most of them failed to show a beneficial effect (Zhang, *et al*., 2013). Most of the data on perioperative AKI are from patients with cardiac surgeries (Sehgal *et al*., 2014).

2.6.1 **Causes of acute kidney disease**

The causes of AKI are often divided into three groups: pre-renal, intrarenal and post-renal. Pre-renal failure, also called prerenal azotemia (PRA), is described as a reversible increase in serum creatinine and urea concentrations resulting from decreased renal perfusion which leads to a reduction in the glomerular filtration rate (GFR). On the other hand, intrarenal diseases affect structures of the nephron such as the glomeruli, tubules, vessels or interstitium, and the most common cause of intra-renal (intrinsic) disease is thought to be acute tubular necrosis (ATN). These two causes have been reported to account for 66 to 75% of all cases of AKI.

Recognition of the cause of AKI especially distinguishing PRA and ATN are widely considered clinically important as fluid resuscitation may improve PRA but can cause tissue edema and worsen ATN. Furthermore, ATN has a much worse prognosis (Shigehiko *et al*., 2012).

2.7 Chronic Kidney Disease

Chronic Kidney Disease (CKD) is defined as a disease characterized by alterations in either kidney structure or function or both for a minimum of three months duration (Nigwekar *et al.*, 2014). Chronic Kidney disease is also defined as the presence of kidney damage manifested by abnormal albumin excretion or decreased kidney function quantified by measured or estimated glomerular filtration rate (GFR) that persists for more than three months (Robert *et al*., 2008). The disease includes conditions that damage the kidneys and decrease their ability to keep them healthy. If kidney disease gets worse, wastes can build to high levels in the blood and make individual feel sick. It may result to complications like high blood pressure, anaemia (low blood count), weak bones, poor nutritional health and nerve damage. Kidney disease also increases the risk of having fluid overload, heart and blood vessel disease. These problems may happen slowly over a long period of time (NKF, 2015a). Earlier recognition of the disease could slow progression, prevent complications, and reduce cardiovascular-related outcomes. However, current estimates of CKD awareness on both patient and provider level remain

unacceptably low. Many of the factors that are possibly associated with CKD awareness of which could help to guide implementation of awareness efforts have yet to be fully examined. Little is also known regarding whether increased patient or provider awareness improves clinical outcomes or whether there are possible negative consequences of awareness for CKD patients. Further research is necessary to continue to design and refine awareness campaigns aimed at both patients and providers. Moreover, there is an immediate need for the dissemination of basic CKD information given both the high prevalence of CKD and its risk factors and the low estimated awareness of CKD (Plantinga *et al*., 2010).

2.7.1 **Causes of chronic kidney disease**

Chronic kidney disease may be caused by diabetes, high blood pressure and other disorders. Early detection and treatment can often keep chronic kidney disease from getting worse. As kidney disease progress, it may eventually lead to kidney failure which requires dialysis or a kidney transplant to maintain life (NKF, 2015a).

People are exposed to various potentially toxic agents and conditions in their natural and occupational environments. These agents may be physical or chemical, may enter the human body through oral, inhalational, or transdermal routes and may exert effects on all organ systems. Several associations exist between CKD and both environmental

agents and conditions, such as heavy metals, industrial chemicals, elevated ambient temperatures, and infections. The effects of these agents may be modulated by genetic susceptibility and other co morbid conditions and may lead to the development of kidney disease (Soderland *et al*., 2010). Nalado *et al.* (2012), reported the prevalence of risk factors for CKD among civil servants in Kano with high positive history of use of traditional medicines; this is important as most of these herbal preparations were not studied and accurately characterized, hence the active ingredient is not known. Some of these herbal preparations were actually reported to be nephrotoxic. The use of analgesic drugs, alcohol ingestion or use of bleaching creams where also recognized as a risk factors for kidney disease. With early identification and treatment of anaemia, renal osteodystrophy, uraemic malnutrition, hyperlipidemia and cardiovascular disease, primary health care physicians and nephrologists together are making significant strides toward extending and improving the lives of patients with chronic renal disease (Robert *et al*., 2008). It was also known that diabetes, hypertension and glomerulonephritis are the main causes of CKD in Nigeria while In the United States, diabetes and hypertension are the commonest causes of CKD while glomerulonephritis plays a less important role (Odubanjo *et al.,* 2011a; Paudel *et al*., 2013).

2.8 Epidemiology of Kidney Disease

The overall incidence of kidney dysfunction after elective or emergency orthopedic surgical procedures is reported to reach 9.1% (Konstantinos *et al.,* 2012). Chronic kidney disease has become a major health problem with about one in ten adults affected worldwide (Thibedi *et al.,* 2014). However, It is estimated that over 20 million Americans have chronic kidney disease (Coresh *et al*., 2007).

The incidence of CRF and End-stage renal disease (ESRD) in any specified area may be influenced by the prevalence of specific disease entities resulting in CRF and by the availability of funds, sophisticated modalities of treatment and expertise are required in the care of the varied types of renal diseases (Asinobi, 1995). ESRD is the final event of a sequence that begins with an initial insult and progresses towards total loss of renal function (Asinobi, 1995).The incidence and the prevalence of ESRD are good indicators of the burden of renal disease in a country. The prevalence is influenced by the number of new cases, mortality and poor socioeconomic status with increased number of non repeated cases (Odubanjo *et al.,* 2011b).

The risk of acute kidney injury (AKI) in surgical patients has been estimated to be approximately 1% of all hospitalized patients. It is known to be an independent predictor of poor in-hospital outcome (Konstantinos *et al.,* 2012). In Nigeria, the actual incidence and prevalence of ESRD is

not clearly known. The prevalence of CRF has been shown in the southern parts of Nigeria to be 1.6%, 3.6%, 6.7%, 8% and 10 % (Odubanjo *et al.,* 2011b). The incidence of CKD in Nigeria was also been shown by various studies to range between 1.6 and 12.4% (Odubanjo *et al.,* 2011a). It has been suggested that the wide variation in the values from various studies appears to be due to variations in the sources of the data consulted (Odubanjo *et al.,* 2011b). The increased prevalence of ESRD among blacks in the United States and South Africa compared with other races also suggests that ESRD may be more prevalent in Africa than in the United States and other developed nations (Odubanjo *et al.,* 2011a).

2.9 Kidney Function Tests

In most cases, the symptoms of renal disease do not show initially until in its clinical cause. Kidney function tests are those evaluating glomerular and tubular functions (Durfour, 2001; Gowda *et al*., 2010). As glomeruler function deteriorates; substances that are normally cleared by the kidneys accumulate in the plasma. The biochemical investigations of renal function can be used to diagnose the presence of renal dysfunction or the severity of the disorder and response to treatment (Mayne, 1994).

Biochemical markers play an important role in accurate diagnosis and also for assessing risk and adopting therapy that improves clinical outcome. Over the decades, research and utilization of biomarkers has

evolved substantially. As markers of renal function, creatinine, urea, uric acid and electrolytes are for routine analysis (Gowda *et al.,* 2010).

Chronic kidney disease typically increases with age and therefore there is an increased risk in older adults. It is found that females are less prone to the risk of the disease (Paudel *et al*., 2013).

2.9.1 **Serum urea**

Urea is manufactured in the liver from carbon dioxide and ammonia resulting from the breakdown of amino acids. It constitutes almost half of the total of the non protein nitrogenous substances of the blood. It is the major execratory product of protein metabolism. Urea is carried by the plasma to the kidney where it is filtered from the plasma by the glomerulus. About 40% of the urea in the glomerular filtrate is reabsorbed by the renal tubules. Most of the urea in the filtrate is excreted in urine while small amounts are excreted through the gastrointestinal tract and the skin (Ochei and Kolhatkar, 2000).

Serum blood urea nitrogen (BUN) is an indirect and rough measurement of renal function; measuring the amount of urea nitrogen in blood and is directly related to the excretory kidney function (Akanda *et al*., 2013). The levels of serum blood urea nitrogen however, may provide supplemental information in regard to renal function as renal proximal tubule cells may increase its reabsorption in the setting of increased neurohormonal activation (Robert *et al.,* 2010).

The amount of urea in the blood is affected by the protein in the diet. When the amount of the urea becomes excessive, the condition is known as ureamia. This condition is usually a result of impaired kidney function. In the elderly, the urea level may be a little higher than normal and low values are found during pregnancy and in full term infants, where as premature infants may have slightly higher values then the adult range (Ochei and Kolhatkar, 2000).

2.9.2 **Serum creatinine**

Creatinine is a nitrogenous product produced from the metabolism of creatine in the skeletal muscles; it is an amino acid derivative with a molecular mass of 113 D. It is filtered by the kidneys and excreted in the urine. Unlike urea, creatinine level is not affected by protein intake. The measurement of creatinine level is a test of renal function, (Ochei and Kolhatkar 2000; Lesley *et al*, 2006). Many studies support the similarity of creatinine clearance to GFR and its reciprocal relationship with the serum creatinine level (Lesley *et al,* 2006). Renal function has routinely been assessed with an estimated creatinine clearance, serum creatinine or an estimated glomerular filtration rate (eGFR) derived from the serum creatinine. Creatinine tests diagnose impaired renal function and measure the amount of creatinine phosphate in the blood (Akanda *et al*., 2013). The loss of kidney function may easily be quantified by measuring the serum creatinine (Sehgal *et al*., 2014). The formation of creatinine is

constant and direct relationship to muscle mass, for this reason varies with age and sex (Ochei and Kolhatkar 2000). Serum creatinine also originates from dietary sources of creatinine such as cooked meat. Creatinine generation from the muscles is proportional to the total muscle mass and muscle catabolism. In people with a relatively low muscle mass, including children, women, the elderly, malnourished patients and cancer patients, the serum creatinine is lower for a given GFR. There is a danger of underestimating the amount of renal impairment in these patients as their serum creatinine is also relatively lower. For example, the GFR may be reduced as low as 20-30 mL/min in a small elderly woman while her serum creatinine remains in the upper range of normal. Creatinine is an imperfect filtration marker, because it is secreted by the tubular cells into the tubular lumen, especially if renal function is impaired. When the GFR is low, the serum creatinine and creatinine clearance overestimate the true GFR. Some drugs (such as cimetidine or trimethoprim) have the effect of reducing tubular secretion of creatinine. This increases the serum creatinine and decreases the measured creatinine clearance. Paradoxically, when these drugs are used, a more accurate measurement of GFR is obtained as it is largely free from the error contributed by the physiological tubular secretion of creatinine (Nankivell, 2001). A large body of evidence suggests that even a mild increase in serum creatinine will have significant negative impact on

kidney (Zhang *et al.*, 2013). Creatinine clearance provides a more accurate assessment of renal function (Nankivell, 2001).

2.9.3 **Serum uric acid**

Uric acid is the product of the xanthine oxidase–catalyzed conversion of xanthine and hypoxanthine; is the final metabolite of endogenous and dietary purine nucleotide metabolism. It is a weak acid, with a p K_a of 5.75; at a physiologic pH of 7.40 in the extracellular compartment, 98% of uric acid is in the ionized form as urate. In the collecting tubules of the kidneys, where the pH can fall to 5.0, uric acid formation is favored (Fahlen, 2015). It is problematic because humans do not possess the enzyme uricase which converts uric acid into the more soluble compound called Allantoin (Guest, 2001). Acute gout attacks are painful therefore attention had been directed towards the pathogenic role of uric acid and evidence was provided that uric acid stone formation is responsible for renal colic (Cucuainu and Brudescà, 2012).

Three forms of kidney disease have been attributed to excess uric acid: acute uric acid nephropathy, chronic urate nephropathy, and uric acid nephrolithiasis. These disorders have different clinical features but common element of excess uric acid or urate deposition (Guest, 2001). However, recent evidence supported the view that uric acid may not be an active player in the pathogenesis of renal disease by causing endothelial dysfunction and intrarenal impairment. Most compelling evidence comes

from animal models in which induced hyperuriceamia in healthy rats caused renal cortical vasoconstriction and glomeruler hypertension that was prevented by allopurinol treatment. In rats with pre-existing renal disease, hyperuriceamia increase renal vascular damage (Daoussis *et al.*, 2009).

The precipitation of uric acid in the renal medulla with formation of characteristics tophi was believed to evoked an inflammatory response leading to fibrosis, a loss of nephron and ultimately to chronic irreversible renal failure. Some emphasized that nearly 100% of the patients with chronic gout also have renal involvement, however, based on the investigation of autopsy cases, chronic uric acid deposit in the kidney (renal tophi) hardly cause irreversible renal failure because in significant number of cases, renal tophi were also found without evidence of renal involvement (Nickeleit and Mihatsch, 1997).

2.9.4 **Serum malondialdehyde**

Malondialdehyde (MDA) is an end-product generated by decomposition of arachidonic acid and larger poly unsaturated fatty Acids (PUFAs) through enzymatic or non enzymatic processes. It has also been proposed that MDA could react physiologically with several nucleosides (deoxyguanosine and cytidine) to form adducts to deoxyguanosine and deoxyadenosine and the resulting major product is a pyrimidopurinone. MDA is an important contributor to DNA damage and mutation. The

MDA-DNA adducts may lead to mutations (point and frameshift), strand breaks, cell cycle arrest, and induction of apoptosis (Ayala *et al*., 2014).

Chronic kidney disease is a pro-oxidant state and the degree of intracellular and extracellular oxidative stress is related to the severity of renal failure. The oxidative stress depends on the excess production free radical coupled with low concentration of antioxidants. It also been observed that, free radical induced lipid peroxidative tissue damage has played a significant role in the pathogenesis of various renal diseases (Raju *et al*., 2013).

Padalkar *et al*. (2012) reported the increased level of serum MDA in kidney disease patients which clearly shows that they were exposed to an increased oxidative stress via lipid peroxidation. Lipid peroxidation is assayed indirectly by the production of secondary products like a water soluble three carbon; low molecular weight reactive aldehyde, Malondialdehyde (Raju *et al*., 2013).

2.9.5 **Serum electrolytes and kidney function**

Electrolytes are positively and negatively charged ions that are found within cells and extracellular fluids including intestinal fluid, blood, and plasma. A test for electrolytes includes the measurement of sodium, potassium, chloride, and bicarbonate. These ions are measured to assess kidney endocrine (glandular) and acid-base functions (Yousafzai *et al*., 2011). Electrolytes are the key to homeostasis and furthermore, their

regulation is dependent upon renal function. Kidney disease is associated with aberrations in the metabolism of electrolytes such as calcium, phosphates, sodium and potassium (Owiredu *et al*., 2012).

The role of electrolytes is extensive particularly that of the cations (positively charged ions) sodium and potassium which exist in the body fluids largely as free ions. As well as maintaining cellular tonicity and fluid balance between the various cellular components; they are involved in most metabolic processes like maintenance of pH and regulation of neural and muscular function. Abnormal levels can be either the cause or result of a wide range of disorders (Cheesbrough, 2009).

2.9.5.1 **Serum sodium**

Sodium is the main extracellular cation. The plasma sodium level is a major factor in the control of water homeostasis and extracellular fluid volume. An increase in plasma sodium normally results in three compensatory mechanisms coming into play thirst prompts oral fluid intake, anti-diuretic hormone (ADH) secretion from the pituitary is increased leading to renal water retention; there is a shift of water from intracellular to extracellular. As the total intake of sodium chloride is almost completely absorbed from the gastrointestinal tract with no active control, regulation of the retained body sodium is maintained by the kidneys with the excess excreted in the urine and fine control carried out by tubular reabsorption. After initial glomerular filtration some 60% of

the filtered sodium is recovered in the proximal tubules together with bicarbonate; 25% is reabsorbed in the Loop of Henle of the renal tubule with chloride; the remainder is reabsorbed in the distal tubules with aldosterone governing its reabsorption; it competes with potassium and hydrogen ions (Cheesbrough, 2009).

Sodium is primarily responsible for maintaining osmotic pressure. Increased serum sodium is present in states of dehydration as a result of diarrhea or vomiting. Low sodium levels usually are a result of too much water in the body (Yousafzai *et al*., 2011). In order for the kidney to excrete excess water by producing a large volume of dilute urine, there must be an adequate glomerular filtration rate. Generally, hyponatremia result in less renal impairment due to intake of large amounts of water. In contrast, hypernatremia may results from renal water loss**.** The hallmark of marked renal water loss is polyuria, defined as a urine volume greater than 3L/24 hours. The common defect in all cases of renal water loss is an inability of the kidney to conserve water appropriately (Richard, 2010).

2.9.5.2 **Serum potassium**

Potassium is the principal intracellular cation, 98% of which is maintained within the cells by the ATP dependent mechanism known as the sodium pump. Any sodium which diffuses into cells is actively excreted in exchange for potassium. Insulin also accelerates the cellular

uptake of potassium and elevated levels of plasma potassium encourage secretion of insulin. In addition to its role in intracellular osmolality, potassium is essential for many enzymatic reactions, the regulation of heart muscle, and for the transmission of nerve impulses. An important factor in the control of potassium cellular transport is the acid/base status. In acidosis the flow of hydrogen ions into cells causes the outflow of an equivalent number of potassium ions. Dietary potassium intake is normally in excess of requirement and the surplus is excreted via the kidneys. Following potassium ingestion, aldosterone secretion is increased to enhance renal clearance and insulin levels rise to increase cellular absorption (Cheesbrough, 2009). Serum potassium is the most convincing electrolyte marker of renal failure. The combination of decreased filtration and decreased secretion of potassium in distal tubule during renal failure cause increased plasma potassium. Hyperkalemia is the most significant and life-threatening complication of renal failure (Gowda *et al.,* 2010). Potassium is a major component in cardiac function; too much potassium in the blood is usually caused by poor kidney function and can cause abnormal and sometimes fatal cardiac arrhythmia. Low potassium levels are usually the result of potassium loss from intake of K^+ lowering drugs, excessive urination or from vomiting (Yousafzai *et al*., 2011).

Many of the disorders causing renal potassium loss are also associated with acid-base disorders. Therefore, numerous causes of renal potassium loss was classified according to whether they typically occur together with metabolic acidosis, metabolic alkalosis or hypokalemia (low serum potassium) with no specific acid-base disorder. On the other hand, when GFR is reduced to <20% of normal, hyperkalemia (high serum potassium) may develop rapidly from exogenous potassium in patients with renal failure (Richard, 2010).

2.9.5.3 **Serum chloride**

Critically ill patients receive large amount of intravenous fluid administration during their ICU stay. Many commercially available crystalloid fluids are rich in chloride, such as the most widely used saline 0.9% that has 40% higher chloride than human plasma. Some animal studies suggest that administration of chloride-liberal fluid induces renal vasoconstriction and a decline in glomerular filtration rate (**Zhang** *et al.,* 2013).

Zhang *et al*. (2013), shows that higher chloride are associated with the development of AKI, indicating that chloride overload during ICU treatment may increase the risk of AKI and also indicated that restricting chloride infusion is no longer beneficial in patients with hypochloremia.

2.9.5.4 **Serum bicarbonate**

Decreasing kidney function causes progressively increased retention of acids, resulting in numerous deleterious consequences, such as protein catabolism and protein-energy wasting, worsening uremic bone disease and an association with decreased functional capacity and with increased mortality in patients with end-stage renal disease. Metabolic acidosis has also been linked directly to kidney damage and to increased progression of CKD, possibly through mechanisms associated with adaptive responses meant to enhance acid excretion in the face of progressive loss of kidney function (Kovesdy, 2012). The association between elevated serum bicarbonate concentrations in patients with kidney disease is positive and should be taking to consideration in every patient with the disease (Khitan, 2015). Sankar *et al.* (2011) reported that low serum bicarbonate levels are associated with death among stage 3 CKD, while high serum bicarbonate levels are associated with death among both stage 3 and stage 4 CKD patients.

2.9.5.5 **Serum calcium**

The adult human body contains approximately 1,300 g of calcium with 99% in skeleton, 0.6% in soft tissues, and 0.1% in extracellular fluid (NKF, 2013). Normal values for serum total calcium concentration vary among clinical laboratories, depending on the methods of measurement,

with a normal range being 2.15 to 2.57mmol/L for adults (Goldman and Bennett 2000; Burtis *et al.*, 2008).

Maintenance of normal calcium balance and serum calcium levels depend on integrated regulation of calcium absorption and secretion by the intestinal tract, the excretion of calcium by the kidney and calcium release from and calcium deposition into bone. Serum calcium level is increased by Parathyroid hormone (PTH) through stimulating bone resorption, kidney distal tubular calcium reabsorption and also activating renal hydroxylation of 25(OH) D_3 to 1, 25$(OH)_2$ D3. Depression in serum levels of calcium by itself stimulates the secretion of preformed parathyroid hormone from parathyroid gland within seconds through the calcium-sensing receptor (CaR) in the parathyroid gland. Subsequently, PTH biosynthesis by parathyroid gland increases over 24 to 48 hours and, if persistent, is followed by parathyroid gland hypertrophy and hyperplasia. Vitamin D metabolites and serum phosphorus levels also regulate PTH levels in blood. These homeostatic mechanisms are distorted in early stages of kidney disease and continue to deteriorate as loss of kidney function progresses (NKF, 2013). Evidence report indicates that hypocalcaemia is a risk for bone disease and for development of secondary hyperparathyroidism and/or increased risk of mortality. Thus, the detection of true hypocalcaemia and its appropriate treatment is important for the management of patients with kidney disease

(Block, *et al*., 1998). Hypercalcaemia poses a risk for kidney patients as it would increase the Ca-P product index in blood (NKF, 2013).

2.9.5.6 **Serum phosphate**

Human phosphate homeostasis is regulated at the level of intestinal absorption of phosphate from the diet, release of phosphate through bone resorption, renal phosphate excretion and involves the actions of parathyroid hormone, 1-25-dihydroxy-vitamin D and fibroblast growth factor 23 to maintain circulating phosphate levels within a narrow normal range which is essential for numerous cellular functions among which are the growth of tissues and bone mineralization (Bergwitz and Jüppner, 2011). Elevated serum phosphate has clinically been associated with vascular stiffness and cardiovascular mortality (Lau *et al*., 2011).

Hyperphosphatemia is one of the most important risk factors associated with cardiovascular disease in CKD patients. The exact mechanism underlying this association remains unclear. It is believed to be related to hyperparathyroidism and vascular calcification which results from high phosphorus levels (Roberts *et al*., 2008). As kidney disease progresses there is diminished filtration and excretion of phosphate resulting in hyperphosphatemia (Owiredu *et al*., 2012).

Mechanistic studies over the past decade regarding local effects of phosphate on the vessel wall have provided insight into various pathways that culminate in vascular calcification. Smooth muscle cell phenotype

change and apoptosis play prominent roles. The sodium-phosphate cotransporter PiT-1 is required for the osteochondrogenic differentiation of smooth muscle cells in vitro. Less is known about phosphate-driven valve interstitial cell calcification and elastin degradation (Lau *et al*., 2011). Serum phosphorus levels should be maintained between 2.7 and 4.6 mg/dL in patients with stages 3 and 4 CKD, and between 3.5 and 5.5 mg/dL in individuals with stage 5 CKD (Roberts *et al*., 2008).

2.9.6 **Serum vitamin D**

Vitamin D is derived from either 7-dehydrocholesterol or ergosterol by the action of ultraviolet radiation (Vasudevan and Sreekumari, 2007). It has been appreciated that vitamin D insufficiency may lead to osteoporotic fractures, overt deficiency states such as rickets and osteomalacia and it may also have important extraskeletal roles in the prevention of cancer, autoimmune disease, diabetes, and other disorders (Aloia *et al.,* 2008). African Americans are particularly susceptible to vitamin D insufficiency because the darker color of their skin limits the amount of ultraviolet light that penetrates, thereby reducing the cutaneous synthesis of vitamin D (Aloia *et al.,* 2008).

The prevalence of vitamin D deficiency in the CKD population has been described to range between 70 and 80% (Nigwekar *et al.*, 2014). Deficiency of 1, 25-dihydroxyvitamin D (1,25 OH_2 D_3) is known to occur during the progression of CKD because the final hydroxylation step of

25-hydroxyvitamin D (25(OH)D_3) to 1,25 OH_2 D_3 (Calcitriol) is mediated by kidney 1-α hydroxylase (Levin, *et al*., 2007), because psatients with kidney disease have reduced activity of the enzyme 1-α hydroxylase (CYP27B1) in the kidneys, which converts 25-hydroxyvitamin D (25(OH)D) to its more active form, 1,25-dihydroxyvitamin D ($1,25(OH)_2D$). As kidney function worsens, low circulating 1, 25-dihyrdoxyvitamin D levels is experienced (Melamed and Thadhani, 2012). A 25(OH) vitamin D (calcidiol) level 75 nmol/L (30 ng/ml) has been identified as a cause of falls which may lead to fracture that responds to treatment with a reduction in falls. 25 (OH) vitamin D deficiencies are very common in renal failure patients (Morley, 2009).

2.10 Body Mass Index (BMI) and Kidney Function

Body Mass Index (BMI) is a person's weight in kilograms divided by the square of height in meters. A high BMI can be an indicator of high body fatness. BMI can be used to screen for weight categories that may lead to health problems but it is not diagnostic of the body fatness or health of an individual {Center for Disease Control and Prevention (CDC, 2015)}. Body mass index is commonly used to diagnose obesity. However, it can be influenced by muscle mass, and its ability to diagnose obesity can vary considerably by predictors of muscle mass, such as age, sex, and race. Among patients with kidney disease who often are elderly and frail, lean body mass may be reduced. Furthermore, volume overload

that often accompanies kidney disease by itself can influence BMI estimation. Therefore, BMI may not accurately reflect excess body fat among patients with kidney disease (Agarwal *et al.,* 2010). Body mass index and prevalence of obesity with kidney disease were found to be higher than in those without the disease in both genders (Nomura, *et al*., 2009). However, Iseki *et al.* (2004) found that, increasing BMI was associated with an increased risk of the development of ESRD in men. Any association between the body mass index (BMI) and kidney disease has so far proved inconclusive (Cohen *et al*., 2013).

2.11 Orthopaedics

Orthopaedics is the branch of medicine that deals with the treatment of deformities, diseases and injuries of bones, joints and muscles (Webster's 2010); it also concerned with tendons and nerves – the skeletal system and all that makes it moves (Solomon *et al.,* 2001). As in all branches of medicine, no condition can exist in true isolation thus there is a defined linking system between general diseases and orthopaedic problems (Obajuluwa, 2014). Conditions that affect skeletal structures (bones, joints, muscles, tendons and nerves) can be congenital and developmental abnormalities, infection and inflammation, arthritis and rheumatic disorders, metabolic and endocrine disorders, tumors and lesions that mimic them, sensory disturbance and muscle weakness as well as injury and mechanical derangement (Solomon *et al.,* 2001). Metabolic bone

disease is a common complication of kidney disease and is part of a broad spectrum of disorders of mineral metabolism that occur in the clinical setting and result in both skeletal and extra skeletal consequences (Kevin and Esther, 2007).

2.11.1 **Fracture and kidney disease**

A fracture is a slight crack or break of a bone. It may be a complete break in the continuity of a bone or incomplete break or crack. Increased bone remodeling leading to micro architectural deterioration and increased fragility may accompany declining kidney function. Patients with kidney disease have higher rates of fracture than the general population (Nickolas *et al*., 2011).

There is a rapid decrease in bone mineral density after renal transplantation over the first year. This decrease in bone is associated with increased risk of fractures. The causes of this increased loss of bone include renal osteodystrophy, Glucocorticoids, immunotherapy, vitamin D deficiency, hypophosphatemia, hypogonadism, and osteoporosis. Bisphosphonates (oral and intravenous), vitamin D, and calcitonin have all been shown to slow the rate of bone loss (Morley, 2009).

Falls and associated fragility fractures are a major cause of morbidity and mortality in older persons with kidney disease. Overall studies suggest that the fall rate is much greater in dialysis patients than in the general population. In the general population over 75 years of age, 30% of

persons fall each year with one in five having an injury. Hip fractures in persons on dialysis occur three to four times more commonly than in the general population (Morley, 2009).

2.11.2 **Burns and kidney function**

Extensive burn is not only a skin injury but also a serious systemic illness often accompanied by various complications. Acute renal failure (ARF) is one of the major complications of burns, carrying an extremely high mortality rate. Although ARF is not commonly encountered in burned patients, this complication merits a special attention depending on the severity and adequate management of the burn injury (Kang *et al*., 2001). The reported incidence and mortality rate of ARF among burned patients varies depending on the severity of the burn injury. ARF occurs either immediately after burn or at a later stage, most often in the third week or later. It is still a life-threatening complication, particularly in patients with extensive third degree burns (Aikawa, *et al*., 1990). Renal pathologies in burns are characterized by the development of extensive inflammation inducing an intensive acute phase response in the kidney. Urinary Malondialdehyde (MDA) is a gross indicator of renal lipid peroxidation and has been shown to increase after burns (Kang *et al*., 2001).

2.11.3 **Rheumatoid arthritis and kidney function**

Rheumatoid arthritis (RA) is a chronic, progressive, inflammatory autoimmune disease associated with articular, extra-articular and

systemic effects. Although some patients have mild self-limited disease, many experience joint destruction, severe physical disability and multiple co-morbidities. It has been reported that RA affects 0.51% of the adult population of developed regions (Choy, 2012). Rheumatoid Arthritis is characterized as a chronic, inflammatory disease in which the immune system destroys synovial joints and accessory structures. As it progresses, this autoimmune condition can cause extra-articular complications within several organ systems, it is the most common autoimmune disease and second most common form of arthritis compared to osteoarthritis **(**Clements, 2011). Hickson *et al*. (2014) reported that patients with RA were more likely to develop reduced kidney function over time.

2.11.4 **Gouty arthritis and kidney function**

Gouty arthritis is an inflammatory arthritis caused by the deposition of monosodium urate crystals into joints cavity, which is therefore considered to represent a metabolic joint disease (Cucuainu and Brudescà, 2012). Gout is the most common inflammatory joint disease in men. Overall the range of prevalence was from 0.03% for Nigerian men to 15.2% for Taiwanese aboriginal men (Smith *et al*, 2010). Based on recent estimates, between 47% and 54% of patients with gouty arthritis are affected with kidney disease (Abdellatif and Elkhalili, 2014).

2.11.5 **Osteoarthritis and kidney function**

Osteoarthritis (OA) is a debilitating condition characterized by pain, joint inflammation and joint stiffness, and results in a substantial degree of physical disability. It is the most common form of arthritis. World Health Organization (WHO) estimates that 25% of adults aged over 65 years suffer from pain and disability associated with this disease globally and every age group is affected. The prevalence increases dramatically after age 50 years in men and 40 years in women. The direct cause of OA is unknown, but it is thought that it results from intrinsic alterations of the articular tissue, or as a response to cumulative mechanical stress, it is also caused primarily by the degradation of the collagen and proteoglycans in cartilage, leading to fibrillation, erosion and cracking in the superficial cartilage layer. Over time, this process spreads to the deeper layers of cartilage, and eventually large, clinically observable erosions are formed. The second and third most commonly involved joints are those of the knee and hip respectively (Breedveld, 2004). Zayed *et al*. (2013) reported middle-aged obese Egyptian patients with knee OA represent a high risk group for renal dysfunction.

2.11.6 **Osteomyelitis and kidney function**

Osteomyelitis is localized bone infection (Berbari *et al.*, 2005). Infection is a condition in which pathogenic organisms multiply and spread within

the body tissues; this usually gives rise to an acute or chronic inflammatory reaction (Solomon *et al.,* 2001).

Osteomyelitis has traditionally been classified into three categories. The first category, hematogenous osteomyelitis, is bone infection that has been seeded through the bloodstream. The second, osteomyelitis due to spread from a contiguous focus of infection without vascular insufficiency which is seen most often after trauma or surgery and is caused by bacteria which gain access to bone by direct inoculation or extension to bone from adjacent contaminated soft tissue. The third category, osteomyelitis due to contiguous infection with vascular insufficiency, is seen almost exclusively in the lower extremities, most commonly as a diabetic foot infection. Each of these three categories of osteomyelitis can present in the acute or chronic phase (Fritz and McDonald, 2008). Griffin *et al*. (1997) reported the association between glomerulonephritis and acute renal failure with osteomyelitis.

2.11.7 **Spinal injury and kidney disease**

Spinal cord injury (SCI) is defined as any injury resulting from an insult to spinal cord that disrupts its major functions, either completely or partially (Dumont *et al*., 2001). The presence of either proteinuria with protein of 500 mg/dl or greater or creatinine clearance less than 60 mL/min is associated independently with increased mortality in the

chronic spinal cord injury population. The presence of both conditions further increases the risk of kidney disease **(**Greenwell *et al*., 2007).

2.11.8 **Spinal tuberculosis and kidney function**

Spinal tuberculosis is one of the oldest diseases known to mankind and has been found in Egyptian mummies dating back to 3400 BC. The disease is popularly known as Pott's spine. Spinal tuberculosis is a destructive form of tuberculosis. It accounts for approximately half of all cases of musculoskeletal tuberculosis. Spinal tuberculosis is more common in children and young adults. Currently, the term 'Pott's disease/Pott's spine' describes tuberculous infection of the spine and the term 'Pott's paraplegia' describes paraplegia resulting from tuberculosis of the spine (Ravindra and Dilip, 2011).

Tuberculosis is caused by a bacillus of the *Mycobacterium tuberculosis* complex. Vertebral infection by the bacillus results from hematogenous dissemination from a primary focus. Infection in the vertebral marrow is followed by a chronic inflammatory response characterized by epithelioid cells, Langhans giant cells, lymphocytes, and inflammatory exudates, which together constitute the typical histopathological lesion called the tubercle with progressive destruction; caseous necrosis occurs to form the cold abscess (Rajasekaran, *et al.,* 2014). Pott's disease should be suspected in end-stage renal disease patients with back pain and/or neuromuscular complaints (El-Shahawy *et al*., 1994).

2.11.9 **Sickle cell disease and kidney function**

Sickle cell disease (SCD) is caused when the glutamic acid in the 6th position of beta chain of Haemoglobin A (HbA) is changed to valine in Haemoglobin S (HbS). The single amino acid substitution leads to polymerization of haemoglobin molecules inside red blood cells which causes a distortion of cells into sickle shape (Vasudevan and Sreekumari, 2007).

The presence of renal failure in sickle cell disease (SCD) ranges from 5 to 18% of the total population of SCD patients (Saborio and Scheinman,1999).Young people with SCD usually have normal renal function. Grossly, the kidneys tend to be hypertrophied, with a characteristic smooth, capsular surface. As people with SCD grow older, the kidneys progress to end-stage renal disease (ESRD). The kidneys eventually shrink, and the capsular surface becomes grossly distorted and scarred (Lerma, 2014).

Sickle cell disease is associated with both proximal and distal tubular abnormalities. The high GFR in association with the increased loss of salt and water leads to a reactive increase in sodium and water reabsorption by the proximal tubule driving the reabsorption of other solutes such as phosphate and β2 microglobulin; hence, many patients have hyperphosphatemia. Other solutes such as creatinine and uric acid have a marked increase in proximal tubular secretion. Up to 30% of the total

creatinine excretion can arise from tubular secretion, resulting in an overestimation of GFR when creatinine-base formulas are used. Distal tubule function is often impaired, leading to reduced potassium and hydrogen ion excretion (Sharpe and Thein, 2O14).

2.11.10 **Diabetes and kidney disease**

Diabetes is a group of metabolic disorders in which an individual has high blood glucose, either because insulin production is inadequate, or the body cells do not respond properly to insulin or both (Halliru *et al.,* 2016). The complications of long standing diabetic mellitus often appear in the foot causing chronic disability. Over 30% of patients attending clinics have evidence of peripheral neuropathy or vascular disease and about 40% of non trauma related amputations in British hospitals are for complication of diabetes (Solomon *et al.,* 2001). Furthermore, factors affecting diabetic foot are predisposition to peripheral vascular disease, damage to nerves which leads to neuropathic joint disease, osteoporosis and reduced resistance to infections (Solomon *et al.,* 2001). Long-term complications of diabetes are usually the result of problems with blood vessels; uncontrolled hyperglycemia that remains over a long period of time causes both the small and large blood vessels to narrow, mainly as a result of complex sugar-based substances that build-up in the walls of blood vessels, leading to microvascular and macrovascular diseases (Halliru *et al.,* 2016). These complications of diabetes cause renal

function to deteriorate following the diabetic nephropathy leading to renal insufficiency, if left untreated (Burtis *et al.,* 2008).

2.11.11 **Hypertension and kidney disease**

Hypertension is a condition in which the blood vessels have persistently raised pressure (WHO, 2016). Previous studies have reported that low muscle strength and impaired physical performance have been linked to chronic diseases including hypertension (Li *et al.,* 2015). Four organs are the most frequent target of hypertension complication which leads to the kidney damage, heart, brain and eye (Damian 2003). High blood pressure is major cause of kidney disease (NKF, 2015a). Some patients with hypercalcaemia may be hypertensive but if the renal damage is not severe the hypertension may respond to reducing the plasma calcium concentration (Mayne, 1994).

CHAPTER THREE

3.0 MATERIALS AND METHODS

3.1 Research Design

This is a prospective randomized study conducted by the researcher at both in- patient and out-patient departments of National Orthopaedic Hospital Dala Kano**.** Weight and height of the patients were measured prior to the sample collection. A semi structured questionnaire was administered to assess the sociodemographic characteristics of the respondents while disease condition, duration of the disease and medication were assessed from the patient's folder.

3.2 Ethical Consideration

Ethical clearance was obtained from the hospital research ethics committee of National Orthopaedic Hospital Dala Kano. (Appendix III)

3.3 Inclusion Criteria

1. Subjects of 20-80 years of age.
2. Subjects that their weight and height can be measured.

3.4 Exclusion Criteria

1. Subjects that are not of 20-80 years of age.
2. Subjects that their weight and height cannot be measured.

3.5 Sample Size Determination

A total of one hundred (100) subjects were recruited for this study, sixty (60) patients and forty (40) apparently healthy individuals of both sexes, calculated from the formula for proportion:

$n=z^2p\ (1-p)/d^2$

Where:

n=minimum sample size

p=prevalence of kidney disease in the literature=3.6% (Alebiosu *et al*., 2006)

Z=constant (1.96) at 95% confidence interval

d= level of precision

$n= (1.96)^2(0.036)\ (1-0.036)^2/\ (0.05)^2 =53.3=53$

An additional minimum of 10% of the calculated sample was added to cover for attrition which makes the sample to 60 while 40 apparently healthy individuals were served as control.

3.6 Sampling Techniques

Arrangement was made with the physicians whereby subjects who satisfy the study inclusion criteria were selected at random. The nature of the study was explained to the subjects using an appropriate language. Informed consent (Appendix IV) for inclusion in to the study was obtained from the subjects.

3.7 Anthropometric Measurement

Anthropometric measurement was adopted from the protocol of the State of Alaska Division of public Health, 2012.

3.7.1 Weight measurement

The scale was set at zero. The patients were asked to remove shoes, heavy outer clothing and empty their pockets to extent possible and patients stepped on the scale platform, facing away from the scale read out, with both feet on the platform, and remained still with arms hanging naturally. The weight value was read to the nearest 0.1 kilogram. The steps were repeated to confirm measurement.

3.7.2 Height measurement

Shoes, hat, and hair ornaments were removed by the patient and asked to stand on the uncarpeted floor with back against the stadiometer rule. The legs were in contact and straight, arms were at sides, and shoulders were relaxed .The back of the patient touched the stadiometer at some point, preferably heels, buttocks, upper back and head was touching the measuring surface. The body was in straight line (mid-auxiliary line parallel to the stadiometer) and the head was in Frankfort plane. The patient was then asked to breathed in and hold while being measured. BMI was calculated as weight (Kg)/ Height (m^2).

3.7.3 Determination of glomerular filtration rate

This was calculated using creatinine-based equations that have been extensively studied and widely applied; the Modification of Diet in Renal Disease (MDRD) study equation.

GFR=186× $(S_{cr})^{1.154}$× (age) $^{0.203}$×0.742 (if the subject is female) ×1.212 (if the subject is black).

GFR is expressed in milliliters per minute per 1.73 m^2 (Stevens *et al.,* 2006).

3.7.4 Blood Sampling/collection

Blood sample was obtained from each subject by venepuncture from the antecubital vein of the forearm using disposable syringes. Five (5ml) of blood sample in each case was delivered in clean, labelled plastic centrifuge tubes. It was allowed to stand for 30 minutes for proper retraction and clotting and then centrifuged for five minutes at 3000 rpm, after which the serum was separated into dry and labeled sample tubes.

3.8 Biochemical Tests

3.8.1 Determination of serum urea by urease bathelot's method (Weatherburn, 1967)

Principle

Urea in the serum is hydrolyzed to ammonia in the presence of urease, ammonia is then measured photometrically by Bathelot's reaction.

$$\text{Urea} + H_2O \xrightarrow{\text{Urease}} 2NH_3 + CO_2$$

NH_3 + hypochlorite + phenol ⟶ indophenol (Blue compound)

Procedure

Reagent 1 (100µL) was added to the test tubes containing 10µL of distilled water, standard and serum respectively. Each Test tube was mixed and incubated at 37ºC for ten minutes. Reagents 2 and 3 (2.50 ml each) was added into blank, standard and test respectively, mixed and incubated for 15 minutes. Absorbance was read at 546 nm using spectrophotometer.

Calculation

Urea concentration (mmol/L) = Abs of sample/Abs of standard × concentration of standard.

3.8.2 Determination of serum creatinine

Kinetic Jaffe's Method was employed using commercially prepared Creatinine Kit as approved by Rosano *et al*. (1990).

Principle

Creatinine in alkaline solution reacts with picric acid to form a colored complex. The amount of the complex formed is directly proportional to the creatinine concentration.

Procedure

Serum/standard (100µL) was added to 1.0mL creatinine working reagent (equal volume of R1a + R1b). It was mixed and incubated for 30 seconds at 25^{o}C. Absorbance (A1) of sample/standard was measured at 492 nm. Exactly 2 minutes later, absorbance (A2) of sample/standard was also measured and the change in absorbance (A2 – A1) calculated.

Calculation

Creatinine concentration (µmol/L) = (A2 – A1) Sample/ (A2 – A1) Standard x Conc. of standard.

3.8.3 Determination of serum uric acid by enzymatic method (uricase method) of Fossali *et al. (*1980)

Principle

Uric Acid is converted by uricase to allantoin and hydrogen peroxide which under the catalytic influence of peroxidase oxidizes 3, 5-Dichloro-2-hydroxybenzenesulfonic acid and 4-aminophenazone to form a red-violet quinoneimine compound.

Uric Acid + O_2+H_2O $\xrightarrow{\text{uricase}}$Allantoin +$CO_2$+$H_2O_2$

2H_2H_2+3, 5-dichloro-2-hydroxybenzenesulfonic acid +4-aminophenazone $\xrightarrow{\text{Peroxidase}}$N-(4-antipyryl)-3-chloro-5-sulfonates-p-benzo-quinoneimine.

Procedure

Reagent 1(1mL) was added to the test tubes containing 25µL of standard and serum respectively. Each Test tube was mixed and incubated at 37ºC

for five minutes. It was read spectrophotometrically at 546 nm against reagent blank.

Calculation

Uric Acid concentration (µmol/L) = Abs sample/Abs standard × conc. of standard.

3.8.4 Determination of serum sodium and potassium by flame photometry

Principle of flame photometry

Using compressed air, diluted serum is sprayed as a fine mist of droplets (nebulized) into a non-luminous gas flame which becomes colored by the characteristic emission of the sodium or potassium metallic ions in the sample. Light of a wavelength corresponding to the metal being measured is selected by a light filter or prism system and allowed to fall on a photosensitive detector system. The amount of light emitted depends on the concentration of metallic ions present. By comparing the amount of light emitted from the sample with that from a standard solution the amount of electrolyte in the sample can be measured.

Procedure

Diluting samples with variable diluter

The variable diluter was turned on. Enough distilled water was placed in the flask and the rubber tube was inserted deeply in the flask. The diluter was primed manually by pressing the start button, until the dispersed water comes out on a smooth flow. The sample volume was selected to

0.02ml for Na^+ and 0.1ml for K^+(the volume of the diluents was fixed at 10ml for both Na^+ and K^+). The standard/sample solution was inserted when red sample indicator light was on. The start button was then pressed and standard/sample aspirated as the green light come on. The start button was pressed to dispense the diluted sample in to plain tube as the red light was on. The variable diluter was turned off.

Flaming with 410-Sherwood flame photometer operation

The flame photometer was turned on and allowed to steam for 2 min. Distilled water container was Inserted and allowed to steam for another 2 min. The gas cylinder was opened and the fuel was turned on while the flame was ignited using the ignite button, and then allowed to stand for another 10 minutes.

The Na^+ filter was selected for Na^+ while K^+ filter was selected for K^+. The coarse adjustment was adjusted to the 3^{rd} point for K^+ or to the 4^{th} part for Na^+. With the Distilled water in places, the standard was set to 5.0 to K^+ or 140 for Na^+ using fine adjustment. The diluted standard was Inserted and set the standard to 5.0 for K^+ or 140 for Na^+ using the fine adjustment. The diluted sample was inserted and readings were taken. The standard setting was rechecked after taking the reading to ensure there was no significant shift. The gas cylinder was then closed and the photometer was allowed to steam with the distilled water and turned off.

3.8.5 Determination of serum bicarbonate (Tietz and Saunders, 1995)

Principle

Carbon dioxide is released from bicarbonate in serum with dilute hydrochloric acid; the excess hydrochloric acid is then titrated with sodium hydroxide using methyl red as an indicator.

Procedure

Into a 25ml conical flask, 1 ml of 0.01N HCl and 0.1ml of serum was added to the mixture, 1ml of carbon dioxide free water was added, shaken for 2 minutes and titrated with 0.01N sodium hydroxide with methyl red as indicator to a faint pink colour end point.

3.8.6 Determination of serum chloride by thiocyanate method (Skeggs and Hochstrasser, 1964)

Principle

$2Cl^- + Hg(SCN)^{2} \longrightarrow HgCl2 + 2SCN^-$

$3SCN^- + Fe^{+2} \longrightarrow Fe(SCN)_2$ (orange)

Procedure

New plastic test tubes were labeled as Blank, Standard and Test.

Reagent A (1.0ml) was transferred into each tube and allowed to come to room temperature (25°C). Sample, standard and Blank reagent (10 µl each) was transferred to respective tubes and mixed by inversion. The

mixture was allowed to stand for five (5) minutes at room temperature. It was read sphectrophotometrically at 540 nm against blank.

Calculation

Chloride conc. (mmol/L) =Test Abs- Blank Abs/ Std Abs- Blank Abs × conc. Of standard.

3.8.7 Determination of serum total 25-hydroxyvitamin D by electro chemiluminescence binding assay (Roche, 2012)

Principle: Competitive protein binding assay

First incubation: The sample (15µL) was incubated with a pretreatment reagent 1 and 2 for 9 minutes. Thereby, the natural VDBP in the sample is denatured to release the bound vitamin D (25-OH).

Second incubation: the pretreated sample is further incubated with a recombinant ruthenium-labeled VDBP to form a complex between vitamin D (25-OH) and the ruthenylated-VDBP.

Third incubation: After the addition of streptavidin-coated microparticles and biotinylated vitamin D (25-OH), unbound ruthenium labeled vitamin D binding proteins become occupied. A complex consisting of the ruthenium-labeled VDBP and the biotinylated vitamin D (25-OH) is formed. The entire complex becomes bound to the solid phase (by the interaction of biotin and which are captured on the surface of the electrode).

The reaction mixture was aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are removed with ProCell/ ProCell M. Application of a voltage to the electrode induces chemiluminescent emission which is measured by a photomultiplier.

Results were determined via an instrument-specific calibration curve which was generated by 2-point calibration and a calibration master curve provided via the reagent barcode.

Procedure

Cobas automated chemistry analyzer was switched on. The serum sample was inserted to the aspirating needle and aspirated. The result was displayed on the screen after 27 minutes and the reading was taken.

3.8.8 Determination of malondialdehyde (MDA)

Malondialdehyde (MDA) concentration was determined as an index to monitor lipid peroxidation. This was determined according to the estimation of serum thiobarbituric acid reactive substances (TBARS) (Method described by Ohkawa *et al.,* 1979).

Principle

Malondialdehyde (MDA) is a secondary product of lipid peroxidation and is used as an indicator of tissue damage. The MDA form a 1:2 adduct with thiobarbituric acid (TBA) and produces a pink colored product which has absorption maximum at 532nm.

Procedure

Normal saline (0.2ml) was pipetted into test tubes labeled as Sample test and Sample blank while 0.2ml of serum was pipetted into the Sample test tubes only. TCA (0.5ml) solution was added to each of the Sample test and the Sample blank tubes, followed by adding 0.1ml of TBA solution to the mixtures in each of the tubes. The mixture in each tube was heated for 60 minteus in a water bath at 95^{o}C. After cooling to room temperature on an ice bath: 3ml of n-butanol was added to the content in each test tube and then mixed vigorously. The butanol phase was separated by centrifugation at 1000 x g for 5 minutes and the absorbance of the Sample test was read against the absorbance of the Sample blank at 532nm.

Calculation

The concentration of TBARS was expressed in terms of Malondialdehyde (MDA) in nmol/ml. Molar extinction coefficient of MDA = 1.56 x 10^{5}cm^{-1}M^{-1}.

Therefore MDA concentration = Absorbance/1.56 x 10^{5}cm^{-1}M^{-1} x path length.

3.8.9 Determination of serum calcium by colorimetric method (Burtis *et al*., 2008)

Principle

Calcium ions form a violet complex with O-Cresolphthalein complexone in an alkaline medium.

Procedure

Working Reagent (1ml of R1+R2) was added to two new plastic test tubes containing 25µL of standard and serum respectively. Each test tube was mixed and incubated at 25ºC for five minutes. It was then read sphectrophotometrically at 570 nm against reagent blank.

Calculation

Calcium concentration (mmol/L) = A sample/A standard × conc. Of standard.

3.8.10 Determination of serum inorganic phosphorus by color method (Teco, 2012)

Principle

Inorganic phosphorus reacts with ammonium molybdate in an acid medium to form a phosphomolybdate complex. This complex is reduced by ferrous ammonium sulfate to produce a molybdenum blue complex. The color produced is measured at 675 nm and its intensity is directly proportional to the concentration of inorganic phosphorus present.

Procedure

New plastic test tubes were labeled as Blank, Standard and Test.

Working reagent (1.0 ml) was transferred into each tube and allowed to stabilize at room temperature (25°C). The sample (20 µl) was transferred to the respective tubes and mixed by inversion. The mixture was allowed

tubes to stand for at least ten (10) minutes. It was then read sphectrophotometrically at 675 nm against reagent blank.

Calculation

Phosphorus concentration (mmol/L) = A sample/A standard × conc. Of standard.

3.9 Statistical Analysis

Graph pad instat (version 3.05 Inc. 2000) was used, results were expressed as mean± SD. One way ANOVA with Dunnett post- Hoc test and unpaired t-test with Welch correction was used as tools of analysis.

CHAPTER FOUR

4.0 RESULT AND DISCUSSION

4.1 Result

Table 1 shows some socio-demographic factors and prevalence of kidney disease among patients attending national orthopedic hospital Dala Kano. The number of males were higher than female patients with value of 71.7% and 28.3%respectively. The male patients were seen to have more patients with kidney disease then female with prevalence of 2.3% and 0% respectively whereas the overall prevalence of kidney disease in this study was 1.7%. No patients with kidney disease were recorded among age groups of 20-40 and 41-60 years while 10 % of the patients within the age group of 61-80 years had kidney disease. The students constitute 30% of the study population followed by civil servants with 20%; business and house wives were 18.3% and 15% respectively. Patients in engineering occupation are 1.7% of the study population with 100% prevalence of kidney disease while butchers, tailors, imams and retirees had 0% prevalence. The patient observed with kidney disease fall within 2- 5 years duration of disease.

TABLE 1: Prevalence of Kidney Disease and Socio-Demographic Factors of the Volunteer Patients of National Orthopaedic Hospital Dala Kano.

Characteristics	Number of Samples n=60, (%)	Patient with Kidney Disease n = 1, (%)
Age group (years)		
20 – 40	33(55.0)	0(0)
41 – 60	17(28.3)	0(0)
61 – 80	10(16.7)	1(10)
Sex		
Female	17(28.3)	0(0)
Male	43(71.7)	1(2.3)
Occupation		
Students	18(30.0)	0(0)
Civil servants	12(20.0)	0(0)
Business	11(18.3)	0(0)
Housewife	9(15.0)	0(0)
Engineering	1(1.7)	1(100)
Butcher	1(1.7)	0(0)
Tailoring	2(3.3)	0(0)
Driving	1(1.7)	0(0)
Farming	2(3.3)	0(0)
Imam	1(1.7)	0(0)
Retiree	2(3.3)	0(0)
Duration of Disease (Years)		
0 – 1	19(31.7)	0(0)
2 – 5	29(48.3)	1(3.4)
6 – 10	5(8.3)	0(0)
11 – 20	6(10.0)	0(0)
21 – above	1(1.7)	0(0)
Overall prevalence	**60**	**1(1.7)**

Table 2, shows mean serum concentrations of Urea, Uric Acid and Creatinine, eGFR and BMI of the Patients with orthopaedic cases and Controls. There was significant difference ($p<0.01$) in mean serum urea concentration among patient with fracture, burns, and muscular injury as compared with controls; significant difference ($p<0.05$) was also observed in mean serum urea among gouty arthritis patients. There was significant difference ($p<0.01$) in mean serum creatinine concentration among patients with gouty arthritis only. There was significant difference ($p<0.01$) in mean serum uric acid concentration among patient with diabetes, SCD, gouty arthritis and muscular injury as compared with controls. There was significant difference ($p<0.01$) in eGFR among patients with SCD, gouty arthritis, rheumatoid arthritis and muscular injury. Significant difference ($p<0.05$) exists between controls and patients with burns, SCD and gouty arthritis; there was also significant difference ($p<0.01$) among septic arthritis patient in body mass index.

TABLE 2: Serum Urea, Uric Acid and Creatinine Concentrations, eGFR and BMI of the Patients and Controls

Disease conditions	Urea (mmol/L)	Creatinine (µml/L)	Uric acid (µml/L)	eGFR (ml/min/1.73m^2)	BMI (kg/m^2)
Fracture	4.7±1.5**	54±9.3	410±161	173±37	23.63±4.3
Dislocation	4.2±0.2	51±2.3	264±39.5	161±12.2	22.21±1.6
Burns	6.3±2.1**	59±8.5	260±1.9	185±31	18.09±0.6*
Hypertension	2.4±0.2*	51±3.8	279±1.8	144±12	23.25±5.1
Diabetes	4.3±1.9	65±12.7	538±74**	157±41	26.35±2.2
Tumor	2.9±1.2	57±0.7	213±10.8	185±5.3	19.72±0.3
SCD	2.4±0.1*	44±1.8	708±79**	263±6.2*	17.87±0.2*
Gouty arthritis	10.2±0.3**	131±1.3**	613±41**	110±2.1*	18.60±2.3*
R /arthritis	5.0±0.1	57±0.8	493±88	128±5.1*	27.95±1.6
Septic arthritis	2.7±0.1	56±18.6	348±21	229±79	15.89±0.3**
Osteo arthritis	3.4±0.1	57±3.4	446±206	170±4.0	21.28±2.2
TB arthritis	4.4±0.1	44±0.8	211±50	182±11	20.35±0.3
Spinal injury	3.9±0.2	59±0.5	498±144	173±3.1	19.92±0.2
Muscular injury	5.6±0.1**	42±1.7	575±42**	270±1.6**	21.34±0.3
Spinal TB	3.5±0.9	48±7.1	368±303	212±10	24.36±0.2
Spondyloisis	3.5±0.1	53±1.5	383±48	182±11	20.71±1.8
Controls	3.8±1.1	53±8.6	308±120	181±46	24.00±3.8

Results are expressed as means ± S.D, N = 100, Nil shows No patients recorded.
Values with * significant difference (P<0.05) when compared to controls
Values with ** significant difference (P<0.01) when compared to controls R=Rheumatoid, TB=Tuberculosis,

Table 3 shows mean serum sodium, potassium, chloride and bicarbonate concentrations of the studied subjects. There was significant difference ($p<0.01$) in mean serum sodium among SCD, TB arthritis and spinal injury patients as compared with controls; there was also significant difference ($p<0.05$) in mean serum sodium among patients with burns as compared with the controls. There was significant difference ($p<0.01$) in mean serum potassium among TB arthritis and spinal injury patients as compared with controls; significant difference also exists ($p<0.05$) in mean serum potassium among patients with SCD, osteoarthritis and spondyloisis as compared with controls. There was significant difference ($p<0.01$) in mean serum chloride in patients with SCD and rheumatoid arthritis and also significant difference ($p<0.05$) was observed in patients with dislocation. There was significant difference ($p<0.01$) in mean serum bicarbonate among patients with burns.

TABLE 3: Serum Electrolytes Concentration of the Patients and Controls.

Disease conditions	Sodium (mmol/L)	Potassium (mmol/L)	Chloride (mmol/L)	Bicarbonate (mmol/L)
Fracture	137±7.9	3.9±0.3	97±6.6	26±1.7
Dislocation	127±6.5	3.9±0.3	90±5.6*	25±0.8
Burns	144±10.7*	3.9±0.3	101±0.9	29±3.2**
Hypertension	141±4.7	3.6±0.1	98±4.2	25±1.3
Diabetes	140±5.7	3.6±0.2	99±6.3	27±1.2
Tumor	132±1.0	3.8±0.1	94±1.9	24±0.7
SCD	160±1.6**	4.4±0.1*	115±1.5**	28±0.7
Gouty arthritis	129±1.1	3.7±0.1	91±1.4	25±1.0
R/ arthritis	125±1.7	4.3±0.1	86±0.9**	26±0.8
Septic arthritis	126±2.3	3.5±0.1	92±5.9	24±0.9
Osteo arthritis	135±12.6	3.4±0.1*	99±10.0	27±1.5
TB arthritis	163±1.2**	3.1±0.1**	114±1.5	28±1.1
Spinal injury	147±1.5**	4.8±0.1**	104±0.9	26±0.7
Muscular injury	134±0.9	3.7±0.1	95±1.5	26±0.5
Spinal TB	131±2.9	3.9±0.1	92±0.9	26±0.5
Spondyloisis	131±3.3	4.4±0.1*	91±0.8	24±0.5
Controls	134±4.1	3.9±0.3	96±2.8	26±1.3

Results are expressed as means ± S.D, N = 100, Nil shows No patients recorded.
Values with * significant difference (P<0.05) when compared to controls, SCD= Sickle cell Disease
Values with ** significant difference (P<0.01) when compared to controls, R=Rheumatoid, TB=Tuberculosis

Table 4 shows mean serum malondialdehyde, vitamin D, calcium and phosphate concentrations of the studied subjects. There was significant difference ($p<0.01$) in mean serum malondialdehyde among patients with burns, tumor, rheumatoid arthritis, septic arthritis, TB arthritis, spinal injury and spinal TB as compared with controls. There was significant difference ($p<0.05$) in mean serum malondialdehyde among patients with osteoarthritis. There was significant difference ($p<0.01$) in mean serum vitamin D among patients with fracture as compared with controls. There was significant difference ($p<0.01$) in mean serum calcium among patients with tumor, rheumatoid arthritis and spinal TB as compared with controls. There was significant difference ($p<0.01$) in mean serum phosphate among patients with SCD and Septic arthritis as compared with controls.

TABLE 4: Serum Malondialdehyde, Vitamin D, Calcium and Phosphate Concentration of the Patients and Controls.

Disease conditions	MDA (nmol/ml)	Vitamin D (ng/ml)	Calcium (mmol/l)	Phosphate (mmol/l)
Fracture	2.70±1.8	69.94±15.3**	2.48±0.4	1.85±0.6
Dislocation	1.91±1.8	52.39±3.1	2.17±0.1	1.91±0.3
Burns	6.11±1.7**	55.69±8.1	2.34±0.4	1.98±0.3
Hypertension	2.31±0.6	37.55±10	2.02±0.1	1.56±0.1
Diabetes	2.39±1.3	70.17±27	2.17±0.2	1.79±0.4
Tumor	8.20±0.2 **	65.05±12	1.87±0.02**	1.91±0.1
SCD	7.40±1.6**	40.26±1.2	2.55±0.2	2.97±0.5**
Gouty arthritis	1.72±0.5	49.30±5.8	2.35±0.1	1.77±0.2
R/ arthritis	4.52±0.4**	57.50±1.5	2.05±0.1	2.11±0.1
Septic arthritis	7.31±3.1**	63.67±17	1.66±0.3**	1.30±0.06**
Osteo arthritis	3.42±4.5*	49.61±2.7	1.95±0.04	2.01±0.2
TB arthritis	7.32±0.9**	69.55±2.2	2.20±0.2	1.91±0.1
Spinal injury	4.11±0.2**	37.12±2.4	1.65±0.2	1.99±0.01
Muscular injury	2.19±0.2	47.12±1.5	2.04±0.01	2.03±0.04
Spinal TB	5.91±0.2**	54.31±11	2.72±0.07**	1.99±0.4
Spondyloisis	1.91±0.2	57.93±9.9	2.14±0.2	1.43±0.3
Controls	2.89±1.7	51.87±16	2.25±0.2	1.76±0.4

Results are expressed as means ± S.D, N = 100.
Values with * significant difference (P<0.05) when compared to controls, SCD= Sickle cell Disease
Values with ** significant difference (P<0.01) when compared to controls, R=Rheumatoid, TB=Tuberculosis

Table 5 compared the Kidney function parameters between males and females. There was significant difference in mean serum potassium, eGFR and BMI ($p=0.0307$, 0.0032 and 0.0112 respectively) between males and females. There was no significant difference ($p>0.05$) in mean serum urea, sodium, chloride, bicarbonate, uric acid, MDA, Vitamin D, phosphate and calcium between both gender.

TABLE 5: Kidney Function Indices in Relation to Gender Among the Patients

	Urea (mmol/l)	Sodium (mmol/l)	Potassium (mmol/l)	Chloride (mmol/l)	Bicarbonate (mmol/l)	Creatinine (µmol/l)	Uric acid (µmol/l)	Phosphate (mmol/l)	Calcium (mmol/l)	MDA (nmol/ml)	Vitamin D(ng/ml)	eGFR (ml/min/1.73m^2)	BMI (kg/m^2)
Male(n= 43) Mean ± S.D.	4.6 ± 1.6	135 ± 10.6	4.0 ± 0.4*	95 ± 8.5	26 ± 2.2	63 ± 36.6	353 ±1.93	1.78 ± 0.4	2.11 ± 0.2	3.72±3.2	58.06±16.7	188±54*	21.28±4.4
Female (n=17) Mean ± S.D.	4.5 ± 3.0	136 ± 10.5	3.8 ± 0.4	99 ± 10.3	26 ± 1.7	56 ± 20.4	418 ± 189	1.94 ± 0.5	2.20 ± 0.4	2.91±2.2	59.09±15.7	152±33	25.48±5.6*

*** Significantly higher at p<0.05 using t- test (two- tailed) Welch corrected.**

4.2 DISCUSSION

This study reveals the overall prevalence of kidney disease among patients attending National Orthopaedic Hospital Dala – Kano as 1.7% (Table 1). The finding is slightly above the 1.6% established by Oyediran and Akingbe (1970) in southern part of Nigeria. The established figure by this research falls within the range of chronic renal failure (CRF) prevalence in various parts of Nigeria which is 1.6-10% according to Odubanjo *et al.* (2011b). However, the value is lower than 3.6% of Olabisi Onabanjo University Teaching Hospital, Sagamu and 10% of Lagos University Teaching Hospital respectively (Mabayage *et al.,* 1992; Alebiosu *et al.,* 2006). This discrepancy may be due to the facts that this study considers diseases different from the former studies, that is, individuals with urogenital problems. The current prevalence is higher in males than females with 2.3% and 0.0% respectively, this could probably be explained by several studies that suggested females are more protected to end stage renal diseases (ESRD) than males (Iseki, 2008).

Observation from the result of this study as shown in Table 2 revealed significant difference ($p<0.01$) in eGFR among patients with fracture as compared with control group. However, the eGFR of both groups do not indicate sign of kidney dysfunctions, this may support the earlier findings by Meghan *et al*. (2013) which shows no association between eGFR and fracture.

The study also revealed a significant increase ($p<0.01$) in mean serum uric acid and eGFR in sickle cell disease (SCD) as compared with controls group with no significant difference ($p>0.05$) in mean serum creatinine between the two groups. The finding is inconsistent with the reports by Triphathi *et al.* (2011) and Pandey *et al.* (2012) that studied the levels of serum uric acids and creatinine in SCD patients but consistent with the work of Idemodia (2015) who reported significant increase in serum uric acid among SCD in Benin. The increased level of serum uric acid in SCD patients could be due to an increase in bone marrow activity and the turnover of nucleic acids associated with the condition. However, the eGFR is significantly higher among SCD patients in this study which may indicate normal renal function and is consistent with the study of Pandey *et al* which concludes that renal insufficiency is not common among SCD patients in India (Pandey *et al.,* 2012). The high eGFR may be due to marked increase in proximal tubular secretion of creatinine and uric acid in SCD patients resulting to overestimation of eGFR (Sharpe and Thein, 2014).

The results (Table 2) indicates hyperuricaemia in all the patients with gouty arthritis; a similar observation with work of Cucuainu and Brudascà (2012). Significant difference ($p<0.01$) in mean serum urea, uric acid and creatinine and significantly low level of eGFR was observed among patients with gouty arthritis which signifies a typical case of

kidney damage. This finding may substantiate the recent incidences by Abdellatif and Elkhalili (2014) that indicated a range of 47% to 54% of patients with gouty arthritis are affected with kidney disease. This may be due to uric acid crystals deposits in the kidney which may develop to kidney stones, a painful condition that obliterates kidney tubules and prevent removal of wastes products. This may lead to scarring and infection that can cause permanent kidney damage (NKD, 2015b).

There was also observed lowered BMI among patients with gouty arthritis in this study; it is in contrast with the study of Iseki *et al.* (2004) that suggested increasing BMI was associated with an increased risk of the development of ESRD in men. Most patients with kidney disease are elderly and frail, hence body mass may be reduced, therefore BMI may not influence eGFR estimation among kidney patients (Agarwal *et al*., 2010). However, the findings of Juraschek *et al.* (2013) suggested an elevated burden of gout in overweight adults.

In this study, there was decreased eGFR in rheumatoid arthritis (RA) patients with age as compared with the control. However research conducted by Hickson *et al*. (2015) indicated a likely reduced kidney function in RA patient overtime by estimating eGFR. On considering the BMI of rheumatoid arthritis patients, the patients in this group falls within the overweight (WHO,1995) while Sandbag *et al.* (2014) associated obesity and rheumatoid arthritis and attributed the overweight at

diagnosis to significant decreases in changes of achieving good control during the early phase of the disease. Higher uric acid was strongly associated with the rheumatoid arthritis and also RA patients with elevated uric acid may require screening for renal dysfunction (Daoussis *et al.*, 2009).

The lower level of mean serum creatinine was observed in patients with tuberculosis arthritis. However, Huh *et al.* (2015) established in his study that serum creatinine reflected muscle mass and serum creatinine is independently associated with bone mineral density in subjects with normal kidney function; this is in line with this study that reported the BMI and eGFR of patients with tuberculosis arthritis as within normal limits.

As shown in Table 2 also, the non significant increase in mean serum creatinine in patients with spinal injury as compared with controls is consistent with the work of Kuhlemeier *et al.* (1984) whereas Rouleau and Guertin (2010) reported significant increase in serum creatinine among patients with spinal cord injury.

There was observed significant increase ($p<0.01$) in mean serum uric acid and eGFR among patients with muscular injury as compared with controls. This suggests that muscle injury caused over production of uric acid and also these abnormalities improve GFR as observed by Knochel *et al*. (1974).

It was also observed that, there is no significant difference ($p>0.05$) in serum electrolyte among all the patients with fracture, however there was significant decrease ($p<0.01$) in mean serum chloride among patients with dislocation as compared with controls. This may be due to the facts that fracture and dislocation are both skeletal diseases, whereas electrolytes are associated with systemic acid – base balance as described by Owiredu *et al.* (2012) hence are mostly affected on systemic disease.

Also as shown in Table 3, the significant increase in serum sodium ($p<0.01$) and bicarbonate ($p<0.05$) among burn patients as compared with controls could be due to the loss in circulating plasma volume (haemoconcentration) which result in dramatic outpouring of electrolytes; increased serum sodium is present in the state of dehydration (Latenser, 2009; Yousofzai *et al.,* 2011). Significant difference ($p<0.01$) in mean serum electrolytes among patients with rheumatoid, Osteo- and tuberculosis arthrites patients as compared with controls could be due to the association of kidney decrease with tubular reabsorption and secretion mechanisms for electrolytes balance; such as sodium and potassium (Owiredu *et al.,* 2012). This discrepancy in serum electrolytes may also affect the endocrine and acid base function of these patients (Yousofzai *et al.,* 2011). There was no significant difference in all the serum electrolytes, creatinine and eGFR among both diabetic and hypertensive patients but observed significant decreased ($p<0.01$) in mean serum urea

among hypertensive patients, this did not agree with previous works (Yasmin *et al.,* 2006*)* which reported decrease in sodium with no significant changes in potassium. This observation could be due to the facts that most of the patients are controlling the conditions by use of some medications, hence this study may not necessarily concur to the fact that diabetes and hypertension are the leading causes of kidney diseases; that may be true for the uncontrolled conditions (Paudel *et al*., 2013).

It was observed that, patients with SCD have significant increase ($p<0.01$) in mean serum sodium, potassium, and chloride as compared with their controls. The findings by Pandey *et al*. (2012), Sharpe and Thein (2O14) and Idemudia (2015) were found to be consistent with this study. The affinity of haemoglobin for oxygen depend on the blood pH among other factors therefore the SCD patients have abnormal affinity of hemoglobin for oxygen which may bring about the abnormal electrolytes (Burtis *et al.,* 2008). As shown in Table 3, the non significant difference ($p>0.05$) in all the electrolytes measured in patients with muscular injury is contrary to the fact that electrolytes have been link to the muscular functions (Cheesbrough, 2009).

Patients with spinal injury considered in this study shows significant increase ($p<0.01$) in mean serum sodium and potassium as compared with controls. Reuleau and Guertin (2010) reported significant increase in serum potassium and chloride in spinal cord injury patients which is

consistent with this study. The neurological functions of spinal cord is attributed to some electrolytes therefore, spinal injury may cause expected electrolyte abnormalities [Institute of Medicine (IM), 2005].

The significant difference ($p<0.01$) between mean serum malondialdehyde among patients with burns as compared with controls (Table 4) agrees with the findings of Singh *et al*. (2015); both studies show increased lipid peroxidation among burn patients. This may result to urinary MDA which is a gross indicator of renal lipid peroxidation that has been shown to increase after burns (Kang *et al.,* 2001). This may be due to the fact that after burn injury tissue adenosine triphosphate (ATP) levels gradually fall and increased adenosine monophosphate (AMP) is converted to hypoxanthine, providing substrate for xanthine oxidase. These reactions produce hydrogen peroxide and superoxide free radicals. Adherent- activated neutrophils produce additional free radicals; furthermore, enhanced free radical generation is also paralleled by impaired antioxidant mechanisms in burn (Horton, 2003); free radicals causes lipid peroxidation and subsequently production of Malondialdehyde (Ayala *et al*., 2014).

The significant difference ($p<0.01$) in MDA level among patients with tumor as shown is consistent with other studies of Nathan *et al.* (2011), which shows increased level of MDA in patients with soft and bone tissue sarcoma (tumor) which shows increased oxidative stress among these

patients. Furthermore, the MDA-DNA adducts may lead to mutations (point and frameshift), strand breaks, cell cycle arrest, and induction of apoptosis (Ayala *et al*., 2014); and therefore may lead to tumor.

The present study also justifies other studies in increased serum malondialdehyde among SCD patients with significant difference ($p<0.01$) as compared with their controls which is an indication of cell membrane damage due to oxidative stress (El-Ghammawy *et al.,* 2014). The non significant difference ($p>0.05$) in mean serum vitamin D and BMI among SCD patients observed in this study is inconsistent with the findings of Hassan *et al*. (2013) carried out in Bahrain. This inconsistency between the two studies may be because of Serum 25(OH) D levels are strongly influenced by the amount of ultraviolet radiation that passes through the outer layer of the skin and reaches vascular tissue. In turn, the latitude of a person's residence and the degree of skin pigmentation determine the amount of radiation (i.e., ultraviolet B [UVB] to which these tissues are exposed. The levels of 25(OH)D are further influenced by genetic variation in receptors and other components of this biological system . It is also generally believed that strong evolutionary selection – working through the metabolic effects of vitamin D - accounts for the clinal variation in skin color seen in human populations in relation to latitude. Other known factors that influence 25(OH)D include age, adiposity, use of steroids and some chronic medical conditions such as

chronic kidney disease (Tayo *et al.,* 2014). Vitamin D deficiency has been associated with bone health, nephropathy, chronic pain and individuals with SCD are susceptible to all of these complications. However, the role of vitamin D as a contributing factor in these complications is unclear (Nolan *et al.,* 2015).

The observed no significant difference ($p>0.05$) in mean serum vitamin D among rheumatoid arthritis patients as compared with controls is not in accord with the result of Hong *et al.* (2014) and suggested that bone loss among rheumatoid arthritis patients is attributed to reduced serum vitamin D levels. Considering the rheumatoid arthritis patients with significant difference ($p<0.05$) in raised value in mean malondialdehyde as compared with the corresponding controls; El-barbary *et al.* (2011) also found similar raised level in serum MDA levels among rheumatoid arthritis patients. Significant increase ($p<0.01$) in mean serum malondialdehyde, calcium and phosphate as observed in septic arthritis patients is consistent with the result of Grbic et *al.* (2014), which indicates that; the oxidants generated by the bacteria can generate more stable MDA and other aldehyde which can be toxic to osteoblast. On the serum vitamin D, this finding is inconsistent with the findings of Signori *et al.* (2015) that reported high level of serum vitamin D among orthopedic patients with septic arthritis having higher eGFR as compared with the controls. Lower BMI was observed in this group of patients

which is significant ($p<0.05$) as compared with their controls. This shows that the patients are underweight as described by WHO (1995).

Observed significant difference ($p<0.01$) in mean serum malondialdehyde among patients with rheumatoid, septic, Osteo and tuberculosis arthritis in this study is an indicator of oxidative stress in these patients as supported by similar findings reported by Ghorbanihghjo *et al.* (2014). Moreover, mycobacterium can also induce ROS production by activating phagocytes which is an important part of the host defense against mycobacteria but also enhanced ROS generation that may promote tissue injury and inflammation (Madebo *et al*., 2003); thus generates more serum malondialdehyde.

The non significant difference ($p>0.05$) in mean serum calcium among patients with dislocation as compared with control is within the normal limit (Goldman and Bennett, 2000; Burtis *et al.,* 2008). Hypercalcaemia increases the Ca – P product index in the blood and thereby pose the risk of kidney disease (NKF, 2013). The significantly ($p<0.01$) observed lower mean serum calcium in patients with tumor may be associated with the kidney disease but is contrary to the fact that, tumor is associated with the high serum calcium (Burtis *et al.,* 2008). In this study also, the non significant difference ($p>0.05$) in mean serum calcium among SCD patients is contrary to the report of Pandey *et al.* (2012) who found an increase in serum calcium. The abnormalities in serum electrolyte among

sickle cell patients could be due to reactive increase in sodium and water reabsorption of other solutes such as phosphate; hence, many SCD patients have hyperphosphataemia (Sharpe and Thein, 2014).

The significant increase ($p<0.01$) in serum calcium in patients with spinal tuberculosis agrees with the findings of Dosumo and Momoh (2006) that reported an increase in serum calcium in newly diagnosed TB patients in Abuja. The cause of hypercalcaemia may be due to spinal tuberculosis as characterized with chronic inflammatory response which constitute histopathological lesion called tubercle with progressive destruction and caseous necrosis which form cold abscess (Rajesekaran *et al.,* 2014).

In Table 5, the non significant difference($p>0.05$) between gender in mean serum urea, sodium, chloride, bicarbonate and creatinine, uric acid, malondialdehyde, vitamin D, phosphate and calcium is in agreement with the work of Paudel *et al* (2013) that reported none of the renal parameters showed significant sex differentials. The non significant difference in mean serum vitamin D between males and females could be due to accumulating evidence from animal and human studies that suggests vitamin D is involved in many functions of the reproductive system in both genders (Anagnostis *et al*., 2013).

Higher eGFR was observed in males than females in this study. However, Nitsch *et al* (2013) reported both sexes face increased risk of lower eGFR. Body mass Index was found to be higher in females than males

also, which is consistent with the findings of Nalado *et al.* (2012) among civil servants in kano and that of Gallapher *et al.* (1996) which reported women have significantly greater amount of total body fat than do men throughout the adult life. However, Wachukwu *et al* reported contrary in the southern part of Nigeria as males are higher in BMI than females; this may be connected with the differences in the socio-demographic factors between the regions (Wachukwu, 2015). BMI can influence muscle mass and sex can considerably affect it (Iseki *et al.,* 2004). Body mass index and prevalence of obesity with kidney disease were found to be higher than in those without the disease in both genders (Nomura, *et al*., 2009). The significant difference ($p>0.05$) in mean serum potassium was higher in males than females and also supported the study of Wysowski *et al* (2003) in the United States that females are more prone to hypokalemia than males because women are more susceptible to the development of QT prolongation and that QT prolongation is associated with hyperkalemia.

CHAPTER FIVE

5.0 SUMMARY, CONCLUSION AND RECOMMENDATIONS

5.1 Summary

This work was done to assess the kidney function status among patients attending National Orthopaedic Hospital, Dala – Kano. A total of 100 subjects were employed in this study. Serum urea, sodium, potassium, chloride, bicarbonate, uric acid, calcium, phosphate, malondialdehyde and vitamin D were estimated while eGFR and BMI were calculated. Prevalence of kidney disease in this study was found to be 1.7%. All patients with burns and tumor were found to have significant increase in mean serum malondialdehyde. There was no significant difference between males and females in all the parameters measured except serum potassium, eGFR and BMI.

5.2 Conclusion

Kidney dysfunction was found to be higher in orthopaedic cases than non orthopaedic cases like diabetes, hypertension and tumor. It is also higher in males than females; related to underweight and is increasing with age. However, most of the biomarkers of kidney function are irrespective of gender. The kidney dysfunction is more frequent among engineering occupation.

5.3 Recommendations

The following recommendations have been proffered based on the findings and conclusions of the study.

1. Testing kidney function should be carried out regularly on patients with orthopaedic cases in order to detect the disease at early stage for prompt diagnosis and treatment.
2. Future research should be carried out on larger sample size, longer duration of research and also to include the types of drugs administered on the patients in order to identify other clinical and laboratory factors that may contribute to the etiology of kidney disease. Analysis of urine samples should also be included in future studies.
3. Future research efforts should be carried out on each disease condition identified in this study in order to provide more extensive data on the status of kidney function among such cases.

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GLOSSARY

ADH	–	Anti-Diuretic Hormone
AKI	–	Acute Kidney Injury
ATN	–	Acute Tubular Necrosis
ATP	–	Adenosine Triphosphate
BMA	–	British Medical Association
BMI	–	Body Mass Index
BUN	–	Blood Urea Nitrogen
CaR	–	Calcium-Sensing Receptor
CDC	–	Centre for Disease Control and Prevention
CKD	–	Chronic Kidney Disease
CRF	–	Chronic Renal Failure
DNA	–	Deoxyribonucleic acid
eGFR	–	Estimated Glomerular Filtration Rate
ESRD	–	End-stage Renal Disease
GFR	–	Glomeruler Filtration Rate
HPTH	–	Hyperparathyroidism
ICU	–	Intensive Care Unit
KD	–	Kidney Disease
KD	–	Kidney Dysfunction
KDOQI	–	Kidney Disease Outcomes Quality Initiative

KI	–	Kidney Injury
MDA	–	Malondialdehyde
MDRD	–	Modification of Diet in Renal Disease
NKF	–	National Kidney Foundation
PRA	–	Prerenal Azotemia
PTH	–	Parathyroid Hormone
PUFAs	–	Poly Unsaturated Fatty Acids
ROS	–	Reactive Oxygen Specie

APPENDICES

APPENDIX I

Urea Reagent Composition

Contents	Initial Concentration of Solutions
Rl.	
EDTA	116 mmol/l
Sodium nitroprusside (R1b)	6 mmol/l
Urease (Rla)	1g/l

The contents of vial Rla was transferred into bottle R1b and mixed gently. Stored at +2 to +8°C.

R2.	Phenol	120 mmol/l.

Contents of bottle R2 Diluted was with 660 ml of distilled water. Bottle was Rinsed thoroughly and mixed, stored in a dark bottle at +2 to +8°C.

R3.	Sodium hypochlorite	27 mmol/l
	Sodium hydroxide	0.14 N

Contents of bottle R3 Diluted was with 750 ml of distilled water. Bottle was Rinsed thoroughly and mixed, stored in a dark bottle at +2 to +8°C.

Urea	Standard	13.3 mmol/l

Calcium Reagent

R1. Buffer

2–amino–2 –methyl –propan–1– ol	3.5 mol/l, pH 10.7

R2. Chromogen

O – Cresolphchalein complexone	0.16 mmol/l
8 – Hydroxyquinoline	6.89 mmol/l
Hydrochloric acid	60 mmol/l

R3. EDTA

Calcium Standard	2.52 mmol/l

Equal volumes of solutions Rl and R2 Mixed to give enough reagent for the number of samples. Stable for 7 days at+2 to +8°C or 3 days at +15 to +25°C.

Uric Acid Reagent

R1a Buffer

Hepes Buffer	50mmol/l, pH 7.0
3,5-Dichloro-2-hydroxy-	
benzenesulfonic acid	4 mmol/l

R1b. Enzyme reagent

4-Aminophenazone	0.25 mmol/l
Peroxidae	>1000 U/l
Uricase	>200 U/l
Uric Acid Standard	595µmol/l

The contents of one vial of Enzyme Reagent RI b with a 15mls of Buffer RIa was Reconstituted and then transfer entire contents to bottle Rla, vial was rinsed several times with Rib. Stored away from light at +15 to +25^{o}C.

Inorganic Phosphorus Reagent

1. Working Reagent

Ammonium Molybdate	2.4 mM,
Sulfuric Acid	750mM,
Ferrous Ammonium Sulfate	10.2 mM,

2. Inorganic Phosphorus Standard Potassium Phosphate in distilled water (5 mg/dl).

Malondialdehyde (MDA) WORKING REAGENTS

1) Thiobarbituric acid (100mg of TBA in 30ml distilled water and 30ml of acetic acid)
2) Trichloacetic acid (TCA) 10%
3) Normal saline solution (0.9% NaCl)
4) n-butanol solution (90%).

Sodium and Potassium

Sodium and Potassium containing 5mmol/l of potassium and 140 mmol/l of sodium.

Serum Total 25-hydroxyvitamin D

The reagent pack (M, RI, R2) and the pre treatment reagents (PT1,PT2) are leveled as VITD-T.

PT1 Pretreatment reagent 1(white cap)

Dithiothreitol	1 g/L, pH 5.5

PT2 Pretreatment reagent 2(gray cap)

Sodium Hydroxide 55g/L

M (transparent cap)

streptavidin-coated microparticles 0.72mg/mL

Preservative

R1 Vitamin D binding protein-BPRu (gray cap)

Ruthenium labeled vitamin D binding protein 150µg/L

Bis-tris propane buffer 20mmol/L

Albumin (Human) 25g/L, pH7.5

Preservative

R2 25- hydroxyvitamin D- biotin (black cap)

Biotinynated VitaminD (25-OH) 14g/L

Bis-tris propane buffer 200mmol/L, pH 8.6

Preservative

Creatinine reagent

R1a Picric Acid 35mmol/L

R1b Sodium hydroxide 0.32 mol/L

Creatinine standard 177mmol/L

Chloride reagent

Reagent A

Mercuric Thiocyanate	0.4Mm
Iron (III) nitrite	21.8Mm

Reagent B

NaCl	30mM

Bicarbonate reagent

Sodium hydroxide	0.01N
Hydrochloric Acid	0.01N
Methyl red	1%

APPENDIX II

DEPARTMENT OF BIOCHEMISTRY

FACULTY OF BIOMEDICAL SCIENCES

BAYERO UNIVERSITY, KANO

QUESTIONERE ON THE TOPIC:

KIDNEY FUNCTION STATUS OF PATIENTS ATTENDING NATIONAL ORTHOPAEDIC HOSPITAL DALA-KANO, NIGERIA

Section A: Personal Information and demography

Name (Optional): .....

Occupation: .....

Age: .....

Sex: .....

Body weight: .....

Body height: .....

Section B: Medical History

1. Disease condition: ....

   a. Fracture
   b. Dislocation
   b. c Arthritis (specify)
   d. Tuberculosis (specify)
   c. e. Others (specify)

2. Duration of the disease:

a. 0-1 year

b. 2- 5years

c. 6-10 years

d.11- 20 year

e. 21 years - above

3. Types of drugs administered:

a. Antibiotic (specify)

b. Analgesic (specify)

c. Anti Inflammatory (specify)

d. Others (specify)

APPENDIX III

Pathology Department,
National Orthopaedic
Hospital,
Dala – Kano.
3rd July, 2015

The Chairman,
Hospital Research Ethics Committee,
National Orthopaedic Hospital,
Dala – Kano.

Dear Sir,

REQUEST FOR RESEARCH ETHICAL CLEARANCE

I hereby write to request for an ethical approval to carry out a Research on the topic: **"Kidney Function Status of Patients Attending National Orthopaedic Hospital Dala-Kano, Nigeria".**

The research is a requirement for the award of M.Sc. Degree in Biochemistry by the Faculty of Biomedical Sciences, Bayero University, Kano. Attached herewith are the copies of the research proposal.

I hope my request will be given kind approval.

Yours faithfully,

SHEHU MUSA ADAMU
NOHD/PER/3305

APPENDIX IV

CONSENT FORM

I am Shehu Musa Adamu , Senior Medical Laboratory Scientist in this hospital; I am conducting a research on kidney function status among patients attending National Orthopaedic Hospital, Dala (N.O.H.D.) as part of my partial fulfillment for the award of M.Sc. in Biochemistry.

The purpose of this research is to determine the condition of the kidney of patients after laboratory investigations. Your weight and height will be measured prior to blood sample collection.

You are to pay only the standard fee for the surgery and Laboratory investigations, there will be no additional charges to you for taking part in this study. Any extra costs of additional investigations outside usually done routinely in relation with this study will be borne by me. In addition, the results of this study will help in providing better care for patients like you in the future.

The information collected from you in this research will be kept confidential. In the event of publication of this research no personal identifying information will be disclosed.

I am therefore requesting for your support by becoming a participant in this study. Your participation in this study is voluntary. It is your choice whether to participate or not. All the services you receive at this hospital will continue and nothing will change. If you choose not participate in this research project, you

will receive the treatment that is routinely offered in this disease. You may change your mind and stop participating even if you agreed earlier.

PART II

I have read the forgoing information or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I consent voluntarily to participate in this research:

Print Name of participant: .....

Signature of participant.....

Date: .....

If illiterate

I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Print name of witness: .....

Signature of witness: ..... AND thumb print of

Date: .....

Statement of the research/person taking the consent

I have accurately read out the information sheet to the participant to the best of my ability and made sure that he/she understands.

I confirm that the participant was given an opportunity to ask question about this study, and all questions asked by the participant have been answered correctly and to best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this informed consent form has been provided to the participant.

Name of researcher: .....

Signature of researcher: .....

Date: .....

Telephone number of researcher; 08030617330

APPENDIX V

PUBLISHED PAPER I

APPENDIX VI

PUBLISHED PAPER II