PREVALENCE OF GLOMERULAR DISEASE AMONG SECONDARY SCHOOL STUDENTS IN ELDORET, KENYA

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A research thesis submitted in partial fulfillment of the requirements for the award of the degree of Master of Medicine in Internal Medicine, Moi University.

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DECLARATION

Student's Declaration

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DEDICATION

I dedicate this work to all secondary school students of my beloved country Kenya.

ABSTRACT

Background: Glomerular pathology contributes significantly to chronic kidney disease (CKD), a global public health problem. CKD has many non specific symptoms and frequently goes unrecognized in its early stages. Early diagnosis is important since measures can be instituted to curb progression. Existence of glomerular disease can be implied by glomerular haematuria, persistent proteinuria and elevated blood pressure.

Objective: To determine the prevalence of glomerular haematuria, persistent proteinuria and elevated blood pressure among secondary school students in Eldoret.

Methods: This was a descriptive cross sectional study. Four public secondary schools were randomly selected. Probabilistic multi-stage sampling was used to enroll participants aged 12 to 19 years between June and July 2013. Data was collected and entered into a predesigned form. Three blood pressure measurements were taken at 5 minute-intervals and the mean calculated. Elevated blood pressure was diagnosed based on United States of America National Heart, Lung and Blood Institute criteria. Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC 7) criteria was used for participants over 17 years. Clean catch, first morning urine samples were obtained. Dipstick urinalysis was done at schools and urine that tested positive for blood and /or protein was transported in a cooler box to laboratory and subjected to microscopy. Participants with proteinuria, haematuria and elevated blood pressures were weighed and blood samples for measurement of serum creatinine drawn. Using Cockroft-Gault formular, their estimated glomerular filtration rate (eGFR) was calculated. Participants with proteinuria and haematuria on first assessment underwent a second test within three months to ascertain the persistence of these findings.

Results: Out of 395 participants, 51%(200) were male. Mean age was 17(SD: 1.5) with a range of 13 to 19 years. The prevalence of glomerular haematuria was 2.8%(11) while that of persistent proteinuria was 2.0%(8). The prevalence of glomerular disease was 3.5%(14). Elevated blood pressure was prevalent at 12.7 % and was found to be strongly associated with presence of glomerular disease; $p<0.0001$. Personal history of features of kidney disease and history of risk factor/s for kidney disease were associated with presence of glomerular disease; $p=0.003$ and $p=0.023$ respectively. There was no association between reduced eGFR (eGFR<90) and glomerular disease; $p = 0.501$.

Conclusion: The prevalence of glomerular disease was 3.5%. Adolescents with elevated blood pressure, personal history of features suggestive of kidney disease and risk factor/s for kidney disease were more likely to have abnormal urinalysis findings consistent with glomerular disease.

Recommendation: Urinalysis together with relevant history and elevated blood pressure should be embraced as screening tool for glomerular disease in adolescent population.

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LIST OF ABBREVIATIONS

AHA	American Heart Association
ART	Anti-Retroviral Therapy
C_{Cr}	Creatinine Clearance Rate
CDC	Centers for Disease Control and Prevention
CKD	Chronic Kidney Disease
CVD	Cardiovascular disease
ESRD	End Stage Renal Disease
eGFR	Estimated Glomerular Filtration Rate
GFR	Glomerular Filtration Rate
HIV	Human Immunodeficiency Virus
HIVAN	Human Immunodeficiency Virus Associated Nephropathy
IREC	Institutional Research and Ethics Committee
JNC 7	Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure

KDIGO	Kidney Disease: Improving Global Outcome
KDOQI	Kidney Disease Outcome Quality Initiative
NACOSTI	National Commission for Science, Technology and Innovation
NKF	National Kidney Foundation
NHANES III	The Third National Health and Nutrition Examination Survey
RRT	Renal Replacement Therapy
RBCs	Red Blood Cells
UNAID	United Nations Programme on HIV/AIDS

DEFINITIONS

Operational definition:

- Glomerular disease in this study is defined by the presence of persistent proteinuria and/or glomerular haematuria.

Standard definitions:

- **Proteinuria -** Presence of protein in urine, defined as an amount in excess of 300 mg per day ($\geq$ 1+ on the urine dipstick) if the specific gravity is $\geq$ 1.020(Kallen RJ, April 2008).

- **Persistent proteinuria -** Proteinuria on more than one occasion and measured within 3 months(Wagner DK, Harris T, & Madans JH, 1994).

- **Haematuria -** Hematuria is defined as the abnormal presence of red blood cells (RBCs) in the urine and is commonly divided into gross (visible) and microscopic hematuria. Gross hematuria can result from as little as 1 mL of blood in 1 L of urine, and therefore the color does not reflect the degree of blood loss. Microscopic hematuria is defined as the presence of more than 2 red blood cells per high power field in a spun urine sediment(Becker G & Fairley K, 1995).

- **Glomerular haematuria -** Haematuria of renal origin as identified by dysmorphic appearance of RBCs or RBC casts on microscopy. This change in morphology is manifested by blebs, budding, and segmental loss of membrane resulting in marked variability in red cell shape and a reduction in mean red cell size.

- **Normal blood pressure -** Average systolic and diastolic blood pressures below 90th percentile for age, gender and height.

- **Pre-hypertension -** Average systolic or diastolic blood pressure between 90th and 95th percentiles for age, gender and height.

- **Hypertension -** Average systolic or diastolic blood pressure above 95th percentile for age, gender and height.

- **Chronic kidney disease -** Kidney damage or a sustained decrease in glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m^2 for 3 or more.

- **Estimated glomerular filtration rate (eGFR)** − Estimate of flow rate of filtered fluid through the kidney. This is based on creatinine clearance rate (C_{Cr}) which is the volume of blood plasma that is cleared of creatinine per unit time. In this study, an estimate of creatinine clearance was ascertained using Cockroft- Gault formula.

- **Features suggestive of kidney disease** - These included any or a composite of the following: facial puffiness, lower limb swelling, loin pain, 'coca cola' coloured urine, smoky urine, anuria or oliguria.

- **History of risk factor/s for kidney disease** - included history of diabetes mellitus, hypertension, kidney disease in family or cardiovascular disease. Cardiovascular disease was considered present if someone had a diagnosis of ischemic heart disease, cerebrovascular disease, chronic heart failure or peripheral vascular disease.

CHAPTER ONE

INTRODUCTION

1.1. Background

Glomerular pathologies contribute significantly to chronic kidney disease (CKD), a worldwide public health problem. CKD is recognized as a common condition that is associated not only with end stage renal disease (ESRD) but also an increased risk of cardiovascular disease(Parfrey PS & Foley RN, 1999; Vanholder R et al., 2005). Globally, there is a rising incidence and prevalence of CKD, with high cost of management and poor outcomes(Coresh J, Astor BC, Greene T, Eknoyan G, & Levey AS, 2003).

In the third National Health and Nutrition Examination Survey (NHANES III) in adults in the United States of America (USA), Coresh estimated that the prevalence of CKD was at 11%. Stratified by stage, 3.3% had stage 1, 3% had stage 2, 4.3% had stage 3, 0.2% had stage 4 and 0.2% had stage 5 CKD(Coresh J et al., 2003). The prevalence of chronic kidney disease stages 1-4 was reported to have increased from 10% in 1988-1994 to 13.1% in 1999-2004(Coresh J et al., 2003). This may be partially explained by the increase in the prevalence of diabetes and hypertension, the two leading causes of chronic glomerulosclerosis and hence chronic kidney disease globally. According to this survey, it was estimated that 6.2 million people aged above 12 years had serum creatinine values above 1.5 mg/dL(132.6 μmol/L),with 8 million people having a GFR below 60 mL/min(Coresh J et al., 2003). This comprised about 3% of the total US population.

Due to non-uniform definition of chronic kidney disease prior to publication of the Kidney Disease Outcomes Quality Initiative (KDOQI) classification in 2002, most patients with earlier stages of chronic kidney disease could not be recognized or adequately treated.

KDOQI of the National Kidney Foundation (NKF) defines chronic kidney disease as either kidney damage or a sustained decrease in glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m^2 for 3 or more months(KDIGO, 2012). Kidney damage is defined as pathological abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies. Irrespective of the underlying etiology, the destruction of renal mass with irreversible sclerosis and loss of nephrons leads to a progressive decline in GFR. The different stages of chronic kidney disease (Appendix 16) therefore, represent a continuum in time.

Glomerular diseases contribute significantly to chronic kidney disease. The most common causes of CKD globally remain to be diabetes mellitus, hypertension, and glomerulonephritis,(Collins AJ et al., 2003) all of which are glomerular diseases. Together, these contribute approximately 75% of all adult CKD cases. Screening for glomerular pathology is therefore appropriate intervention to diagnose early stageCKD and curb its progression.

1.2. Problem Statement

Chronic kidney disease (CKD) is a major public health problem. While cerebro-vascular diseases, cardiovascular diseases, and cancer remain the major causes of mortality resulting from chronic diseases, CKD has assumed epidemic proportions and is among the leading causes of death in the industrialized world(Eknoyan G, Lameire

N, & Barsoum R, 2004). Reports from two metropolitan areas of China, Beijing and Shanghai, indicated that in 2002, the annual incidence of haemodialysis was 146.4 per million population and 148.1 per million population(Wang H, Zhang L, & Lv J, 2005), respectively. These rates were almost double the incidence reported in 1999. The same trend has been observed in low and middle income countries.

CKD has many non specific symptoms and is frequently unrecognized in its early stages. In Kinshasa, Sumaili *et al* demonstrated that the estimated proportion of those with CKD based on eGFR was 12% to12.4%. Only 3% of those with CKD were aware of their condition(Sumaili K et al., 2009). A survey conducted by Hallan *et al* in Norway in 2006 involving 65,604 people demonstrated that a high-risk screening model targeting only those with diabetes or hypertension would identify less than half of those with CKD(Hallan SI et al., 2006). Moreover, particularly in low and middle income countries, many individuals are not aware that they have diabetes, hypertension or other glomerular pathology causing proteinuria and/or haematuria. Among 1,243 subjects with high blood pressure in Dharan, Nepal, 47% were newly detected during a screening exercise(Sharma SK et al., 2007). Such findings imply that a significant number of people in all spectra of economic set ups live with undiagnosed CKD and hence miss opportunity to have appropriate interventions that could slow down progression to ESRD.

Traditionally, people who were recommended for screening included people with hypertension or history of cardiovascular disease, those with diabetes mellitus, obesity, those aged > 60 years, those with a history of renal disease in the past, as well as people with relatives diagnosed to have kidney disease requiring dialysis. Screening included calculation of estimated GFR/1.73 m^2 from the serum creatinine level, and

measurement of urine-to-albumin creatinine ratio (UACR) in a first morning urine specimen as well as dipstick screen for hematuria. There are no health programmes directed at screening for glomerular disease in Kenya. Early identification of glomerular disease can potentially reduce morbidity and mortality due to CKD.

The presence of chronic kidney disease confers a markedly increased risk of cardiovascular disease(Sarnak MJ et al., 2003). It is recognized that the most common cause of death in people with CKD is cardiovascular disease rather than renal failure. Other than CVD, it has also been noted that patients with end-stage renal disease are at increased overall risk for cancer(Maisonneuve P et al., 1999). This risk is particularly high in younger patients and gradually diminishes with age.(Maisonneuve P et al., 1999)

Chronic glomerulonephritis affects predominantly young adults in low and middle income countries. Young adults presenting with symptomatic CKD due to chronic glomerulonephritis must have had a long period of asymptomatic insidious disease that may not have been diagnosed and managed appropriately leading to rapid progression to ESRD and hence need for early renal replacement therapy which is not readily available to all for various reasons.

The prevalence of hypertension in Kenya is high with an age-standardized prevalence of 21.4% in the rural areas(Hendriks ME et al., 2012). Being a silent disease, it means that many Kenyans are being exposed to complications of unmanaged hypertension including CKD, without their knowledge. Not only can hypertension cause renal

disease, but it might also be initial pointer to existence of glomerular disease especially in young people.

1.3. Justification

Given the magnitude of the problem as stated above, this study sought to address the challenge of late diagnosis of CKD by screening for glomerular disease which contribute to over 75% of all CKD cases. Early identification of patients with kidney disease is recommended since measures may be instituted to slow down progression to ESRD. This may be achieved through mass screening of the communities using simple appropriate and affordable tools such as used in this study to identify those with glomerular pathology.

Information on the existence of glomerular disease can be achieved by doing dipstick urinalysis and blood pressure measurements. Persistent proteinuria, glomerular haematuria, pre-hypertension and hypertension independently or in combination imply presence of glomerular disease.

Considering the high prevalence and the silent nature of hypertension, it is justified to pro-actively find, optimally manage and control it especially in young people. Un-identified, hypertension invariably causes hypertensive glopmerulosclerosis and hence CKD whose management is more complicated and expensive.

In 2003, the American Heart Association (AHA) issued a directive that persons with CKD should be regarded as the highest risk group for subsequent cardiovascular disease(Sarnak MJ et al., 2003). Noting that glomerular pathologies contribute to over 75% of CKD, the potential benefit of proactive detection and management of glomerular disease is reducing mortality and morbidity from cardiovascular diseases.

Additional benefits include reducing progression to ESRD amongst patients with CKD, and mitigating the cancer risk that is now known to be significantly increased in young adults with ESRD(Maisonneuve P et al., 1999).

1.4. Research Question

What is the prevalence of glomerular disease among secondary school students in Eldoret.

1.5. Study Objectives

1.5.1. Primary objective

To determine the prevalence of glomerular disease among secondary school students in Eldoret as defined by the presence of persistent proteinuria and/or glomerular haematuria.

1.5.2. Secondary objectives

- To determine the prevalence of proteinuria among secondary school students in Eldoret.

- To determine the prevalence of glomerular haematuria among secondary school students in Eldoret.

- To determine the prevalence of pre-hypertension and hypertension among secondary school students in Eldoret.

- To estimate renal function and correlate it with urinalysis findings among secondary school students in Eldoret.

CHAPTER TWO

LITERATURE REVIEW

2.1. Background

Glomerular pathologies contribute significantly to chronic kidney disease (CKD), a global public health problem. CKD is defined by the presence of kidney damage or decreased kidney function for three or more months, irrespective of the cause. The persistence of damage or decreased function for at least three months is necessary to distinguish CKD from acute kidney disease. Kidney damage refers to pathologic abnormalities, whether established through kidney biopsy or imaging studies, or inferred from markers such as urinary sediment abnormalities i.e. haematuria or increased rates of urinary albumin excretion. Decreased kidney function refers to a decreased glomerular filtration rate (GFR), which is usually estimated (eGFR) using serum creatinine and one of several validated equations. Individuals who have an eGFR below 60 mL/min per 1.73 m^2 are defined as having CKD(KDIGO, 2012).

Glomerular filtration rate (GFR) describes the flow rate of filtered fluid through the kidney. Creatinine clearance rate (C_{Cr}) is the volume of blood plasma that is cleared of creatinine per unit time and is a useful measure for approximating the GFR. The results of these tests are important in assessing the excretory function of the kidneys. In clinical practice, estimates of creatinine clearance based on the serum creatinine level are used to measure GFR. Creatinine, a breakdown product of creatinine phosphate which is found in muscle, is produced naturally by the body. It is freely filtered by the glomerulus, but also actively secreted by peritubular capillaries in very small amounts

such that creatinine clearance overestimates actual GFR by 10-20%(Stevens LA, Coresh J, Greene T, & Levey AS, June 2006).

A commonly used formular for estimating creatinine clearance is the Cockcroft-Gault (CG) formula (Appendix 15), which in turn estimates GFR in mililitres per minute. It utilizes serum creatinine measurements and a patient's weight to predict the creatinine clearance and is commonly applied because of ease in calculating it, though it does not cater for variations in race(Cockcroft DW & Gault MH, 1976). Other formulae include Modification of Diet in Renal Disease (MDRD) formula, Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula and Mayo Quadratic formula, which though complex to calculate are deemed to be more accurate(Levey AS et al., March 1999; Levey AS, Stevens LA, & Schmid CH, May 2009; Rule AD et al., December 2004). In children under 12 years, the Schwartz formula which is derived from body length and serum creatinine is used(Schwartz GJ, Haycock GB, Edelmann CM, & Spitzer A, August 1976).

Chronic kidney disease (CKD) is a worldwide public health problem. In the United States (US), the prevalence of end-stage renal disease has been noted to be increasing(KDIGO, 2012). The number of people enrolled to the end-stage renal disease (ESRD) Medicare-funded program rose from approximately 10,000 beneficiaries in 1973 to 86,354 in 1983, and to 547,982 in 2008(United States Renal Data System, 2010).

The disease pattern in Sub-Saharan Africa (SSA) is markedly different from other regions. Middle-aged and elderly populations are predominantly affected in developed countries whereas in Sub-Saharan Africa, CKD mainly affects young people between the ages of 20 and 50 years with hypertension, diabetes and infections(Arogundade FA

& Barsoum RS, 2008). According to review done by Barsoum and published in 2009, chronic glomerulonephritis and interstitial nephritis were the principal causes of CKD in low and middle income countries, reflecting the high prevalence of bacterial, viral, and parasitic infections that affect the kidneys directly or indirectly(Barsoum RS, 2009).

2.2. Major risk factors for glomerulosclerosis and CKD.

2.2.1. Hypertension and pre-hypertension

Traditionally, hypertension has been recognized as a major cause of glomerulosclerosis and CKD. It is a leading cause of CKD in sub- Saharan Africa, and was documented to contribute 25% of CKD cases in Senegal, 29.8% in Nigeria, 45.6% in South Africa, 48.7% in Ghana(Naicker S, 2003). In a survey conducted by Naicker *et al* in South Africa, hypertension affected about 25% of the adult population, was more in blacks and was the cause of ESRD in 21% of patients on renal replacement therapy(Naicker S, 2003).

In a screening survey of adults living in the largest urban slum in Nairobi Kenya in 2014, Joshi *et al* found the age standardized prevalence of hypertension of 22.8%. Only 20% were aware of their hypertensive status and among the known and drug treated hypertensive people, 49% had achieved control(Joshi MD et al., 2014). 59.3% had pre-hypertension in the same survey. Screening in a rural low income setting in western Kenya conducted by Pastakia *et al* in 2014 utilizing home-based and community-based strategies revealed rates of 6% and 13% respectively(Pastakia SD et al., 2013). This could have been an under estimate since cut-off systolic blood pressure (SBP) of $\geq$ 160 mmHg was used in order to triage screened participants for referral to the local

clinic for diagnostic testing. Although these studies were carried out among the adult population, it is clear that the burden of hypertension is high. Similar picture may be extrapolated to the adolescent population considering that elevation in both systolic and diastolic blood pressure tracks age. This then, implies that many people in Kenya are exposed to complications of hypertension including CKD. Pre-hypertension is associated with development of hypertension(Vasan RS, Beiser A, Seshadri S, 2000).

2.2.2. Glomerulonephritis

Glomerular disease is more prevalent in Africa and the most common mode of presentation is nephrotic syndrome, with the age of onset at five to eight years. It is estimated that 2 to 3% of medical admissions in tropical countries are due to renal-related complaints, the majority being the glomerulonephritides(Naicker S, 2003).

 In 2006, Barsoum noted that chronic glomerulonephritis and interstitial nephritis were the principal causes of CKD in developing countries given the high prevalence of implicated infectious aetiologies like malaria, schistosomiasis, infective endocarditis and viral hepatitis(Barsoum RS, 2009).

Although epidemiologic data from many areas in Africa are sparse, the incidence of glomerular disease, particularly nephrotic syndrome, seems to be higher in Africa, has been observed to be of a more severe form than that found in Western countries, and is characterized by poor response to treatment and progression to renal failure(Barsoum RS & Francis MR, 2000).

2.2.3. HIV infection

HIV infection is endemic in sub-Saharan Africa. According to UNAID regional fact sheet of 2012, an estimated 23.5 million(22.1–24.8 million) people living with HIV resided in sub-Saharan Africa, representing 69% of the global HIV burden. In 2011,

92% of pregnant women living with HIV resided in sub-Saharan Africa. More than 90% of children who acquired HIV in 2011 lived in sub-Saharan Africa. Women in sub-Saharan Africa were disproportionately impacted by the HIV epidemic, and accounted for 58% of all people living with HIV in the region in 2011(Joint United Nation Programme on HIV and AIDS, November 2012).

The number of new infections has been declining, with increasing numbers of patients on anti-retroviral therapy (ART). In 2011, there were an estimated 1.8 million(1.6million–2 million) new HIV infections in sub-Saharan Africa compared to 2.4 million (2.2million–2.5 million) new infections in 2001, a 25% decline(Joint United Nation Programme on HIV and AIDS, November 2012).

Data on the prevalence of HIV-related glomerular disease in Africa are scarce. This relates to the late presentation in Africa of patients with the disease. Oftentimes, patients require dialysis at the time of presentation. Reported prevalence of CKD in HIV-infected ART-naive patients in SSA ranges from 6 to 45%(Naicker S & Fabian J, 2010). Screening studies in South Africa reported proteinuria in 5.5–6%, with HIV-associated nephropathy (HIVAN) on biopsy in 5–83%(Han TM, Naicker S, Ramdial PK, & Assounga AG, 2006). In a study looking at the burden of renal disease among ART naïve, HIV infected children at Moi Teaching and Referral Hospital Eldoret, Cheptinga reported the prevalence of renal disease at 27.6%(Cheptinga PK, 2011). Koech documented persistent proteinuria rate of 9.6% in his study looking at Human Immunodeficiency Virus (HIV)-associated nephropathy among antiretroviral naïve adults with persistent proteinuria at the Moi Teaching and Referral Hospital(Koech KM, 2013). None of those with persistent proteinuria had histological lesion consistent

with HIVAN. These findings allude to multiple other aetiologies of kidney disease in the setting of HIV with possible regional variability.

Studies have shown that the risk for HIVAN is linked to the *MYH9* gene polymorphism, with the risk variant accounting for all or nearly all of the increased risk for focal segmental glomerulosclerosis (80%) and HIV-associated collapsing glomerulopathy (100%) that characterize African Americans(Kopp JB, Smith MW, & Nelson GW, 2008). The *APOL1* variant has been reported to be more strongly associated with focal segmental glomerulosclerosis(Tzur S et al., 2010).

An increasing burden of HIV associated CKD may be anticipated, with increasing life expectancy on ART, aging of HIV-infected populations, and nephrotoxicity of the various drugs used in this population. It is worth noting, however, that early initiation of ART may impact on the burden of CKD due to HIV infection. A study in south Africa by Fabian *et al* showed that the response of both microalbuminuria and proteinuria to ART was rapid and sustained, resolving to normal limits within 3–6 months(Fabian J, Naicker S, & Venter WD, 2009).

2.2.4. Diabetes mellitus

Diabetic nephrosclerosis is notably the leading cause of end-stage renal disease in the Western world(Ballard DJ et al., 1988; Raine AE, 1993). Published data on nephropathy in the African diabetic population are scarce. However, there appears to be a racial difference in the prevalence of diabetic nephropathy and end-stage renal failure. African-American patients have been reported to have a greater risk of diabetic nephropathy and kidney damage than their Caucasian counterparts(Crook ED, 2002). In the past three decades, the prevalence of microalbuminuria in African diabetic patients

has varied greatly(Erasmus RT, Oyeyinka G, & Arije A, 1992; Rahlenbeck SI & Gebre-Yohannes A, 1997; Wanjohi FW, Otieno FC, Ogola EN, & Amayo EO, 2002). A study carried out by Alebiosu *et al* suggested that diabetic nephropathy could be assuming an increasing role as a cause of chronic kidney disease in Africa(Alebiosu CO & Ayodele OE, 2006).

2.2.5. Proteinuria

The kidneys play a major role in the retention of plasma proteins, using renal tubules to reabsorb them as the proteins pass through the glomerular filtration barrier. Normal urine protein excretion is up to 150 mg/day. Detection of abnormal quantities of protein in the urine is therefore considered an early sign of significant glomerular disease(KDIGO, 2012).

Proteinuria occurs in various forms and at different levels of severity. Protein excretion can vary on a day-to-day basis depending on factors such as vigorous physical activity. Persistent proteinuria, defined as being present on two or more occasions, therefore needs to be confirmed by retesting within 3 months before interventions to correct it are undertaken(Wagner DK et al., 1994). Persistent proteinuria is believed to reflect structural renal disease and may progress to chronic renal insufficiency. Persistent proteinuria in excess of 500 mg/day is more likely the result of significant glomerular disease especially when associated with active urine sediment (dysmorphic red blood cells and red cell casts), hypoalbuminemia, lipiduria, edema, abnormal renal function, hyperlipidemia and hypertension(KDIGO, 2012).

Proteinuria may accelerate kidney disease progression to end-stage renal failure. Evidence indicate that this process occurs through multiple pathways, including induction of tubular chemokine expression and complement activation that lead to

inflammatory cells, predominantly macrophages, infiltration in the interstitium and sustained fibrogenesis(Abbate et al., 2006). This in turn worsens kidney damage. Persistent proteinuria therefore warrants treatment with angiotensin converting enzyme inhibitors.

2.3. Glomerular haematuria as an indicator of glomerular disease.

Hematuria of glomerular origin is often the result of a structural disruption in the integrity of glomerular basement membrane which may result from immune-mediated injury to the glomerular capillary wall, or in non-inflammatory glomerulopathies such as thin basement membrane nephropathy from localized gaps in the glomerular capillary wall(Collar JE, Ladva S, Cairns TD, & Cattell V, 2001). The structural alteration causes red blood cells to be filtered and get altered in morphology as they traverse the filtration barrier and tubular system.

Among patients with hematuria, a variety of findings on urinalysis favor the diagnosis of glomerular bleeding. These include the presence of red cell casts, proteinuria, dysmorphic red cells and, in patients with gross hematuria, a smoky brown color of urine. On the other hand, blood clots are almost always indicative of extraglomerular bleeding.

Evaluation of red cell morphology may be helpful in identifying the cause of hematuria. The red cells are typically uniform and round with extra renal bleeding, but usually have a dysmorphic appearance with renal lesions(Birch DF, Fairley KF, & Whitworth JA, 1983; Fairley KF & Birch DF, 1982; Pollock C, Liu PL, & Györy AZ, 1989), particularly but not only glomerular diseases(Pollock C et al., 1989). This change in morphology is manifested by blebs, budding, and segmental loss of membrane,

resulting in marked variability in red cell shape and a reduction in mean red cell size(Shichiri M, Hosoda K, & Nishio Y, 1988).

2.4. Elevated blood pressure as a predictor glomerular disease and progression of CKD.

It has been postulated that the renal abnormality that contributes to essential hypertension in the general population is a reduced number of nephrons. A major pathophysiological aspect of this concept is hyperfiltration and increased intraglomerular pressure in the remaining glomeruli causing haematuria and proteinuria. Hyperfiltration is associated with glomerular enlargement which is accompanied by maladaptive changes progressing to glomerular sclerosis which can present with elevated systemic blood pressure. Pre-hypertension, defined in the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC7),(Chobanian AV et al., 2003) is associated with increased risk for developing hypertension(Vasan RS, Beiser A, & Seshadri S, 2000). Identification and management of individuals with pre-hypertension is recommended as an important strategy to inhibit progression to hypertension and thereby reduce the risk of CKD in the general population.

Hypertension is a critical risk factor for progression of CKD(Fox CS, Larson MG, & Leip EP, 2004; Mainous AG III, Everett CJ, & Liszka H, 2004) and a predictor of development to ESRD(Klag MJ, Whelton PK, & Randall BL, 1996). Both early detection and appropriate intervention during the initial stages of CKD are necessary for prevention of a rapid progression to ESRD.

2.5. Screening strategies for chronic kidney disease

Until recently, screening for chronic kidney disease was accepted practice only in patients with hypertension or diabetes mellitus,(American Diabetes Association, 2006; Williams B et al., 2004) but also more widespread screening has increasingly been proposed.(de Jong PE & Brenner BM, 2004; Remuzzi G & Weening JJ, 2005). The United Kingdom chronic kidney disease guidelines also recommend at least annual screening of all adults at risk of obstructive kidney disease and those with cardiovascular diseases, while the US kidney disease outcomes quality initiative (US KDOQI) guidelines use age >60 years for additional inclusion(KDIGO, 2012). Even more expanded, the International Society of Nephrology advocates proactive screening for minor renal damage in all patients visiting general practitioners, similar to the screening for high blood pressure or dyslipidemia(International Society of Nephrology, 2005). Although there is general agreement that screening for chronic kidney disease (CKD) in adults is of great importance(Narva A, 2007), screening for CKD among children is more controversial. The primary reason for this controversy is the uncertainty as to whether early detection of renal disorders in childhood will lead to effective interventions and reduction in the number of individuals who develop end-stage renal disease (ESRD). In December 2007, the American Association of Paediatrics published its recommendations, in which no urinalyses were recommended at any age during childhood (American Paediatrics Association, 1995).

There appears to be a clear consensus, however, among Asian investigators that screening for CKD inco-operated into public health programs in these countries has led to early detection and effective intervention(Cho BS, Kim S D, Choi Y M, & Kang HH, 2001; Kitagawa T, 1988; Murakami M, Yamamoto H, Ueda Y, Murakami K, &

Yamauchi K, 1991). Comparing the situation in Japan and the United States, Murakami noted a fourfold lower incidence of patients <20 years of age reaching ESRD in Japan (Murakami M, Hayakawa M, Yanagihara T, & Hukunaga Y, 2005). The evidence was notably striking in the 15 to 19 years age group where the number of patients starting ESRD therapy was 6 per million in Japan compared with 30 per million in the United States. However, the role of primary screening in producing this disparity is unclear. The cause for the lower rate in Japan may be multi-factorial and may include issues such as differences in disease type and presence of co-morbidities such as obesity, which may have contributed to a higher rate of progression in U.S. children. The lower rates may at the same time be a reflection of the positive impact of screening that has been entrenched in this country.

Screening programs are not well developed in most African countries. In Kinshasa, More than 15 000 adults were screened at churches, schools, and industrial sites by volunteer health care personnel. The prevalence of hypertension and proteinuria were 40% and 12% respectively(Sumaili K et al., 2009). In a study in Nigeria carried out amongst school children, Ikimalo demonstrated that although the yield from mass urinary screening was low, majority of those detected to have significant urinary abnormalities had persistence of those abnormalities when followed up(Ikimalo FE, Eke FU, Nkanginieme KE, & Ikimalo J, 2003). They recommended screening as part of school health programme. In Nairobi, Muraguri and colleagues found the prevalence of proteinuria, haematuria, other urinary abnormalities and hypertension to range between 1 and 3.5% among teenage secondary school students. Most were asymptomatic and had no significant associations(Muraguri PW, McLigeyo SO, & Kayima JK, 1997).

CHAPTER THREE

MATERIALS AND METHODS

3.1. Study Population

This consisted of public secondary school students in Eldoret municipality. There are sixteen public secondary schools in this region with a total student population of 5200.

3.2. Setting

The study was carried out in four randomly selected public secondary schools within Eldoret municipality in Uasin-Gishu County. These schools were Kapsoya, Ilula, Kapsaos and Kapkeben. All are mixed secondary schools, located within a radius of fifteen kilometers from Eldoret town where Moi Teaching & Referral Hospital (MTRH) and Moi University School of Medicine (MUSOM) are located. Serum creatinine measurements and microscopic urinalysis were done in MTRH main laboratory and MUSOM microbiology laboratory.

3.3. Study design

Descriptive cross sectional survey was carried out to find out the prevalence of glomerular disease among secondary school students in Eldoret.

3.4. Inclusion Criteria

All consenting students aged 12 to 19 years.

3.5. Exclusion Criteria

Females having menses or those who had completed menses within two days of collection of urine.

3.6. Sample Size

The sample size was calculated using Fischer's formula for prevalence studies. Thus;

The sample size, $\mathbf{n} = \dfrac{Z^2_{\left(1-\frac{\alpha}{2}\right)} . P(1-P)}{D^2}$

Where **n**=sample size; **Z**= the z value corresponding to 95% confidence (1.96); **α**=significance level (5%); **P** = estimated prevalence; **D** = Precision.

Using a precision of 5% and estimated prevalence of 50%, a sample of **384** patients was obtained. Being a population-based prevalence study with no recent research data providing the baseline prevalence of the measures being studied, estimated prevalence of **50%** was used in the formula in order to arrive at a minimum acceptable sample size. **395** students were finally included in the study.

3.7. Sampling technique

A total of 395 students were enrolled to participate in the study using probabilistic, multistage sampling. Representative public boarding secondary schools, clusters, were randomly selected. Total student population in the selected schools was ascertained.

Selected schools were then stratified by class levels/forms i.e. form 1 to form 4 and by class streams i.e. stream A, stream B etc. Proportionate sample size for each school was calculated by dividing school population by total number of students in the selected schools and multiplying by the sample size, **n**. A stream in each class level was selected by simple random sampling and a proportionate sample size for each class was

calculated by dividing class population by school population and multiplying by school sample size.

Simple random sampling was then used to identify the pupils from each selected class stream that would be included in the study.

3.8. Study Procedure

The study participants were interviewed using a questionnaire (Appendix 1) that was pre-designed to give relevant demographic information as well as the information about the presence of symptoms of renal disease and recognized predisposing factors for renal disease. Blood pressure measurements were taken according to the guidelines provided in the Seventh Report of the Joint National Committee on Prevention Detection, Evaluation and Treatment of High Blood pressure (JNC VII). Each participant was settled in a quiet room, in a relaxed sitting position, back and elbow supported, with no tight fitting clothing on the upper arm or any thick clothes like sweaters. Three, right arm, readings were taken at 5 minute - intervals. Mean of the three readings was calculated, unless the difference between the readings was >10mmHg, in which case the mean of the two closest of the three measurements was used. Heights were measured in Centimeters and height/stature percentile for every participant ascertained based on Centers for Disease Control and Prevention (CDC) height percentiles for boys and girls developed in 2000 by National Center for Health Statistics in collaboration with The National Center for Chronic Disease Prevention and Health Promotion (Appendix VIII & IX). Normal blood pressure, pre-hypertension and hypertension were defined based on the blood pressure levels by age and height percentile charts contained in the fourth report on the diagnosis, evaluation, and treatment of high blood

pressure in children and adolescents by National Heart, Lung and Blood Institute (Appendix VI and VII). JNC VII criteria was used for participants older than 17 years.

Each participant was also given code-labeled, sterile urine specimen bottle and instructed to empty their bladders before going to bed at night and to collect clean catch first morning urine just after waking up and before engaging in any physical activity. Instructions on how to collect mid-stream sample were given to the participants and prior cleansing of the external genitalia was not required. Girls, not having menses at the time, were required to part the labia majora and boys to reflect back the prepuce in order to collect clean catch, mid stream urine. Urinalysis was performed using multifunctional dipstick. Proteinuria of 1+ (30mg/dl) or more was accepted as significant and haematuria of trace and above was also recorded. The urine specimens that tested positive for blood and /or proteins were stored in a cooler box with ice packs and transported to the laboratory where it was centrifuged at 3000rpm for 3-5 minutes. Supernatant was poured out and the sediment subjected to light microscopy. All urine specimens were analyzed within 4 hours of collection. Urine analyzed within 4 hours of collection has yielded valid results(Ikimalo FE et al., 2003).

 All the participants with proteinuria and/or haematuria, pre-hypertension or hypertension were weighed and blood samples taken for estimation of serum creatinine. Estimated GFR was then calculated using Cockroft-Gault formula (Appendix 11). All the participants with proteinuria and/or haematuria on first urinalysis underwent a second test after one month to ascertain the persistence of proteinuria and/or haematuria.

Those who were found to have glomerular haematuria and /or persistent proteinuria, pre-hypertension or hypertension were appropriately referred for further evaluation and appropriate management.

3.9. Data Management and Analysis

3.9.1. Data Collection

Data was collected by the researcher on a data entry form. Each data entry form had a unique identifier, which was the participant's number. Data collected in the data entry form included relevant demographics, history relevant to kidney disease, urinalysis findings, blood pressure findings and categories. Data was later transferred to computer epidata software. Double entry while entering data on a computer was used to ensure accuracy.

3.9.2. Data Analysis

Data analysis was done using STATA version 13 SE. Categorical variables were summarized as frequencies and their corresponding percentages. Continuous variables that assumed the Gaussian distribution were summarized as mean and their corresponding standard deviation (SD). Continuous variables that violated the Gaussian assumption were summarized as median and their corresponding inter quartile ranges (IQR). Gaussian assumption was assessed empirically using Shapiro Wilk test and graphically using normal probability plots. Persistent proteinuria was determined using the second dipstick urinalysis test done within three months that confirmed proteinuria. Glomerular haematuria was determined by presence of dysmorphic red blood cells or red blood cell casts on first light microscopy and its persistence was confirmed by the second light microscopy. Presence of renal disease was determined by the presence of glomerular haematuria on first light microscopy and/or persistent proteinuria. A decline in renal function was defined by glomerular filtration rate (GFR) less than 90 mLs/minute.

Association between categorical variables was assessed using Pearson's Chi square test. Difference between two continuous variables was evaluated using two sample t-test if normally distributed or using two sample Wilcoxon rank sum test if they were skewed. Relative rates between any two groups were computed and reported alongside the corresponding 95% confidence limits. Similarly, the prevalence was reported alongside the corresponding 95% confidence limits. Results were presented using tables.

3.10. Study Limitations

- Light microscope was used in urinalysis. Though acceptable, it is less sensitive in showing dysmorphism in red blood cells compared to electron/phase contrast microscope.

- White coat effect may have exaggerated the rate of elevated blood pressure measurements. Ambulatory blood pressure measurement, which is ideal, was beyond the scope of this study.

- Estimation of renal function was based on single measurement of serum creatinine.

3.11. Ethical Considerations

3.11.1. Approval

Approval was sought from the Institutional Research and Ethics Committee of MTRH and Moi University, National Council for Science Technology and Innovation, County Education Officer and Principals of participating schools.

3.11.2. Specimen collection and handling

Infection prevention and safety was observed in the collection, processing and disposal of urine specimens so as not to endanger the participants, the general population and the research assistants.

3.11.3. Risks

There were no anticipated risks to the participants in this study.

3.11.4. Benefits.

The participants who were found to have glomerular haematuria and /or persistent proteinuria, pre-hypertension and hypertension were appropriately referred for further evaluation and appropriate management. Participating schools' fraternity was sensitized on kidney disease through brief talks by the researcher.

3.10.5. Informed consent

The principals, teachers and students of participating schools were sensitized about the study. This was done through health talks focusing on kidney disease and relevance of the study.

Principals of the study schools were educated about the study by the investigator. They were then asked to consent in writing, on behalf of enrolled students, to their participation in the study.

All students provided written assent before participating in the study. They did so by free will and those who declined to assent were not discriminated against in any way.

CHAPTER FOUR

RESULTS

4.1 Demographic variables and baseline characteristics

A total of 395 participants, from four public secondary schools were included in the study, 51 %(n = 200) being male. The overall mean age was 17(SD: 1.5) years with a range of 13 to 19 years. About one third, 127(32%), had personal history of features suggestive of kidney disease which included any or a composite of loin pain, facial puffiness, limb swelling, cola colored urine, smoky urine and anuria/oliguria. 23% (n = 91) of participants reported presence of risk factor/s for kidney disease which included diabetes mellitus, hypertension, cardiovascular disease or kidney disease in family.

The median systolic blood pressure (SBP) was 117(IQR: 110-126) mm Hg while the median diastolic blood pressure (DBP) was 70(IQR: 63-76) mm Hg. Of all participants, 23(5.8%), 95% CI 3.7%, 8.6% were pre-hypertensive while 27(6.8%), 95% CI 4.6%, 9.8% were hypertensive. The prevalence of elevated blood pressure was 12.7 %(95%) CI: 9.5%, 16.3%.

Table 1: Overall baseline characteristics

Variable	Levels	Total
Age in years; *mean(SD)*		17(1.5)
SBP in mmHg; *median(IQR)*		117(110-126)
DBP in mmHg; *median(IQR)*		70(63-76)
Sex; *n(percentage)*	Male	200(51%)
Personal history of features suggestive of kidney disease; *n(percentage)*	Present	127(32%)
History of risk factor/s for kidney disease; *n(percentage)*	Present	91(23%)
Pre-hypertension; *n(percentage)*	Yes	23(5.8%)
Hypertension; *n(percentage)*	Yes	27(6.8%)
Elevated blood pressure; *n(percentage)*	Pre-hypertensive and Hypertensive	50(12.7%)
Schools; *n(percentage)*	Ilula	119(30%)
	Kapsaos	123(31%)
	Kapkeben	79(20%)
	Kapsoya	74(19%)

4.2 Gender differences in the participants characteristics

Male participants were significantly older than the female participants, 16.9(SD: 1.5) versus 16.5(SD: 1.4) years, p=0.030. There was no significant differences in systolic blood pressures (SBP) among the male participants compared to the female participants, 117(IQR: 110-124) versus 117(IQR: 110-126), p=0.886. However, the male participants had significantly higher diastolic blood pressures (DBP) compared to the female participants, 80(IQR: 77-83) versus 70(IQR: 60-73), p=0.0001.

There were also significant differences in the proportions of those who had personal history of features suggestive of renal disease and those who reported history of risk factor/s for kidney disease i.e. diabetes mellitus, hypertension, kidney disease in family or cardiovascular disease, among male compared to female, 78(39%) versus 49(25%), p=0.003, and 33(17%) versus 58(30%), p=0.002.

There was no statistically significant gender difference in the occurrence of pre-hypertension, hypertension, and overall elevated blood pressure; p=0.088, 0.320, and 0.130 respectively. Gender distribution was different from school to school, p=0.024

Table 2: Gender differences in the participants' characteristics

Variable	Levels	Male	Female	P (test for difference)
Age in years, *median(SD)*		16.9(1.5)	16.5(1.4)	0.030^t
SBP in mmHg, *mean(IQR)*		117(110-124)	117(110-126)	0.886^w
DBP in mmHg; *mean(IQR)*		80(77-83)	70(60-73)	0.0001^w
Personal history of features suggestive of kidney disease, *n(percentage)*	Present	78(39%)	49(25%)	0.003
History of a risk factor/s for kidney disease; *n(percentage)*	Present	33(17%)	58(30%)	0.002
Pre-hypertension; *n(percentage)*	Yes	8(4%)	15(8%)	0.088^f
Hypertension, *n(percentage)*	Yes	12(6%)	15(8%)	0.320^f
Elevated blood pressure; *n(percentage)*	Yes	20(10%)	30(15%)	0.130^f
Schools	Ilula	62(31%)	57(29%)	0.024
	Kapsaos	64(32%)	59(30%)	
	Kapkeben	29(15%)	50(23%)	
	Kapsoya	45(23%)	29(15%)	

^{f} – Fisher's exact test was reported since the expected cell counts in at least one of the cells of the 2x2 tables that were created was <5.
^{w} – Two sample Wilcoxon ranks sum test
^{t} – Two sample t-test.

4.3 Outcome variables

Table 3: Overall outcome variables

Variable	Levels	Total
Proteinuria (First dipstick test)	Nil	n=387(98.0%)
	Present	n=8(2.0%)
Persistent proteinuria (second dipstick test)	Yes	n=8(2.0%)
Haematuria (First dipstick test)	Nil	n=361(91.4%)
	Present	n=34(8.6%)
Haematuria (First Light Microscopy)	Nil	n=375(94.5%)
	Normal red blood cells	n=9 (2.3%)
	Dysmorphic red blood cells	**n=11(2.8%)**
Persistent Haematuria (Second dipstick test)	Yes	n=12 (3.0%)
Persistent Haematuria (Second Light Microscopy)	Normal red blood cells	n=3 (1.0%)
	Dysmorphic red blood cells	n=8 (2.0%)
Persistent proteinuria and First light microscopy glomerular hematuria	Yes	n=6 (1.5%)
¥Reduced GFR (GFR<90 mls/min)	Yes	n=30 (39.5%)
Glomerular disease present (Persistent proteinuria and/or glomerular hematuria)	Yes	**n=14(3.5%)**

¥ - Sample size = 76.

The prevalence of glomerular haematuria was 2.8 %(95% CL: 1.4%, 4.9%) while the prevalence of persistent proteinuria was 2.0 %(95% CL: 0.9%, 4.0%). There were 6(1.5%, 95% CL: 0.6%, 3.3%) participants who had both persistent proteinuria and glomerular haematuria. The prevalence of glomerular disease, defined by glomerular hematuria on first light microscopy and/or persistent proteinuria, was 3.5% (95% CL: 2.0%, 5.9%). 76 participants, consisting of those who had elevated blood pressure, first dipstick test haematuria and/or proteinuria were evaluated for renal function using Cockroft-Gault formular to estimate their glomerular filtration rate. Of these, there were 30(39.5%, 95% CI: 28.4%, 51.4%) participants with reduced GFR of less than 90 mLs/min.

4.4 Gender differences in outcome variables

Stratified by gender, there was no statistically significant differences, between male and female participants, in the rates of proteinuria on first dipstick test (p=0.624), and persistent proteinuria on second dipstick (p=0.624).

There was a significant difference in the rate of haematuria using first dipstick test between the male and female participants, 10(5.0%) versus 24(12.3%), p=0.008. However, first microscopic analysis of the same urine samples did not show any difference in the rates of glomerular haematuria between males and females, 3(1.5%) versus 8(4.1%), p=0.102.

The rate of glomerular haematuria on the first light microscopy, and the rate of persistent glomerular haematuria on second light microscopy were not different among the male compared to the female participants, 3(1.5%) versus 8(4.1%), p=0.139, and 3(1.5%) versus 5(2.6%), p=0.147, respectively. The rates of glomerular disease and decreased GFR were not different between male compared to female participants, 5(2.5%) versus 9(4.6%), p=0.194 and 11(39.3%) versus 19(39.6%), p=0.588, respectively.

Table 4: Gender differences in the outcome variables

Variable	Levels	Male n (%))	Female n (%)	P value Test for differences
Proteinuria(First dipstick test)	Nil	196(98%)	191(98%)	0.624^f
	Present	4(2%)	4(2%)	
Persistent proteinuria(Second dipstick test)	Yes	4(2.0%)	4(2.1%)	0.624^f
Haematuria (First dipstick test)	Nil	190(95.0%)	171(87.7%)	0.008^f
	Present	10(5.0%)	24(12.3%)	
Haematuria (FirstLight Microscopy)	Nil	194(97.0%)	181(92.8%)	0.139^f
	Normal RBCs	3(1.5%)	6(3.1%)	
	Dysmorphic RBCs	3(1.5%)	8(4.1%)	
Persistent Haematuria (Second dipstick test)	Nil	197(98.5%)	186(95.4%)	0.064^f
	Present	3(1.5%)	9(4.6%)	
Persistent Haematuria (Second Light Miscroscopy)	Nil	197(98.5%)	187(95.9%)	0.147^f
	Normal RBCs	0	3(1.5%)	
	Dysmorphic RBCs	3(1.5%)	5(2.6%)	
Glomerular hematuria (First light microscopy)	Yes	3(1.5%)	8(4.1%)	0.102^f
Persistent proteinuria and First light microscopy glomerular hematuria	Yes	3(1.5%)	3(1.5%)	0.645^f
$^¥$Reduced GFR (GFR<90 mL/min)	Yes	11(39.3%)	19(39.6%)	0.588^f
Glomerular disease present	Yes	5(2.5%)	9(4.6%)	0.194^f

$^¥$ - Sample size = 76.

^{f} – Fisher's exact test was reported since the expected cell counts in at least one of the cells of the 2x2 tables that were created was <5.
^{w} – Two sample Wilcoxon ranks sum test.

4.5 Associations between glomerular disease other variable

The association between the presence of glomerularl disease and, elevated blood pressure, personal history of features suggestive of kidney disease, risk factor/s for kidney disease and decreased GFR were assessed. Elevated blood pressure, history of features suggestive of kidney disease and presence of risk factor/s for kidney disease were all significantly associated with presence of glomerular; p<0.0001, p = 0.003, p = 0.023 respectively(Table 5). There was no association between reduced GFR (GFR<90) and glomerular disease, p = 0.501(Table 6).

Table 5: Associations between glomerular disease and participants' characteristics

	Glomerular disease present(n=14)	Glomerular disease absent(n=381)	P value
Elevated BP	9(64.3%)	41(10.8%)	<0.0001[f]
Personal history	10(71.4%)	117(30.7%)	0.003[f]
Presence of risk factor/s	7(50%)	84(22%)	0.023[f]

[f] – Fisher's exact test was reported since the expected cell counts in at least one of the cells of the 2x2 tables that were created was <5.

Table 6: Association between glomerular disease and decreased renal function

	Glomerular disease present(n=14)	Glomerular disease absent(n=62)	P value
Decreased GFR	6(42.9%)	24(38.7%)	0.501[f]

[f] – Fisher's exact test was reported since the expected cell counts in at least one of the cells of the 2x2 tables that were created was <5.

CHAPTER FIVE

DISCUSSION

Proteinuria and glomerular haematuria are recognized urinalysis findings that may imply presence of glomerular disease and ought to prompt keen investigation. This study set out to measure these important markers of glomerular disease among teenage population in Eldoret. The prevalence of proteinuria on first dipstick test in this study was 2%. There was a high rate of persistence of this finding making the prevalence of persistent proteinuria in our study to be 2%. We utilized the easily available regular multi-detector dipsticks as opposed to microalbumin dipsticks that are more sensitive and can detect protein excretion of less than 300g per day. It is therefore possible that the rates of proteinuria we found underestimated the true picture of pathological protein excretion consistent with glomerular disease in the study population. The urinalysis dipsticks we used are readily available and cheap and though they cannot detect microalbuminuria, they are relevant in screening glomerular disease.

Glomerular haematuria is oftentimes pathological, especially if it occurs concurrently with proteinuria. The rate of haematuria on first dipstick urinalysis was 5%. When similar urine samples were subjected to microscopic analysis, the prevalence of glomerular haematuria was found to be 2.8%. This observation perhaps brings into focus the critical role of microscopic urinalysis in evaluating pathological haematuria and determining whether it is due to glomerular pathology or otherwise. In this study, 56% of haematuria found using dipstick urinalysis turned out to be of glomerular origin.

There was statistically significant gender difference in the rates of haematuria using first dipstick test.12.3 % of female participant had dipstick haematuria whereas male participants had a 5% rate (p=0.008). Considering that menstruating females were excluded from the study, it may be possible that etiological factor/s for non-glomerular haematuria played a role in girls more than boys. Sub clinical urinary tract infections being more common in girls, because of anatomical relations of the urethral meatus in the perineum and the shorter length of the urethra compared to boys, may be responsible for the observed gender difference.

In our study, glomerular disease was defined by presence of glomerular haematuria and/or persistent proteinuria. The prevalence of glomerular disease was 3.5%. No gender difference in occurrence of glomerular disease was observed. This can be explained by probable similar etiologies of glomerular disease across gender since both male and female participants in this study had comparable ages and came from similar geographic environment.

In Nairobi, Muraguri and colleagues found the prevalence of significant proteinuria and dipstick haematuria to be 2.2% and 3.5% respectively among teenage secondary school students(Muraguri PW et al., 1997). Although their study did not report persistence in proteinuria nor microscopic evaluation of haematuria, their findings compare well with our study with respect to dipstick urinalysis and gender distribution.

A study carried out amongst primary school children by Ikimalo *et.al* in Nigeria found the prevalence of asymptomatic proteinuria to be 1% and that of asymptomatic dipstick haematuria to be 0.6% with no statistically significant gender difference(Ikimalo FE et al., 2003). These are lower rates than those we found in our study, perhaps because of younger average age of their study participants. It is worth

noting that when stratified by age, the prevalence of haematuria in Ikimalo study was 4.76% in those aged between 15 and 17 years, results that compare favorably with those we found. Participants in the Ikimalo study demonstrated high rate of persistence in both proteinuria and haematuria like in our study. Ikimalo pointed out the high prevalence of bladder schistosomiasis in their study population especially among the male which could explain the similarity in rates of occurrence of dipstick haematuria in males and females. This contrasts to the Nairobi study by Muraguri and our study where the dipstick haematuria occurred at a significantly higher rate in females compared to males.

Elevated systemic blood pressure is a recognized risk factor for glomerular disease. In our study, both pre-hypertension and hypertension were considered to constitute elevated blood pressure. The prevalence of pre-hypertension and hypertension were 5.8% and 6.8% respectively. The prevalence of elevated blood pressure thus was 12.7%. Mean diastolic blood pressure was noted to be higher in male participants. Physiologically, male exhibit higher blood pressure values. Although the mechanisms responsible for the gender differences in blood pressure control are not clear, there is significant evidence that androgens, such as testosterone, play an important role in gender-associated differences in blood pressure regulation by stimulating renin angiotensin aldosterone system(Reckelhoff JF, 2001).

There was a high variability in the rates of hypertension in our study compared with other studies around the country. Muraguri *et al* found hypertension prevalence of 1% among secondary students in Nairobi two decades ago whereas Kimama, using similar blood pressure categorization as we used, found a very high prevalence of 30.6 % among secondary school students in Nairobi in 2014. Similar variability has also been

noted among adults as well. Pastakia and colleagues in a screening survey conducted in a rural low income setting in western Kenya among adult population in 2014, utilizing home-based and community-based strategies, revealed rates of 6% and 13% respectively(Pastakia SD et al., 2013). Hendriks in 2012 carried out a survey and documented hypertension prevalence of 23.7% in Nandi County, Kenya(Hendriks ME et al., 2012). This high variability in hypertension rates that cuts across all ages may point to possible unequal regional distribution in known risk factors for hypertension including lifestyle.

Elevated blood pressure was significantly associated with presence of glomerular disease, $p < 0.0001$. Pre- hypertension is well recognized to be associated with the risk of developing hypertension and both are independently considered risk for and/or a feature of renal disease(Chobanian AV et al., 2003; Vasan RS, Beiser A, & Seshadri S, 2000). Brenner *et al* in 1988 postulated that a renal abnormality that contributes to essential hypertension in the general population is a reduced number of nephrons. A major pathophysiological aspect of this concept is hyperfiltration and increased intraglomerular pressure in the remaining glomeruli, causing haematuria and proteinuria. Hyperfiltration is associated with glomerular enlargement which is accompanied by maladaptive changes progressing to glomerular sclerosis which can present with hypertension(Brenner BM, Garcia DL, & Anderson S, 1988). This may be the reason for the significant association between glomerular disease and hypertension in our study. Glomerulonephritides may also present with elevation in blood pressure as part of nephritic syndrome. This as well can explain the observed association between glomerular disease and hypertension in our study.

Ikimalo study did not show similar relationship between presence of active sediment on urinalysis and hypertension(Ikimalo FE et al., 2003). It is possible that blood pressure abnormalities had already become established in our cohort of participants with glomerular disease unlike in the Ikimalo study where the participants were primary school pupils, majority of who were less than 15 years. Elevation in blood pressure parallels increasing age and progression in glomerular disease.

Participants with personal history of features suggestive of kidney disease were more than twice likely to have glomerular disease compared to those without such history, p=0.003. Similarly, presence of a risk factor/s for kidney disease was associated with increased occurrence of glomerular disease compared to those without, p=0.023. These findings bring into focus the controversy surrounding the role of mass urinalysis for screening renal disease in children and adolescents. Although there is general agreement that screening for chronic kidney disease (CKD) in adults is of great importance(Narva A, 2007), screening for CKD among children and adolescents is more controversial. In December 2007, the American Association of Paediatrics published its recommendations, in which no screening urinalysis was recommended at any age during childhood (American Paediatrics Association, 1995). Going by the results of this study, however, application of urinalysis as a screening tool may be appropriate for the cohort of children and adolescents with elevated blood pressure, personal history of features suggestive of kidney disease and those with risk factor/s for kidney disease.

There was no association between reduced GFR (GFR<90) and presence of glomerular disease, p = 0.501. In other words, presence of glomerular disease, as detected by screening urinalysis, was not associated with significant decline in renal function. This

implies that urinalysis as screening test appropriately offers opportunity for detection of early stage disease. This also concurs with KDIGO screening guidelines that emphasize the markers of kidney damage rather than markers of decline in function.

CHAPTER SIX

CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusions

- Urinalysis, used as screening test for glomerular disease among secondary school students in Eldoret, yielded prevalence of glomerular disease of 3.5 %. The prevalence of glomerular haematuria and persistent proteinuria was 2.8% and 2% respectively. Majority of those detected to have haematuria and/or proteinuria had persistence of these abnormalities when followed up.

- The prevalence of pre-hypertension and hypertension was 5.8% and 6.8% respectively.

- Presence of glomerular disease, as detected by screening urinalysis, was not associated with significant decline in renal function.

- Given the significant associations, utility of urinalysis as screening tool could improve in yield if applied in a cohort of children and adolescents with elevated blood pressure, personal history of features suggestive of kidney disease and those with risk factor/s for kidney disease, instead of all children and adolescents.

6.2 Recommendations

- Dipstick and microscopic urinalysis, together with relevant history and blood pressure measurement ought to be embraced as screening tool for glomerular disease in adolescent population.

- Screening for glomerular disease should focus on markers of damage (proteinuria, glomerular haematuria) and not function.

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Vasan RS, Beiser A, Seshadri S, (2000). Residual lifetime risk for developing hypertension in middle-aged women and men: the Framingham Heart Study. *Journal of the American Medical Association, 287*(6), 1003-1010.

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APPENDICES

6.1. Appendix I – Data Entry Form

1. Participant's Number [＿＿＿＿＿] Age [＿＿] Gender [＿＿＿＿]

Telephone Number [＿＿＿＿＿] Address [＿＿＿＿＿＿＿＿]

Weight ＿＿＿＿＿ **Kgs**. Height ＿＿＿＿＿ **Cms**

2. Has the participant had any of the following symptoms previously? (Tick where approriate)

Loin pain [ ] Facial puffiness [ ] Limb swelling [ ]

Cola colored urine [ ] Smoky urine [ ] Anuria/Oliguria [ ]

3. Has the participant been diagnosed to have any of the following diseases (Tick where appropriate)

Diabetes mellitus [ ] Hypertension [ ]

Kidney disease [ ] Cardiovascular disease [ ]

4. Has the participant's kin been diagnosed to have any of the following diseases (Tick where appropriate)

Diabetes mellitus [ ] Hypertension [ ]

Kidney disease [ ] History of proteinuria [ ]

5. Blood pressure levels:

Systolic [ ] percentile [ ] <u>Category</u>**:**

Normal………….. [ ]

Pre-hypertension… [ ]

Hypertension……… [ ]

Diastolic ☐   Percentile ☐   <u>Category</u>**:**

                                                Normal…………. ☐

                                                Pre-hypertension. ☐

                                                Hypertension……. ☐

6. Urinalysis findings: First visit ☐ , Second visit ☐

Proteinuria: (Tick where appropriate and indicate level)

None ☐   Trace ☐   2+ ☐   3+ ☐

Persistence of proteinuria within three months

Yes ☐   No ☐

Haematuria on dipstick noted

Yes ☐   No ☐

Haematuria with dysmorphic RBCs and/or RBC casts on microcopy

Yes ☐   No ☐

6.2. Appendix II - Informed Consent Agreement: English Version

My name is Dr. Peter K. Koech. I am a student at Moi University School of Medicine pursuing Masters Degree course in internal medicine. I am carrying out a study titled; **Prevalence of Glomerular Disease among Secondary School Students in Eldoret, Kenya.** I am interested in finding out the extent of abnormal findings on urine analysis and blood pressure measurements among secondary school students that may point to existence of underlying kidney disease.

We shall ask the participants questions relevant to kidney disease and enter the answers they provide on the data entry sheet. We shall also do blood pressure measurements and ask the participants to provide early morning urine samples which shall be analyzed for the purposes of this study.

Participation in this study is voluntary. Refusal to participate will involve no penalty or loss of benefit to which you (your students) are entitled. You (your students) may discontinue participation at any time without penalty or loss of benefit. The principal investigator may decide to withdraw a student from the study if we are unable to obtain urine sample.

There are no risks to participants in this study.

If a student will be found to have significant urine findings and /or abnormal blood pressure, he/she will be weighed and a blood sample drawn for estimation of kidney function. The parent/guardian shall be informed and both shall be referred to MTRH for further evaluation and appropriate management.

Records relating to student's participation in the study will remain confidential. Students' names will not be used in any report resulting from this study. The urine and

blood samples obtained from this study will not be used for any other purpose other than the ones stated in the protocol and consent form. You will receive a signed copy of this consent form.

I therefore ask your permission to carry out this study amongst your students who will be selected randomly to participate.

If you grant permission, kindly fill in the declaration below.

I ………………………………………..(name of school principal) having full capacity to consent for students, do hereby consent to their participation in the research study**; Prevalence of Glomerular Disease among Secondary School Students in Eldoret.**

The methods and means by which the study will be conducted; and the risk which may be reasonably expected have been explained to me by…………………….(Researcher's name).

I have been given the opportunity to ask questions concerning this study and any such questions have been answered to my full and complete satisfaction. I understand that I may at any time during the course of this study revoke this consent and withdraw my students from the study without prejudice.

Principal'signature …………………   date……………………..

6.3. Appendix III - Informed Consent Agreement: Kiswahili Version

<u>Cheti cha idhini</u>

Jina langu ni Daktari Peter K.Koech. Ninasomea shahada ya pili katika chuo kikuu cha Moi Kitivo cha Afya.

Niko na nia ya kufanya utafiti kwa ajili ya kukusanya takirimu kuhusu ugonjwa wa figo ambayo inajulikana kama glomerular disease, miongoni mwa wanafunzi kwenye shule za upili za umma katika manispaa ya Eldoret. Kichwa cha utafiti huu ni;

Prevalence of Glomerular Disease among Secondary School students in Eldoret, Kenya.

Matarajio ya atafiti huu ni kuchunguza kama kuna dalili za mapema za ugonjwa huu, ambazo zaweza kuonekana kwenye mkojo au kiwango cha pressure ya damu. Utafiti huu utahusisha kujibu maswali kadhaa kuhusu ugonjwa wa figo, high blood pressure na kisukari. Tutapima mkojo na damu pia.

Hakuna madhara tunayotarajia kuwakumba watakaoshiriki kwenye utafiti huu.

Mkojo na damu itatumika kwa sababu iliyotajwa pekee, wala si kwa sababu zingine zozote.

Iwapo mkojo wa mwanafunzi yeyote utapatikana kuwa na ishara ya itilafu kwenye figo au iwapo kipimo cha pressure ya damu hakitakuwa sawa, yeye na mzazi/mlezi wake watashauriwa kwenda kwenye kituo cha matibabu cha MTRH kwa uchunguzi zaidi na matibabu yanayofaa. Maswala yote yanayohusu wanafunzi yatawekwa siri na wala hakuna hatakayetambuliwa kwa jina au njia nyingine yeyote.

Ninachokusihi ni kwamba uniruhusu nifanye utafiti huu miongoni mwa wanafunzi kwenye shule yako.

Kama unakubali kutoa ruhusa huu, tafadhali weka sahihi yako kwa nafasi iliyoko;

Jina…………………………   Sahihi………………   Tarehe…………

6.4. Appendix IV - Student's Assent Form: English Version

Hallo! My name is Dr. Peter K. Koech. I am a student at Moi University School of Medicine pursuing a Masters degree course in internal medicine. I am carrying out a study titled: **Prevalence of Renal Glomerular Disease among Secondary School students in Eldoret, Kenya.**

I am interested in enumerating the extent of abnormal findings on urine analysis and blood pressure measurements among secondary school students that may point to existence of underlying kidney disease.

This will involve asking you questions relevant to kidney disease and entering the answers you provide on the data entry sheet. We shall also measure your blood pressure and ask you to provide early morning urine sample which shall be analyzed for the purposes of this study.

There are no risks to participant in this study.

If you will be found to have significant urine findings and /or abnormal blood pressure, your weight will be measured and a blood sample will be drawn for estimation of kidney function. Your parent/guardian will be informed and you will be referred to MTRH for further evaluation and appropriate management.

The urine and blood samples obtained from this study will not be used for any other purpose other than the ones stated in the protocol and assent form. Records relating to your participation in this study will remain confidential. Your name will not be used in any report resulting from this study. You will receive a signed copy of this assent form.

I therefore ask your permission to participate in this study.

If you agree to participate in this study, kindly fill in the declaration below.

I …………………………………………….. (Name of student), do hereby agree to participate in the research study. The purpose, methods and means by which the study will be conducted; and the risk which may be reasonably expected have been explained to me by ....…………………………………….. (Researcher's name).

I have been given the opportunity to ask questions concerning this study and any such questions have been answered to my full and complete satisfaction.

I understand that I may at any time during the course of this study revoke this assent and withdraw from the study without prejudice.

Student'ssignature ………………….…   date…………………………….

Study number …………………………

6.5. Appendix V - Student's Assent Form: Kiswahili Version

<u>Cheti cha idhini ya mwanafunzi</u>

Jina langu ni Daktari Peter K.Koech. Ninasomea shahada ya pili katika chuo kikuu cha Moi Kitivo cha Afya.

Niko na nia ya kufanya utafiti kwa ajili ya kukusanya takirimu kuhusu ugonjwa wa figo ambayo inajulikana kama glomerular disease, miongoni mwa wanafunzi kwenye shule za upili za umma katika manispaa ya Eldoret. Kichwa cha utafiti huu ni; **Prevalence of Glomerular Disease among Secondary School students in Eldoret, Kenya.**

Matarajio ya atafiti huu ni kuchunguza kama kuna dalili za mapema za ugonjwa huu, ambazo zaweza kuonekana kwenye mkojo au kiwango cha pressure ya damu yako. Utafiti huu utahusisha kujibu maswali kadhaa kuhusu ugonjwa wa figo, high blood pressure na kisukari. Tutapima mkojo na damu pia.

Hakuna madhara tunayotarajia kuwakumba watakaoshiriki kwenye utafiti huu. Mkojo utatumika kwa sababu iliyotajwa pekee, wala si kwa sababu zingine zozote.

Iwapo mkojo wako utapatikana kuwa na ishara ya itilafu kwenye figo au iwapo kipimo cha pressure ya damu yako hakitakuwa sawa, wewe na mzazi/mlezi wako mtashauriwa kwenda kwenye kituo cha matibabu cha MTRH kwa uchunguzi zaidi na matibabu yanayofaa.

Maswala yote yanayokuhusu yatawekwa siri na wala hautatambuliwa kwa jina au njia nyingine yeyote.

Ninakusihi kwamba uniruhusu uwe mmoja wa wale nitakao kusanya takirimu kwao.

Kama unakubali, tafadhali weka sahihi yako kwa nafasi iliyoko;

Jina………………………. Sahihi……………. Tarehe………………

6.6. Appendix VI – NACOSTI Research Authorization

NATIONAL COMMISSION FOR SCIENCE, TECHNOLOGY AND INNOVATION

Telephone: +254-20-2213471,
2241349, 310571, 2219420
Fax: +254-20-318245, 318249
Email: secretary@nacosti.go.ke
Website: www.nacosti.go.ke
When replying please quote

9th Floor, Utalii House
Uhuru Highway
P.O. Box 30623-00100
NAIROBI-KENYA

Ref: No.

Date:

19th December, 2013

NACOSTI/P/13/5171/442

Dr. Peter Kipruto Koech
Moi University
P.O.Box 3900-30100
ELDORET.

RE: RESEARCH AUTHORIZATION

Following your application for authority to carry out research on *"Prevalence of renal disease among secondary school students in Eldoret,"* I am pleased to inform you that you have been authorized to undertake research in **Uasin Gishu County** for a period ending **1st July, 2014.**

You are advised to report to **the County Commissioner and the County Director of Education, Uasin Gishu County** before embarking on the research project.

On completion of the research, you are expected to submit **two hard copies and one soft copy in pdf** of the research report/thesis to our office.

DR. M. K. RUGUTT, PhD, HSC.
DEPUTY COMMISSION SECRETARY
NATIONAL COMMISSION FOR SCIENCE, TECHNOLOGY & INNOVATION

Copy to:

The County Commissioner
The County Director of Education
Uasin Gishu County.

COUNTY COMMISSIONER
UASIN GISHU COUNTY

National Commission for Science, Technology and Innovation is ISO 2008: 9001 Certified

6.7. Appendix VII – Formal IREC Approval

INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471//2/3

MOI UNIVERSITY
SCHOOL OF MEDICINE
P.O. BOX 4606
ELDORET
Tel: 33471/2/3 Reference

Reference: IREC/2013/136
Approval Number: 0001051
Dr. Peter Koech,
Moi University,
School of Medicine
P.O.Box 4606-30100,,
ELDORET-KENYA.

14th April, 2015

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
14 APR 2015
APPROVED
P.O. Box 4606-30100 ELDORET

Dear Dr. Koech,

RE: APPROVAL OF AMENDMENT
The Institutional Research and Ethics Committee has reviewed the amendment made to your proposal titled:-

"Prevalence of Glomerular Disease among Secondary Students in Eldoret, Kenya".

We note that you are seeking to make an amendment as follows:-

1. To change the title as above from: *Prevalence of Renal Disease Among Secondary School Students In Eldoret*

The amendment has been approved on 14th April 2015 according to SOP's of IREC. You are therefore permitted to continue with your research.

You are required to submit progress(s) regularly as dictated by your proposal. Furthermore, you must notify the Committee of any proposal change(s) or amendment(s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. The Committee expects to receive a final report at the end of the study.

Sincerely,

DR. WILSON ARUASA
DEPUTY CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc: Director - MTRH   Dean - SPH   Dean - SOM
     Dean - SOM   Dean - SOD   Dean - SON

6.8. Appendix VIII - Blood pressure for boys by age and height percentile

Blood pressure levels for boys by age and height percentile

Age, year	BP, percentile	Systolic BP, mmHg Percentile of height							Diastolic BP, mmHg Percentile of height						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
1	50th	80	81	83	85	87	88	89	34	35	36	37	38	39	39
	90th	94	95	97	99	100	102	103	49	50	51	52	53	53	54
	95th	98	99	101	103	104	106	106	54	54	55	56	57	58	58
	99th	105	106	108	110	112	113	114	61	62	63	64	65	66	66
2	50th	84	85	87	88	90	92	92	39	40	41	42	43	44	44
	90th	97	99	100	102	104	105	106	54	55	56	57	58	58	59
	95th	101	102	104	106	108	109	110	59	59	60	61	62	63	63
	99th	109	110	111	113	115	117	117	66	67	68	69	70	71	71
3	50th	86	87	89	91	93	94	95	44	44	45	46	47	48	48
	90th	100	101	103	105	107	108	109	59	59	60	61	62	63	63
	95th	104	105	107	109	110	112	113	63	63	64	65	66	67	67
	99th	111	112	114	116	118	119	120	71	71	72	73	74	75	75
4	50th	88	89	91	93	95	96	97	47	48	49	50	51	51	52
	90th	102	103	105	107	109	110	111	62	63	64	65	66	66	67
	95th	106	107	109	111	112	114	115	66	67	68	69	70	71	71
	99th	113	114	116	118	120	121	122	74	75	76	77	78	78	79
5	50th	90	91	93	95	96	98	98	50	51	52	53	54	55	55
	90th	104	105	106	108	110	111	112	65	66	67	68	69	69	70
	95th	108	109	110	112	114	115	116	69	70	71	72	73	74	74
	99th	115	116	118	120	121	123	123	77	78	79	80	81	81	82
6	50th	91	92	94	96	98	99	100	53	53	54	55	56	57	57
	90th	105	106	108	110	111	113	113	68	68	69	70	71	72	72
	95th	109	110	112	114	115	117	117	72	72	73	74	75	76	76
	99th	116	117	119	121	123	124	125	80	80	81	82	83	84	84
7	50th	92	94	95	97	99	100	101	55	55	56	57	58	59	59
	90th	106	107	109	111	113	114	115	70	70	71	72	73	74	74
	95th	110	111	113	115	117	118	119	74	74	75	76	77	78	78
	99th	117	118	120	122	124	125	126	82	82	83	84	85	86	86
8	50th	94	95	97	99	100	102	102	56	57	58	59	60	60	61
	90th	107	109	110	112	114	115	116	71	72	72	73	74	75	76
	95th	111	112	114	116	118	119	120	75	76	77	78	79	79	80
	99th	119	120	122	123	125	127	127	83	84	85	86	87	87	88
9	50th	95	96	98	100	102	103	104	57	58	59	60	61	61	62
	90th	109	110	112	114	115	117	118	72	73	74	75	76	76	77
	95th	113	114	116	118	119	121	121	76	77	78	79	80	81	81
	99th	120	121	123	125	127	128	129	84	85	86	87	88	88	89
10	50th	97	98	100	102	103	105	106	58	59	60	61	61	62	63
	90th	111	112	114	115	117	119	119	73	73	74	75	76	77	78
	95th	115	116	117	119	121	122	123	77	78	79	80	81	81	82
	99th	122	123	125	127	128	130	130	85	86	86	88	88	89	90

Blood pressure levels for boys by age and height percentile, continued

Age, year	BP, percentile	Systolic BP, mmHg Percentile of height							Diastolic BP, mmHg Percentile of height						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
11	**50th**	**99**	**100**	**102**	**104**	**105**	**107**	**107**	**59**	**59**	**60**	**61**	**62**	**63**	**63**
	90th	**113**	**114**	**115**	**117**	**119**	**120**	**121**	**74**	**74**	**75**	**76**	**77**	**78**	**78**
	95th	**117**	**118**	**119**	**121**	**123**	**124**	**125**	**78**	**78**	**79**	**80**	**81**	**82**	**82**
	99th	**124**	**125**	**127**	**129**	**130**	**132**	**132**	**86**	**86**	**87**	**88**	**89**	**90**	**90**
12	50th	101	102	104	106	108	109	110	59	60	61	62	63	63	64
	90th	115	116	118	120	121	123	123	74	75	75	76	77	78	79
	95th	119	120	122	123	125	127	127	78	79	80	81	82	82	83
	99th	126	127	129	131	133	134	135	86	87	88	89	90	90	91
13	**50th**	**104**	**105**	**106**	**108**	**110**	**111**	**111**	**60**	**60**	**61**	**62**	**63**	**64**	**64**
	90th	**117**	**118**	**120**	**122**	**124**	**125**	**126**	**75**	**75**	**76**	**77**	**78**	**79**	**79**
	95th	**121**	**122**	**124**	**126**	**128**	**129**	**130**	**79**	**79**	**80**	**81**	**82**	**83**	**83**
	99th	**128**	**130**	**131**	**133**	**135**	**136**	**137**	**87**	**87**	**88**	**89**	**90**	**91**	**91**
14	50th	106	107	109	111	113	114	115	60	61	62	63	64	65	65
	90th	120	121	123	125	126	128	128	75	76	77	78	79	79	80
	95th	124	125	127	128	130	132	132	80	80	81	82	83	84	84
	99th	131	132	134	136	138	139	140	87	88	89	90	91	92	92
15	**50th**	**109**	**110**	**112**	**113**	**115**	**117**	**117**	**61**	**62**	**63**	**64**	**65**	**66**	**66**
	90th	**122**	**124**	**125**	**127**	**129**	**130**	**131**	**76**	**77**	**78**	**79**	**80**	**80**	**81**
	95th	**126**	**127**	**129**	**131**	**133**	**134**	**135**	**81**	**81**	**82**	**83**	**84**	**85**	**85**
	99th	**134**	**135**	**136**	**138**	**140**	**142**	**142**	**88**	**89**	**90**	**91**	**92**	**93**	**93**
16	50th	111	112	114	116	118	119	120	63	63	64	65	66	67	67
	90th	125	126	128	130	131	133	134	78	78	79	80	81	82	82
	95th	129	130	132	134	135	137	137	82	83	83	84	85	86	87
	99th	136	137	139	141	143	144	145	90	90	91	92	93	94	94
17	**50th**	**114**	**115**	**116**	**118**	**120**	**121**	**122**	**65**	**66**	**66**	**67**	**68**	**69**	**70**
	90th	**127**	**128**	**130**	**132**	**134**	**135**	**136**	**80**	**80**	**81**	**82**	**83**	**84**	**84**
	95th	**131**	**132**	**134**	**136**	**138**	**139**	**140**	**84**	**85**	**86**	**87**	**87**	**88**	**89**
	99th	**139**	**140**	**141**	**143**	**145**	**146**	**147**	**92**	**93**	**93**	**94**	**95**	**96**	**97**

BP: blood pressure.

The 90th percentile is 1.28 SD, 95th percentile is 1.645 SD, and the 99th percentile is 2.326 over the mean.

From the Fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. National Heart, Lung and Blood Institute. National Institutes of Health. May 2004.

6.9. Appendix IX - Blood pressure for girls by age and height percentiles

Blood pressure levels for girls by age and height percentile

| Age, year	BP, percentile	Systolic BP, mmHg Percentile of height							Diastolic BP, mmHg Percentile of height						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
1	**50th**	**83**	**84**	**85**	**86**	**88**	**89**	**90**	**38**	**39**	**39**	**40**	**41**	**41**	**42**
	90th	**97**	**97**	**98**	**100**	**101**	**102**	**103**	**52**	**53**	**53**	**54**	**55**	**55**	**56**
	95th	**100**	**101**	**102**	**104**	**105**	**106**	**107**	**56**	**57**	**57**	**58**	**59**	**59**	**60**
	99th	**108**	**108**	**109**	**111**	**112**	**113**	**114**	**64**	**64**	**65**	**65**	**66**	**67**	**67**
2	50th	85	85	87	88	89	91	91	43	44	44	45	46	46	47
	90th	98	99	100	101	103	104	105	57	58	58	59	60	61	61
	95th	102	103	104	105	107	108	109	61	62	62	63	64	65	65
	99th	109	110	111	112	114	115	116	69	69	70	70	71	72	72
3	**50th**	**86**	**87**	**88**	**89**	**91**	**92**	**93**	**47**	**48**	**48**	**49**	**50**	**50**	**51**
	90th	**100**	**100**	**102**	**103**	**104**	**106**	**106**	**61**	**62**	**62**	**63**	**64**	**64**	**65**
	95th	**104**	**104**	**105**	**107**	**108**	**109**	**110**	**65**	**66**	**66**	**67**	**68**	**68**	**69**
	99th	**111**	**111**	**113**	**114**	**115**	**116**	**117**	**73**	**73**	**74**	**74**	**75**	**76**	**76**
4	50th	88	88	90	91	92	94	94	50	50	51	52	52	53	54
	90th	101	102	103	104	106	107	108	64	64	65	66	67	67	68
	95th	105	106	107	108	110	111	112	68	68	69	70	71	71	72
	99th	112	113	114	115	117	118	119	76	76	76	77	78	79	79
5	**50th**	**89**	**90**	**91**	**93**	**94**	**95**	**96**	**52**	**53**	**53**	**54**	**55**	**55**	**56**
	90th	**103**	**103**	**105**	**106**	**107**	**109**	**109**	**66**	**67**	**67**	**68**	**69**	**69**	**70**
	95th	**107**	**107**	**108**	**110**	**111**	**112**	**113**	**70**	**71**	**71**	**72**	**73**	**73**	**74**
	99th	**114**	**114**	**116**	**117**	**118**	**120**	**120**	**78**	**78**	**79**	**79**	**80**	**81**	**81**
6	50th	91	92	93	94	96	97	98	54	54	55	56	56	57	58
	90th	104	105	106	108	109	110	111	68	68	69	70	70	71	72
	95th	108	109	110	111	113	114	115	72	72	73	74	74	75	76
	99th	115	116	117	119	120	121	122	80	80	80	81	82	83	83
7	**50th**	**93**	**93**	**95**	**96**	**97**	**99**	**99**	**55**	**56**	**56**	**57**	**58**	**58**	**59**
	90th	**106**	**107**	**108**	**109**	**111**	**112**	**113**	**69**	**70**	**70**	**71**	**72**	**72**	**73**
	95th	**110**	**111**	**112**	**113**	**115**	**116**	**116**	**73**	**74**	**74**	**75**	**76**	**76**	**77**
	99th	**117**	**118**	**119**	**120**	**122**	**123**	**124**	**81**	**81**	**82**	**82**	**83**	**84**	**84**
8	50th	95	95	96	98	99	100	101	57	57	57	58	59	60	60
	90th	108	109	110	111	113	114	114	71	71	71	72	73	74	74
	95th	112	112	114	115	116	118	118	75	75	75	76	77	78	78
	99th	119	120	121	122	123	125	125	82	82	83	83	84	85	86
9	**50th**	**96**	**97**	**98**	**100**	**101**	**102**	**103**	**58**	**58**	**58**	**59**	**60**	**61**	**61**
	90th	**110**	**110**	**112**	**113**	**114**	**116**	**116**	**72**	**72**	**72**	**73**	**74**	**75**	**75**
	95th	**114**	**114**	**115**	**117**	**118**	**119**	**120**	**76**	**76**	**76**	**77**	**78**	**79**	**79**
	99th	**121**	**121**	**123**	**124**	**125**	**127**	**127**	**83**	**83**	**84**	**84**	**85**	**86**	**87**
10	50th	98	99	100	102	103	104	105	59	59	59	60	61	62	62
	90th	112	112	114	115	116	118	118	73	73	73	74	75	76	76
	95th	116	116	117	119	120	121	122	77	77	77	78	79	80	80
	99th	123	123	125	126	127	129	129	84	84	85	86	86	87	88

Blood pressure levels for girls by age and height percentile, continued

Age, year	BP, percentile	Systolic BP, mmHg Percentile of height							Diastolic BP, mmHg Percentile of height						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
11	50th	100	101	102	103	105	106	107	60	60	60	61	62	63	63
	90th	114	114	116	117	118	119	120	74	74	74	75	76	77	77
	95th	118	118	119	121	122	123	124	78	78	78	79	80	81	81
	99th	125	125	126	128	129	130	131	85	85	86	87	87	88	89
12	50th	102	103	104	105	107	108	109	61	61	61	62	63	64	64
	90th	116	116	117	119	120	121	122	75	75	75	76	77	78	78
	95th	119	120	121	123	124	125	126	79	79	79	80	81	82	82
	99th	127	127	128	130	131	132	133	86	86	87	88	88	89	90
13	50th	104	105	106	107	109	110	110	62	62	62	63	64	65	65
	90th	117	118	119	121	122	123	124	76	76	76	77	78	79	79
	95th	121	122	123	124	126	127	128	80	80	80	81	82	83	83
	99th	128	129	130	132	133	134	135	87	87	88	89	89	90	91
14	50th	106	106	107	109	110	111	112	63	63	63	64	65	66	66
	90th	119	120	121	122	124	125	125	77	77	77	78	79	80	80
	95th	123	123	125	126	127	129	129	81	81	81	82	83	84	84
	99th	130	131	132	133	135	136	136	88	88	89	90	90	91	92
15	50th	107	108	109	110	111	113	113	64	64	64	65	66	67	67
	90th	120	121	122	123	125	126	127	78	78	78	79	80	81	81
	95th	124	125	126	127	129	130	131	82	82	82	83	84	85	85
	99th	131	132	133	134	136	137	138	89	89	90	91	91	92	93
16	50th	108	108	110	111	112	114	114	64	64	65	66	66	67	68
	90th	121	122	123	124	126	127	128	78	78	79	80	81	81	82
	95th	125	126	127	128	130	131	132	82	82	83	84	85	85	86
	99th	132	133	134	135	137	138	139	90	90	90	91	92	93	93
17	50th	108	109	110	111	113	114	115	64	65	65	66	67	67	68
	90th	122	122	123	125	126	127	128	78	79	79	80	81	81	82
	95th	125	126	127	129	130	131	132	82	83	83	84	85	85	86
	99th	133	133	134	136	137	138	139	90	90	91	91	92	93	93

From the Fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. National Heart, Lung and Blood Institute. National Institutes of Health. May 2004.

6.10. Appendix X - CDC Height Percentiles for Boys

CDC Growth Charts: United States
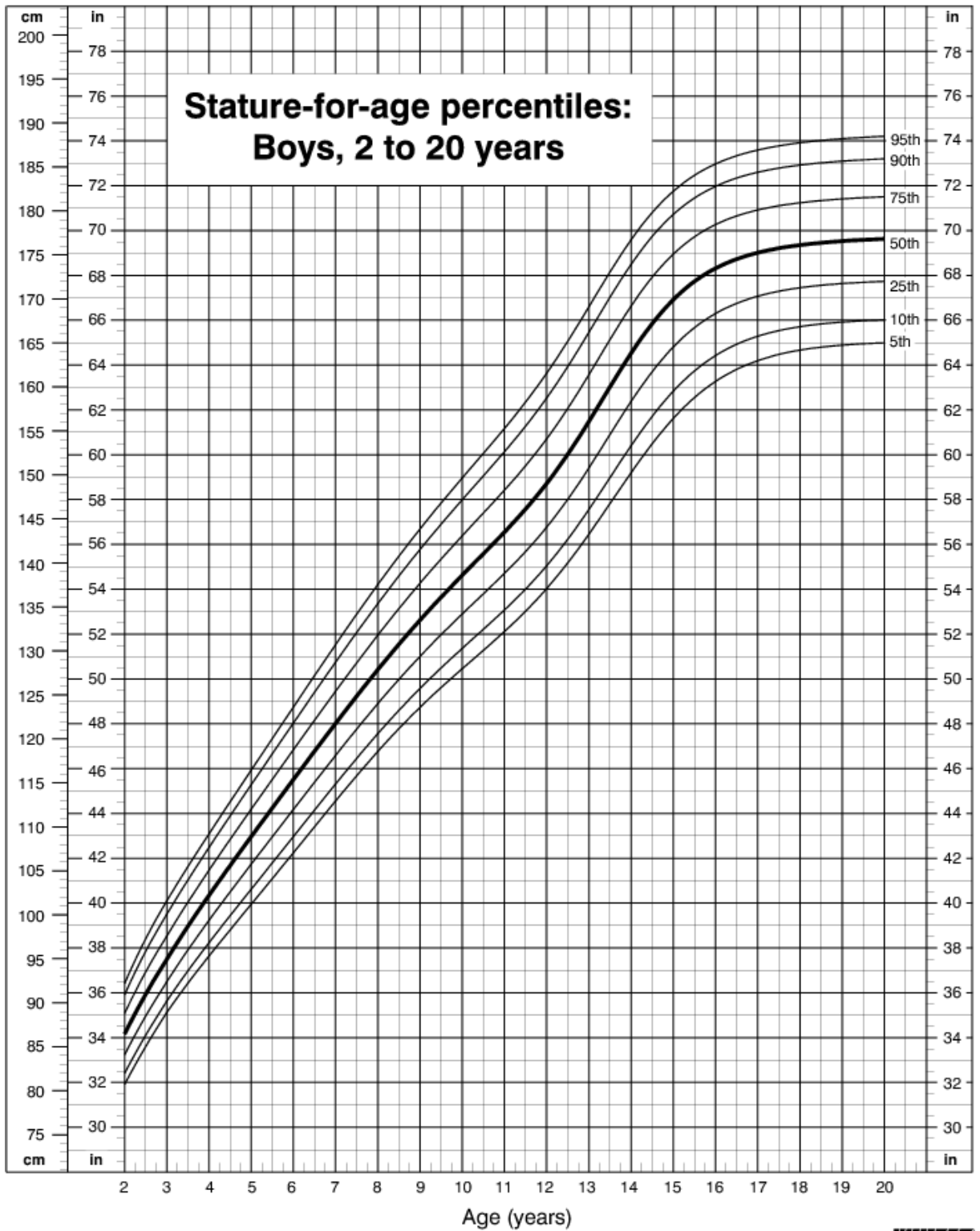
**Stature-for-age percentiles:
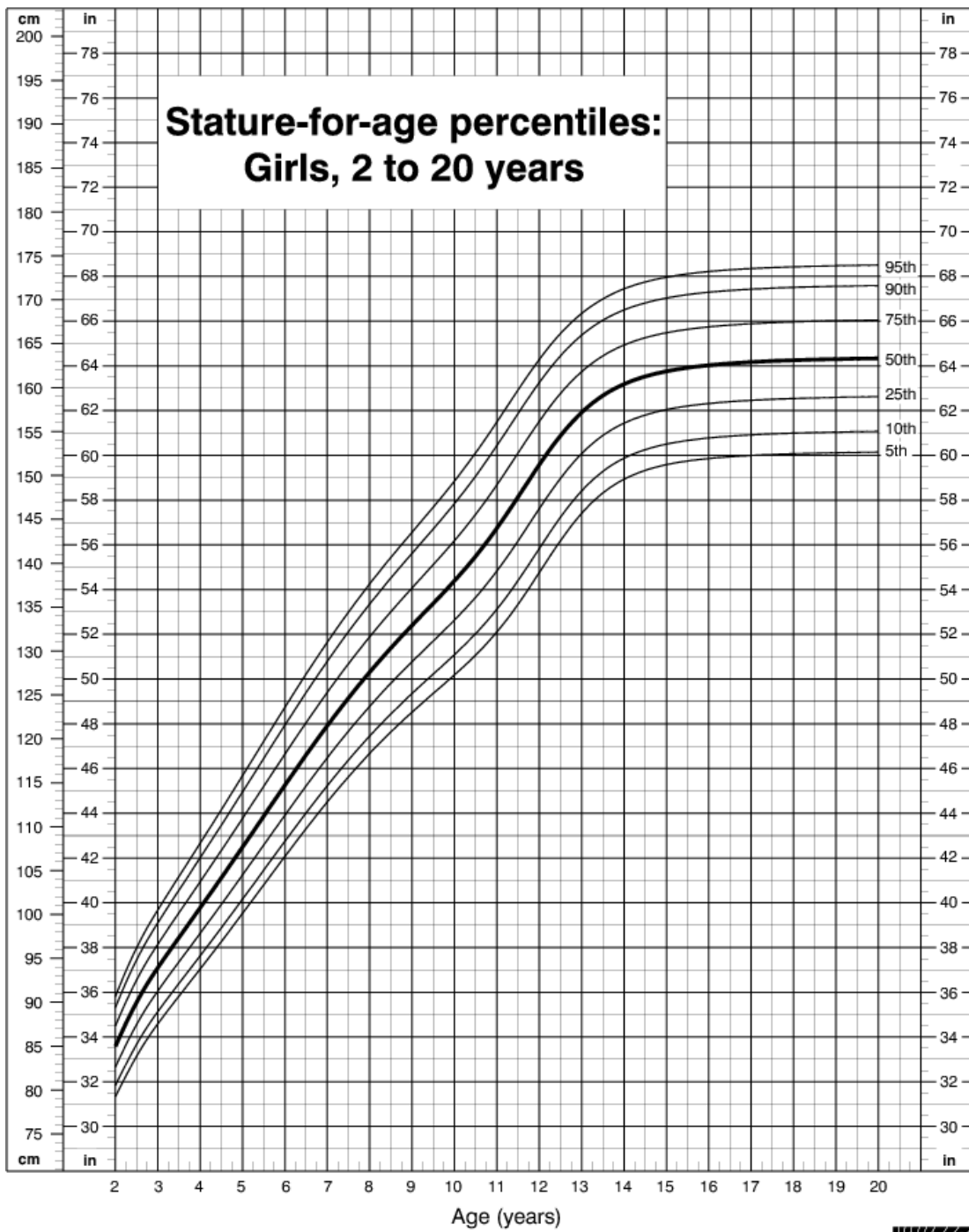Boys, 2 to 20 years**

Published May 30, 2000.
SOURCE: Developed by the National Center for Health Statistics in collaboration with
the National Center for Chronic Disease Prevention and Health Promotion (2000).

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6.11. Appendix XI - CDC Height Percentiles for Girls

CDC Growth Charts: United States

Stature-for-age percentiles:
Girls, 2 to 20 years

Published May 30, 2000.
SOURCE: Developed by the National Center for Health Statistics in collaboration with
the National Center for Chronic Disease Prevention and Health Promotion (2000).

6.12. Appendix XII - Procedure for Urinalysis

Dipstick urinalysis:

A Uristix® strip (siemensHealthcare Diagnostics, 1717 Deerfield Road,Deerfield, IL 60015-0778, USA) was briefly immersed in the urine specimen, covering all the reagent area.

The edge of the Uristix® strip was run against the rim of the container to remove excess urine. The strip was then held in a horizontal position.

The strip measures proteinuria based on protein error of pH indicators' principle. This principle states that at constant pH, development of any green colour is due to the presence of protein. The results range from yellow for negative test results to yellow green to green blue for positive test result. The test pad contains a pH dye indicator bromphenol blue. The presence of negatively charged albumin in urine increases the pH resulting in a positive test.

The colour change on strip was read visually and compared to that on the Uristix® colour chart. The results were recorded and strip discarded.

Microscope urinalysis:

Urine was centrifuged at 3000 rpm for 5 minutes and the supernatant then poured out. Using a micro-pipette, a drop of urine was put on a glass slide and a cover slip applied. This was then observed under a high power field of a light microscope.

The red blood cells per high power field were counted and their shape was noted as well.

6.13. Appendix XIII - Procedure for determining serum creatinine.

Blood in plain Vacutainer® bottles was taken to the laboratory within 24 hours at 2 to 25ºC.

The bottle was set on a centrifuge and spun at 3000 rpm for 3 minutes to separate the serum from the blood cells. The supernatant (serum) was carefully suctioned using a micropipette and transferred to a sample cup.

The sample cups were then systematically set on a rack that goes onto a Cobas Integra® 400 plus analyzer. This is an auto analyzer that uses the Jaffe reaction to quantify creatinine; creatinine reacts with picric acid in the presence of alkaline pH to produce a yellow red complex that has a maximum absorbance at 512nm. The rate of dye formation is proportional to the level of creatinine in the sample. The analyzer reads out this absorbance and based on its software it calculates the serum creatinine. It prints out results on paper.

The results were reported in µmol/L alongside reference serum creatinine levels.

6.14. Appendix XIV - Procedure for drawing blood

The procedure was explained to the participant and verbal consent sought.Universal precautions were observed.A tourniquet was applied 5 cm proximal to the selected venipuncture site. Participant was asked to make a fist without pumping the hand. The site was cleaned with methylated spirit starting from the centre and working outwards then allowed to dry.

The patient's arm was grasped firmly using the thumb to keep the skin taut and anchor the vein. A sterile needle mounted on the sterile syringe was inserted gently into the lumen of the vein at an angle of 15- 30º, and approximately 2 mls of blood drawn. It was then emptied into a plain blood specimen bottle.

After adequate blood was drawn the tourniquet was released and an alcohol impregnated swab applied at the site under pressure for a minute. The site was then assessed for continued bleeding, and dressed with a dry gauze and tape.

6.15. Appendix XV - Cockroft - Gault formula.

The Cockcroft-Gault equation allows the creatinine clearance to be estimated from the serum creatinine in a patient with a stable serum creatinine:

$$CCr \ (mL/min) \ = \ \frac{(140 - Age) \ x \ lean \ body \ weight \ [kg] \ x \ 0.85 (if \ female)}{Cr \ [mg/dL] \ x \ 72}$$

This formula takes into account the increase in creatinine production with increasing weight, and the decline in creatinine production with age. For women, the formula requires multiplication by 0.85 to account for smaller muscle mass compared to men. The equation is not adjusted for body surface area and race.

6.16. Kidney Disease Outcome Quality Initiative (KDOQI) Staging of Chronic Kidney Disease

Stage	Definition	eGFR
I	Normal or increased GFR	>90 mL/min/1.73m^2
II	Mild reduction in GFR	60 - 89 mL/min/1.73m^2
III	Moderate reduction in GFR	30 - 59 mL/min/1.73m^2
IV	Severe reduction in GFR	15 -29 mL/min/1.73m^2
V	Kidney failure	< 15 mL/min/1.73m^2

Loss of proteins in urine is regarded as an independent marker for worsening of renal function and cardiovascular disease. As a result, British guidelines append the letter "P" to the stage of chronic kidney disease if there is significant protein loss.