SONOGRAPHIC AND LABORATORY FINDINGS IN HYPERTENSIVE PATIENTS SUSPECTED TO HAVE RENAL ARTERY STENOSIS AT MOI TEACHING AND REFFERAL HOSPITAL, ELDORET, KENYA.

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Thesis submitted to School of Medicine, Moi University in partial fulfillment for the award of a Master of Medicine in Diagnostic Radiology and Imaging

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DECLARATION

I declare that this thesis is my original work written in partial fulfillment for the award of a degree in Master of Medicine in Diagnostic Radiology and Imaging. It has not been submitted to any other university or organization.

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This thesis has been submitted with our approval as the university supervisors.

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LIST OFABBREVIATIONS

ACE –Inhibitor	Angiotensin Converting Enzyme Inhibitor.
ARB	Angiotensin Receptor Blocker
BMI	Body mass index
EDV	End diastolic velocity
FMD	Fibromuscular Dysplasia
IREC	Institutional Research and Ethics Committee
MTRH	Moi Teaching and Referral Hospital
MUSOM	Moi University School of Medicine
PSV	Peak Systolic Velocity
RAR	Renal-to- aortic ratio
RAS	Renal Artery Stenosis
RI	Resistive Index
RRI	Renal resistive index
WHO	World Health Organization

OPERATIONAL DEFINITION OF TERMS

Hypertension

Based on the Eighth Joint National Committee (JNC 8) guidelines, any blood pressure measurement of ≥140/90 mmHg was considered high.

Known hypertensive patient

A known hypertensive patient was someone who reported history of hypertension, which was also confirmed from the patient's file.

Malignant hypertension

Blood pressure >180/120 that develops rapidly and causes some type of organ damage.

Accelerated hypertension

Recent significant increase over baseline blood pressure that is associated with target organ damage.

Resistant hypertension

Blood pressure that remains above goal despite concurrent use of three antihypertensive agents of different classes.

Lipid profile

The following figures were considered deranged, as per the current lipids management guidelines: Low Density Lipoprotein (LDL) >2.6mmol/l; Triglycerides >1.7mmol/l; Total Cholesterol >5.17mmol/l and HDL <1.29mmol/l for female and <1.03mmol/l for male patients

Renal function Test

The following figures were considered deranged

Urea > 8.3mmol/l

Creatinine > 80mmol/l

Potassium > 5.1mmol/l

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ABSTRACT

Background: Renal artery stenosis is the leading cause of secondary hypertension. Global prevalence of hypertension is 22% and across the WHO regions it is highest in Africa (30%). Up to 5% (3.5 to 4 million) of all occurrences of hypertension in the United States are caused by renal artery stenosis. The prevalence varies according to the population examined. This prevalence in our region is unknown and the diagnosis is probably missed in many patients. Timely diagnosis is important since renal artery stenosis is a correctable cause of hypertension.

Objectives: To describe sonographic findings and determine the prevalence of renal artery stenosis and its association with age, gender, renal functions, lipid profile and Body Mass Index in adult hypertensive patients suspected to have renal artery stenosis at Moi Teaching and Referral Hospital.

Methods: This was a cross sectional study done at the ultrasound room in the Department of Radiology and Imaging, Moi Teaching and Referral Hospital, Eldoret between October 2015 and October 2016. Consecutive sampling technique was used on consenting adult hypertensive patients with clinical features suggestive of renal artery stenosis as per the American Heart association Guidelines of 2005 who underwent renal Duplex Doppler ultrasonography. A 3.5- 7 MHz curvilinear phase array transducer of a Philips HD11 XE machine model 2006 was used. All the images were reviewed by two consultant radiologists. Descriptive statistics were summarized for patient socio-demographics. Frequency tables were generated for categorical variables. Inferential statistics were done using Chi-square and Fishers exact tests. Results were presented using tables and charts.

Results: The study included 169 participants with a median age of 46 (IQR 30). One hundred and five (62.1%) of them were females. In the findings; Sonographic prevalence of renal artery stenosis was 33.7%. Areas of aliasing was present in 62.5% of those with renal artery stenosis, post stenotic turbulence in 75.4% and thickening and calcification of arterial wall in 3.6%. Tardus- Parvus waveform pattern was seen in 66.1% (on the right) and 64.9% (on the left) in patients with renal artery stenosis. Echogenic kidneys were seen in 25 (43.9%) and loss of corticomedullary differentiation in 15 (26.3%) of the patients with renal artery stenosis. More females (63.2%) had renal artery stenosis than males, and majority, (43.8%) of those with renal artery stenosis were above 55 years. There was a significant association ($p < 0.05$) between elevated creatinine (above 80mmol/l) elevated urea (above 8.3mmol/l), elevated potassium(above 5.1mmol/l)and presence of renal artery stenosis.

Conclusion The sonographic prevalence of renal artery stenosis in adult hypertensive patients with specific clinical clues at MTRH was 33.7%. Parvus- Tardus was the commonest waveform pattern seen and there was an association between presence of renal artery stenosis and elevated levels of urea, creatinine, potassium,total cholesterol and triglyceride levels.

Recommendation: We need to have a high index of suspicion for renal artery stenosis whenever parvus- tardus waveform pattern is encountered during renal Duplex Doppler ultrasonography.

CHAPTER ONE

INTRODUCTION

1.1 Background of the Study

Renal artery stenosis (RAS) refers to the narrowing of the main or branch of renal artery. It is so far the commonest cause of secondary hypertension and may result in renal ischemia with resultant renal failure (Baxter et al, 1996) . Over the last decade, there has been increased awareness of renovascular disease as a potentially correctable cause of hypertension and renal insufficiency (Olin, 2004).

Globally the prevalence of hypertension in adults was 22% in 2014 and across the WHO regions the prevalence is highest in Africa, where it ranges from 25% - 35% in adults aged 25- 64 years (WHO, 2013). In Kenya the prevalence of hypertension is 21% (Joshi et al, 2014).

More than 72 million Americans have hypertension and majority have essential hypertension. However a significant subset has a secondary cause. The most common cause of secondary hypertension is renal vascular hypertension of which renal artery stenosis is the leading etiology. Up to 5% of all occurrences of hypertension are caused by RAS, equating to as many as 3.5 to 4 million occurrences in the United States (Hartman and Kawashima, 2009). In Africa and Kenya this prevalence is unknown.

Renal artery stenosis is the most common surgically or interventionally curable cause of hypertension. Screening and diagnostic tests are still needed to establish its presence (Karasch and Rubin, 1998).

Timely diagnosis is important because this condition carries a worse prognosis than essential hypertension and seems to be less amenable to drug treatment (Derkx and Schalekamp, 1994).

Because of the possibility of cure, screening measures for renal artery stenosis are warranted in hypertensive patients with clinical features suggestive of renovascular disease. Diagnosing these patients is therefore important, since interventional treatment may eliminate or reduce the need for antihypertensive therapy and also preserve renal function (Hirsch et al, 2006).

Duplex Doppler ultrasound is a non-invasive method which is an important part of the diagnostic algorithm in patients with diseases characterized by vascular involvement such as hypertension (Lubomirova et al, 2006).It has been extensively used in detecting renovascular diseases, showing to be a non-invasive, safe, low cost and repeatable tool (Spatola and Andrulli, 2016).

Renal duplex Doppler ultrasonography is used in many centers as the first line imaging modality for renovascular diseases. It has been shown to have comparable outcome with angiography which is the gold- standard (Abuagla and Pei, 2014), (Appel et al, 1995) , (Olin et al, 1995) and (Strandness, 1994).

Studies done in the United States of America show that Duplex Doppler scanning of renal artery stenosis show agreement with angiography and it is considered a valid, non-invasive screening or diagnostic test for renovascular hypertension (Simoni et al, 1991). Modern ultrasound machines are now able to outline with great detail both main renal

vessels and intraparenchymal vasculature of the kidney using colour and power Doppler techniques.

Despite the availability of Renal Duplex Doppler Ultrasound, Evaluation of hypertensive patients in our setting is mostly by history taking and clinical examination and radiological investigations are hardly ordered by the clinicians unless co morbid conditions exist for example renal failure. Unpublished data from our Ultrasound register (2015) revealed that few renal Duplex Doppler studies are done in our department every month, with mostly Gray- scale ultrasound of the kidneys being requested for hypertensive patients.

There are no local published studies done on renal Duplex Doppler in hypertensive patients. This study aims to describe the sonographic findings and determine the prevalence of renal artery stenosis and associated laboratory findings in hypertensive patients attending the Medical and Renal outpatient clinics and in the medical wards at MTRH. It is anticipated that the findings will encourage clinicians to send all patients with clinical features suggestive of renal artery stenosis for a Renal Duplex Doppler Ultrasound and this will have a positive impact in the management of secondary hypertension since RAS is a modifiable factor.

1.2 Problem Statement

Hypertension and its complications is one of the leading causes of morbidity and mortality in adults. It contributes to the burden of heart disease, stroke, kidney disease and premature mortality.

Renovascular hypertension is the commonest secondary cause of hypertension and may lead to the development of renovascular disease and significant associated morbidity in terms of hypertension and nephropathy (Jennings et al, 2014). Up to 5% (3.5- 4 Million) of all occurrences of hypertension in the United States are caused by Renal artery stenosis (Hartman and Kawashima, 2009).

The exact prevalence of renal artery stenosis is not known and the diagnosis is probably missed in many patients (Ram, 1997). An autopsy study by Kuroda *et al* (2000) found prevalence of renal artery stenosis to be 14.7% in hypertensive patients and these cases were not picked when the patients were alive.

Renovascular disease is an important cause of chronic renal failure, accounting for renal failure in 14% of patients over the age of 50 accepted for renal replacement therapy and more importantly, one of the few causes that is treatable (Adam and Dixon, 2008).

The prevalence of RAS is on the rise, owing to an increasing prevalence of diabetes and atherosclerotic disease among the aging population. This rise in RAS prevalence poses major challenges for clinicians making diagnostic and treatment decisions (Karasch and Rubin, 1998).

Renal artery stenosis continues to be a problem for clinicians, and the diagnosis has remained a challenge to the nephrologists and the radiologists (Abuagla and Pei, 2014) with no clear consensus on how to investigate and assess the clinical significance of stenotic lesions and manage findings (Jennings et al, 2014). Pathophysiologic manifestations of RAS (hypertension, renal dysfunction and left ventricular failure) are nonspecific and often attributed to other processes hence making the clinical identification of patients with renovascular hypertension imprecise and complex that the very diagnostic quest for this condition has been questioned (Ram, 1997).

Although the anatomical lesions in atherosclerotic renal artery stenosis are relatively easy to depict, there is need to identify diagnostic methods to establish the functional significance of the stenosis (Karasch and Rubin, 1998).Furthermore, atherosclerotic renal artery stenosis is a common and progressive disease and it is likely that many cases are never detected (Safian and Textor, 2001).

1.3 Justification of the Study

The prevalence of renal artery stenosis varies with the population examined. The prevalence in our region is unknown and the diagnosis probably missed in many patients.

Literature search reveals few studies done on this subject in Sub-Saharan Africa and In Kenya. There is no similar published study done in our hospital and the entire Western region. Results of studies in other regions of the world may not be applicable to us because of ethnic and geographical variations.

Data on renal Duplex Doppler ultrasound findings and prevalence of RAS in our population is needed to create awareness among health care providers and the general population on the critical role of sonography in the diagnosis and management of the hypertensive patient.According to WHO, basic diagnostics is one of the 6 important components of any country's initiative to address hypertension (WHO, 2015).

1.4 Research Question

What are the sonographic findings in adult hypertensive patients suspected to have renal artery stenosis at Moi Teaching and Referral Hospital and what is the association with laboratory findings?

1.5 Objectives

1.5.1 Broad Objective

To determine the sonographic findings and prevalence of renal artery stenosis and its association with age, gender, renal functions, lipid profile and Body Mass Index (BMI) in adult hypertensive patients suspected to have renal artery stenosis in MTRH.

1.5.2 Specific Objectives

1. To determine the sonographic prevalence of renal artery stenosis in adult hypertensive patients with clinical features of renal artery stenosis in MTRH.

2. To describe the Duplex Doppler Ultrasound findings in adult hypertensive patients with clinical features of renal artery stenosis in MTRH.

3. To describe the association between presence of renal artery stenosis and age, gender, renal functions, lipid profile and body mass index and sonographic findings.

CHAPTER TWO

LITERATURE REVIEW

2.0 Introduction

Renal artery stenosis (RAS) refers to narrowing of an artery to the kidneys. The most common cause is atherosclerosis (a buildup of plaque, which is a deposit of fatty substances, cholesterol, cellular waste products, calcium and fibrin in the inner lining of an artery) and fibromuscular dysplasia.

Renovascular disease is a general term used to describe lesions of the renal artery, including stenoses and occlusions that can result in significant reduction in renal parenchymal perfusion (Norris et al, 1984).

2.1 Aetiology of renovascular disease.

Atherosclerosis accounts for 90% of the renovascular diseases while fibromuscular dysplasia (FMD) accounts for less than 10% (Safian and Textor, 2001). Less common causes are arteritis, thrombosis, arterial dissection and stenosis in a transplanted kidney (Derkx and Schalekamp, 1994).

Peng *et al,* (2015) retrospectively analysed the etiology of RAS in 2047 patients diagnosed with RAS at Fuwai Hospital, China between 1999-2014. They found the causes as atherosclerosis 81.5%, Takayasu's arteritis 12.7%, fibromuscular dysplasia 4.2%, and other causes 1.6% .

2.2 Location of Renovascular Pathology.

Primary diseases of the renal arteries often involve the large renal arteries, whereas secondary diseases are frequently characterized by small vessel and intrarenal vascular disease (Safian and Textor, 2001).

Atherosclerosis accounts for 90% of the cases of renal artery stenosis and usually involves the ostium and proximal third of the main renal artery and the perirenal aorta whereas fibromuscular dysplasia accounts for less than 10%. 90 % of cases of fibromuscular dysplasia involve the media. It tends to affect girls and women between 15-50 years of age and frequently involves the distal two thirds of the renal artery and its branches (Safian and Textor, 2001).

2.3 Clinical Features Suggestive of Renovascular Disease.

Atherosclerotic RAS may present with one or more of the following; hypertension, renal failure (Ischemic nephropathy), refractory angina, recurrent episodes of congestive heart failure and flash pulmonary edema. Fibromuscular dysplasia commonly presents with hypertension, which can be frequently cured or significantly improved with percutaneous balloon dilation (Olin, 2004).

Guidelines regarding who to investigate for RAS were published by the American College of Cardiology /American Heart Association in 2005 (Hirsch et al,2006).

They recommend screening anyone with the following;

- Onset of hypertension before age of 30 years or severe hypertension after age 55years.
- Accelerated, resistant or malignant hypertension.
- Development of new azotemia or worsening renal function after administration of an ACE Inhibitor or ARB.
- Unexplained atrophic kidneys or size discrepancy > 1.5cm between kidneys.
- Sudden, unexplained pulmonary edema.
- Unexplained renal dysfunction, including patients starting renal replacement therapy.
- Multivessel coronary artery disease or peripheral arterial disease.
- Unexplained congestive heart failure or refractory angina.

2.4 Imaging Modality

Duplex Doppler ultrasound of the renal arteries has replaced other modalities as the screening test of choice in many centers (Olin, 2004) and it is the diagnostic procedure of choice for screening outpatients for RAS (White and Olin, 2009).

It combines traditional ultrasound imaging with a Doppler technique to measure blood flow velocities in the renal arteries.

Renal Doppler sonography correctly identifies the presence of renovascular disease with an overall accuracy of approximately 95% (Appel et al, 1995) and is widely accepted as the first line diagnostic imaging test because of its availability and cost (Lao et al, 2011).

It is an ideal test as it is non-invasive and can predict the presence of RAS with a high degree of accuracy (Olin et al, 1995) and does not require use of contrast media which may be nephrotoxic.

Renal Doppler ultrasound has also been found to be accurate in the diagnosis of significant RAS by Abuagala and Pei (2014) who compared the sensitivity, specificity, accuracy and predictive values of Doppler ultrasonography using contrast- enhanced magnetic resonance imaging as the gold standard for diagnosing RAS. 57 consecutive patients with clinical findings suggestive of RAS were referred to University Kebangsaan Medical Centre, Kuala Lumpur to be screened for RAS using Doppler ultrasonography and Contrast Enhanced Magnetic Resonance Imaging (CEMRA) as gold standard. They found all the measured Doppler ultrasonography parameters were positive for the detection of RAS with an accuracy of 98.3% (Abuagla and Pei, 2014).

Strandness *et al* (1994) compared results of renal Duplex Doppler scanning with arteriograms in a study done to determine the accuracy of ultrasonic Duplex Doppler scanning in detecting and classifying RAS in Washington. Duplex Doppler scanning identified the location of the renal artery stenosis with an accuracy of 95%. The study concluded that Duplex Doppler scanning is an accurate method of detecting RAS and provides a suitable method of estimating the degree of narrowing.

Olin *et al* (1995) established that Duplex Doppler ultrasound of renal arteries can predict presence of RAS with a high degree of accuracy using a prospective blinded study in a large unnamed referral Centre.

The overall sensitivity of Duplex ultrasound compared with arteriography was 0.98, the specificity was 0.98, positive predictive value was 0.99 and negative predictive value was 0.97.

2.5 Screening for Renovascular Disease

The kidneys are usually supplied by a single main renal artery that arises from the aorta just inferior to the origin of the superior mesenteric artery. The main renal arteries travel posterior to the corresponding vein and the right renal artery passes posterior to the inferior vena cava. Accessory renal arteries occur in approximately 20% of the kidneys. The renal arteries branch into multiple segmental arteries that travel from the renal hilum into the renal sinus. The segmental arteries branch into the interlobar arteries and arcuate arteries (Kurtz and Hertzberg, 2004).

The normal intrarenal arteries are rarely visible on gray-scale sonography but are visible with colour Doppler analysis.

The highest frequency probe that gives measurable waveforms should be used, supplemented by color or power Doppler to help vessel localization.

Several parameters of the Doppler wave can be measured in the signal obtained from the main renal artery and interlobar arteries. Peak systolic velocity (PSV), End diastolic velocity (EDV), peripheral resistance index(RI), acceleration time, acceleration index and renal /aortic ratio (RAR) (Miralles et al, 1996).

Doppler tracings should be obtained from within the renal arteries and also from within the kidney (Rumack et al , 2005).

The Doppler spectrum of the normal renal artery shows continuous forward flow into the kidney with relatively high velocities maintained throughout diastole indicating low intrarenal vascular resistance (low resistance pattern) as illustrated in the image below.

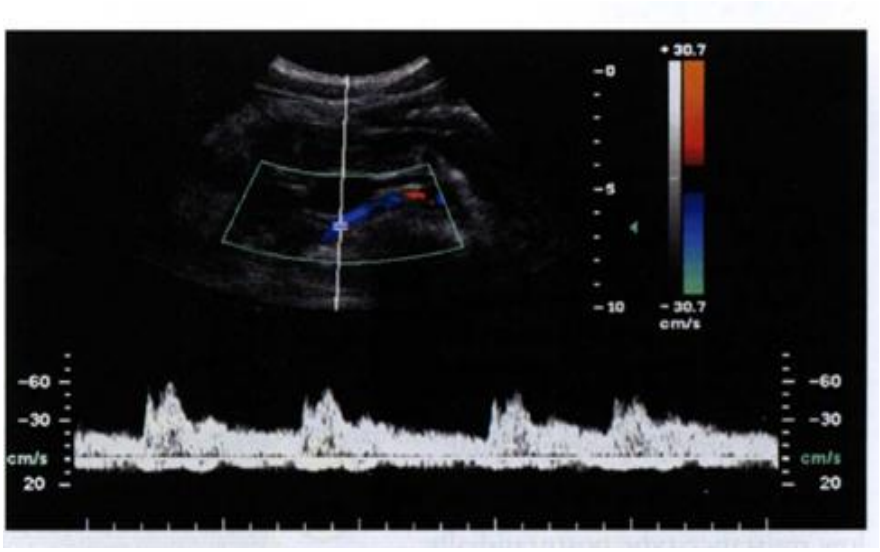


Figure 1. The above image shows the Doppler tracing from a right renal artery demonstrating the usual early systolic spike that is seen in normal patients.

2.6 Renal Artery Stenosis

Abnormalities seen on spectral Doppler include focal areas of aliasing and localized perivascular tissue vibration. Turbulent flow with spectral broadening and flow reversal is present downstream from the stenosis (Brant, 2001)

Pulsed Doppler analysis of abnormal areas identified on color Doppler imaging will reveal a PSV exceeding 200cm/sec and a peak renal artery velocity – to peak aortic velocity ratio (RAR) of greater than 3.5 (Kurtz and Hertzberg, 2004).

Accuracy is increased if the velocity in the renal artery is compared to that in the aorta (renal artery to aorta velocity ratio, RAR).

A proximal stenosis will also cause blunting of the waveform from distal arteries. This dampening of the distal arterial waveforms has been referred to as the parvus-tardus effect (slowed systolic upstroke and a delayed time to peak systole).

In less severe cases, the effect can be detected quantitatively by measuring the early systolic acceleration. Values more than 300cm/sec are considered abnormal (Kurtz and Hertzberg, 2004).

The image below demonstrates Doppler tracing about a stenotic region.

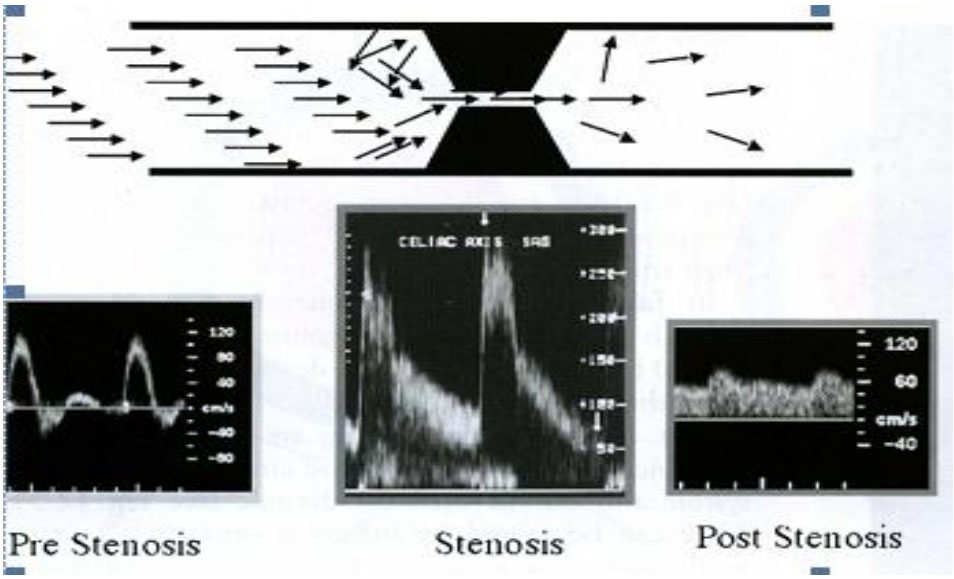


Figure 2. Doppler tracings about a stenotic region.

The image on the left shows tracing at the pre- stenotic region: forward flow of blood is impeded by the narrowing resulting in a high resistance or aortic type tracing.The middle image shows Doppler tracing at the stenotic region. The flow is typically of a high velocity and turbulent with disruption of the normal laminar flow pattern.

The image on the right shows the Doppler tracing post stenosis where there is typically relatively little blood relative to the size of the vessel , so flow has a “parvus- tardus” pattern.

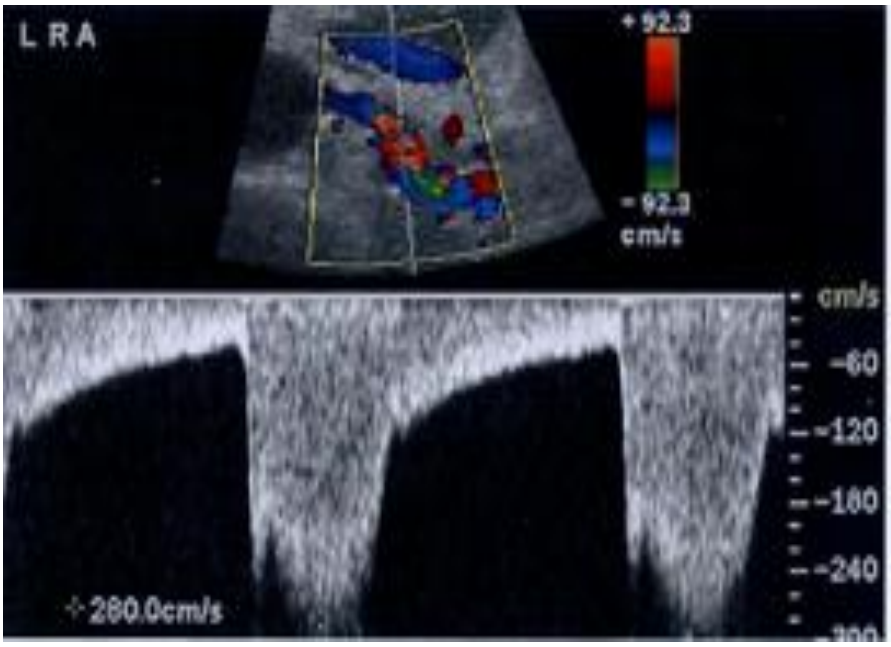


Figure 3. A pulsed Doppler waveform at a stenotic region showing elevated peak systolic velocity of 280cm/ sec.

The largest study to date was done by AbuRahma *et al,* (2012) in USA, to compare Renal Doppler ultrasound imaging vs. angiography and to assess various published Doppler criteria. 313 patients (606 renal arteries) were assessed with both Doppler imaging and angiography. RAS was classified as normal, <60%, >60-90% and occlusion. PSV of 285cm/s or RAR of 3.7 were found to be better than any combination of PSV, EDVs or RARs in detecting more than 60% stenosis (AbuRahma et al, 2012).

The resistive index (RI) measures the degree of intrarenal arterial impedance. It is calculated using the formula :([PSV- EDV] / PSV) and a mean of 3 measurements at each kidney is usually considered. As resistance to blood flow progressively increases from the hilar arteries towards the more peripheral parenchymal vessels, it is recommended that sampling for RRI should be done at the level of the arcuate or interlobar arteries, adjacent to medullary pyramids. Measurements should preferentially be repeated in different parts of both organs (superior, median and lower) when at least three reproducible waveforms have been obtained (Tublin et al, 2003).

Several studies have shown that a normal mean RI is approximately 0.60 (Keogan et al, 1996), (Kim et al, 1990). In general, most sonologists now consider 0.70 to be the upper threshold of the normal RI in adult, (Platt, et al 1991).

The image below demonstrates normal resistive index of 0.6.

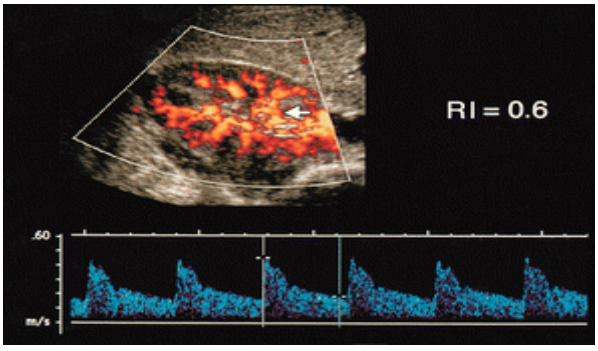


Figure 4:Normal resistive index in 25-year-old healthy woman.

Thickening and calcification of the wall of the renal artery indicate the presence of atherosclerotic plaque, but not necessarily significant stenosis (Helenon et al, 1995).

Fibromuscular dysplasia affects the mid and distal renal artery and is more difficult to visualize than atherosclerotic disease (Kurtz and Hertzberg, 2004). The beaded appearance

characteristic of FMD may be visualized on gray-scale ultrasound of the main renal artery (Helenon et al, 1995).

2.7 Renal Artery Occlusion

Occlusion of the renal artery occurs with embolus, thrombosis, trauma or surgical error. Occlusion of the main renal artery results in global infarction whereas occlusion of an accessory or branch of renal artery results in focal or segmental infarction. With acute infarction, appearance of the kidney remains normal on gray-scale ultrasound (Brant, 2001).

Color Doppler shows the occluded stump of the renal artery with no blood flow in 60% of cases. Intrarenal arteries may show no detectable Doppler signal in 80% of cases or a severe Tardus – parvus spectrum in 20 % of cases (Helenon et al, 1995).

2.8 Renal Sizes

Normal renal length (ultrasonic measurement) ranges between 10- 12 cm with a volume of 50 -200cm^3. This should be related to the patient's age and build, including height and weight (Emamian et al, 1993).

Musa,(2014) in Sudan studied renal changes in hypertensive patients in high altitude and found reduced kidney length and volume in patients with renal artery stenosis and hypertension compared to those with hypertension alone. On the right he found a mean kidney length of 8.8cm and mean volume of 57±8.11cm^3 and on the left a mean length of 9.0cm and renal volume of 55±9.2 cm^3 in patients with RAS. In those without RAS he

found a mean length of 9 ± 0.4 cm and volume of 85.8 ±17.3 cm^3 on the right and 9.5±6.2cm and a volume of 89.2±16.7 cm^3 on the left.

In South Western Nigeria Adedeji *et al,* (2010) evaluated renal volumes in hypertensive patients by ultrasound and found normal kidney volumes. The range of renal volume obtained was 51.6- 205 cm^3 with a mean of 114cm^3 for the left kidney and (47.37-177.5$cm^{3)}$ with a mean of 106.14cm^3 for the right kidney.

2.9 Prevalence of Renal Artery Stenosis

The prevalence of RAS depends upon the population examined (White and Olin, 2009). In the general hypertensive population, the prevalence of renovascular disease varies between 1% and 5% (Derkx and Schalekamp, 1994). In patients who exhibit specific clinical clues that indicate renovascular hypertension, the probability of having the disease increases to 20% to 40% (Hypertension, 1987).

In the United States of America, Benjamin *et al*, (2014) at Bayer Heart and Vascular Hospital found a prevalence of 24.2%, whereas Hansen *et al* (2005) In the cardiovascular health study, found the prevalence of renovascular disease to be 6.8%, demonstrated by renal Duplex Doppler sonography in the general hypertensive population. RAS was present in almost twice as many men as women (9.1% versus 5.5%). There was no difference in the prevalence of RAS in whites (6.9%) compared to African Americans (6.7%).

Derkx and Schalekamp (1994), found the prevalence of renovascular disease to be 1 % in the general population of hypertensives, 5 % in hospital- based populations and up to 40% in patients referred to hypertension clinics.

The prevalence tends to be higher in patients with peripheral vascular disease. Wachtell *et al*, (1996), found the prevalence of renal artery stenosis to be 34% in a subgroup of patients with hypertension and peripheral vascular disease in Glostrup University Hospital – Denmark.

In France, Helenon, *et al* (1995), studied 187 native kidneys in 96 patients to determine the colourDuplex Doppler ultrasound characteristics of renovascular disorders and found 40 cases of renal artery stenosis, renal artery thrombosis (3 cases), renal artery aneurysm (4 cases), renal vein thrombosis (3 cases), arteriovenous fistula (3 cases), peripheral infarction (1 case of bilateral infarct) and distal occlusive disease (3 cases).

In Mulago Hospital, Ameda, (2009), found a prevalence of 26.6% similarly for peripheral arterial diseases in general.

At Kenyatta National Hospital, prevalence of arterial disease was found to be 11.9%, (Maritim, 2007) whereas Nikita, (2016) found a prevalence of 36%..

2.10 Relationship between RAS and Age, Gender, Renal Functions, Lipid Profile and Body Mass Index.

Several laboratory and patient characteristics have been associated with atherosclerosis which subsequently predisposes to renal artery stenosis. They include advanced age, gender, deranged renal functions, elevated lipids (total cholesterol and Low density lipoproteins) and obesity.

Harding *et al*, (1992) studied the prevalence and associated risk factors for renal artery stenosis in patients undergoing routine cardiac catheterization at Duke University Medical

Centre. They found older age to be the most important predictor of significant renal artery stenosis. The mean age of patients with significant renal artery stenosis was 66 ± 10 years compared to 58 ± 11 years for patients without renal artery stenosis. They also found elevated creatinine levels not to be an important predictor for renal artery stenosis.

Hansen *et al*,(2002) estimated the population based prevalence of renovascular disease and defined its association with age, gender, race and other potential risk factors among participants in the Cardiovascular Health Study in Forsyth County, North Central US. They found increasing participant age (p= 0.028 OR, 1.34; 95%, CI, 1.03, 1.73), low HDL (high density lipoproteins) and increasing systolic blood pressure to be significantly and independently associated with presence of renal artery stenosis.

Buller *et al*, (2004) in Vancouver Hospital, Canada studied the profile of cardiac patients with renal artery stenosis and found severe renal artery stenosis was associated with age, female gender, reduced creatinine clearance, increased systolic blood pressure and peripheral or carotid artery disease.

Caps *et al*, (1998) at the University of Washington studied the risk of atrophy in kidneys with atherosclerotic renal artery stenosis in 122 subjects and found the severity of renal artery stenosis was associated with worsening renal functions.

Kuroda *et al*, (2000) studied the prevalence of atherosclerotic renal artery stenosis in 2,167 patients at the National Cardiovascular Centre Hospital in Osaka, Japan. They found renal insufficiency, hypertension, female gender and presence of carotid artery stenosis as independent predictors of renal artery stenosis. They found a mean creatinine level of 221µmol/l (elevated) in those with renal artery stenosis and 124µmol/l (normal) in those with normal renal arteries.

In a study by Harding *et al*, (1992) of RAS in patients undergoing routine cardiac catheterisation at Duke Medical Centre, they found majority (53%) of the patients with RAS had elevated cholesterol levels (mean of 11mmol/l).

In the cardiovascular health study in Forsyth County, North Central US 18.6% of the participants had hypercholesterolemia (Total cholesterol > 13mmol/l), 16.8% had elevated LDL (> 7.2mmol/l) and 16.4% had decreased HDL (<2.2mmol/l) and 29.4% of the participants were obese having 130 % of their ideal body weight (Hansen et al, 2002).

Postma *et al*, (2012) in Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands in a study to find out the prevalence of RAS among patients with diabetes found 33% of the patients were obese (mean BMI 31.4 ± 5.6).

CHAPTER THREE

METHODOLOGY

3.1 Study Site

The study was carried out in the ultrasound room of Radiology and Imaging Department in Moi Teaching and Referral Hospital. MTRH is the second National Referral hospital in Kenya. The hospital is located along Nandi Road, Eldoret Town in Uasin- Gishu County. With a bed capacity of 800, MTRH receives patients from Western Kenya, Eastern Uganda and even parts of Southern Sudan. MTRH was selected as the study site due to its diversity in patient population and patient diagnosis and availability of the necessary equipment.

3.2 Study Design

A cross-sectional hospital based study was done within a period of one year from October 2015 October 2016. Adult hypertensive patients with clinical features suggestive of renal artery stenosis who met the inclusion criteria and were referred for a Duplex Doppler ultrasound of the kidneys were assessed.

3.3 Study Population

Adult hypertensive patients with clinical features suggestive of renal artery stenosis who presented to hospital during the study period were eligible to participate in the study.

Patients with clinical features of renal artery stenosis were selected since in the general hypertensive population the prevalence varies between 1- 5% unlike in patients with suggestive clinical features where it varies from 20 – 40% hence without selection it would

require a very large sample size to calculate the prevalence which would have required a longer study period to achieve.

Before commencement of the study sensitization was done to the clinicians in the accident and emergency department, medical and renal outpatient clinics and the wards concerning the study and recruitment protocol and they were asked to refer the patients with clinical features of renal artery stenosis for sonography.

3.4 Eligibility Criteria

3.4.1 Inclusion Criteria

The following inclusion criteria was applied:

- Adult hypertensive patients with clinical features suggestive of renal artery stenosis as per the attached protocol.

3.4.2 Exclusion Criteria

- Patients who had undergone any surgical procedure to the renal arteries as this might have led to post surgical stricture.

3.5 Sampling

3.5.1 Sample Size Determination

Studies have shown that the prevalence of RAS among patients with clinical features suggestive of renovascular disease is 40% (Derkx and Schalekamp, 1994). Thus in order to be 95% sure that we get the prevalence of RAS within plus or minus 5% of the study population prevalence of 40% we need to estimate the sample size using the following formula (Cochran, 1965).

$$n = \left(\frac{Z_{1-\alpha/2}}{\delta}\right)^2 \times P(1-P)$$
$$= \left(\frac{1.96}{0.05}\right)^2 \times 0.4(1-0.4)$$
$$= 369$$

Where:

n_0 = estimated minimal sample size in infinite population

$Z_{1-\alpha/2}$ is the $\left(1-\alpha/2\right)\times 100\%$ quartile of the standard normal distribution with type I error of $\alpha = 5\%$.

P - is the prevalence of RAS among the patients with hypertension.

δ _ is the margin of error taken to be 5%.

The population of hypertensive patients with clinical features of RAS seen in MTRH in 2015 was 311. This figure excluded revisits. Correction for a finite population size of 311 was done as shown below and a sample size of 196 patients was arrived at.

$$n \geq \frac{n_0}{1+\frac{n_0}{N}} = \frac{369}{1+\frac{369}{311}} = 169$$

This is the minimum sample size required.

Where:

n – is the estimated minimal sample size for finite population

N- estimated population of hypertensive patients with clinical features of RAS seen in MTRH for 1 year

3.5.2 Sampling Procedure

Consecutive sampling was employed because of the limited study period.

3.6 Study Procedure

Adult hypertensive patients with clinical features suggestive of RAS who met the inclusion criteria were booked for a renal Duplex Doppler ultrasound examination in the Radiology and Imaging Department.

All the examinations were performed by the principal investigator and the images archived. A Phillips HD XE machine model 2006 with 3.5 - 5 MHz curvilinear phase array transducer was used. Every effort was made to use a Doppler angle of less than 60 degrees to provide consistency in Doppler velocity measurements.

Patients were examined after an overnight fast in the prone, anterior and lateral decubitus positions and portions of the main renal artery from the origin to the hilum were examined. Hilar examination was also performed by the flank approach with the patient in the right and left decubitus positions. This was particularly useful in patients with excessive bowel gas and obese patients.

The length, width, depth and cortical thickness of each kidney were recorded from the flank position using the B- mode imaging.

The renal volume was calculated using the formula L X W X AP X 0.523 (Hricak, 1983)and the volume that was considered normal was 50 -200$cm^{3.}$

Renal parenchymal Doppler signals were also acquired during this examination. Zero degree Doppler angle and a sample volume size of 2mm was used to record spectral

waveforms from the renal parenchyma of the upper and lower poles of each kidney. Patients were asked to hold their breath during the Doppler sampling.

The abdominal aorta was identified in the sagittal plane at the level of the origin of the superior mesenteric artery; probe rotated to 90 degrees and each renal artery origin was located using the left renal vein as a landmark. Doppler sampling and velocity waveforms were obtained from the origin, proximal, middle and distal renal arteries. Peak systolic velocities (PSVs) and end- diastolic velocities (EDV) along both renal arteries from the aortic origin to the renal hilum were also recorded. The RAR was calculated by dividing the highest PSV in the renal artery by the PSV in the aorta.

Resistive index was calculated using the formula ([PSV- EDV] / PSV) and a mean of 3 measurements at each kidney was considered. A value of 0.70 was considered as the upper threshold of normal RI, (Platt et al, 1991).

All duplex Doppler scans were interpreted by two qualified radiologists. RAS was diagnosed by combining both direct (proximal) and Indirect (distal) criteria. In the direct criteria a peak systolic velocity PSV exceeding 200cm/sec in any abnormal areas, and Renal artery to aortic velocity ratio (RAR) of greater than 3.5 were considered abnormal. In the indirect criteria the Doppler wave characteristics used were presence of any areas of aliasing, localized perivascular tissue vibration , post stenotic turbulence and Parvus-Tardus waveform pattern. Any one or more of the above features were diagnostic of RAS.

Atherosclerotic plaque was diagnosed based on presence of thickening (more than 6mm) and calcification of the wall of the renal artery. Renal artery occlusion was diagnosed when

there was no flow signal in the renal artery and a low amplitude velocity signal from the renal parenchyma.

3.7 Data Collection Procedures

Data was collected using a structured questionnaire.

3.8 Quality Control

All US scans were done at MTRH ultrasound room that had internal quality controls. The scans were done by the Principal Investigator conducting the study based on a standardized evaluation criteria. Images were then reviewed by two consultant radiologists oblivious of the study.

3.9 Data Management

Collected data was entered into an appropriate database. The data was de-identified and the databases encrypted to ensure confidentiality was maintained. Data was accessed by the principle investigator only. The data collection forms and questionnaires were kept in safe cabinets under lock with key kept by the investigator to ensure safety and confidentiality. The databases were also backed up to avoid loss of data.

3.10 Data Analysis

The categorical variables were summarized as frequencies and percentages. Test of associations between such variables were conducted using Pearson's Chi-square test and Fishers exact test. The normally distributed continuous variables were summarized as mean and standard deviation or as median and quartiles for the skewed variables. All the analysis was performed using R statistical package.

3.11 Ethical Considerations

This study posed no risk to the health or wellbeing of study participants. The study results will benefit the health system by providing evidence on the benefits of renal Doppler sonography in the diagnosis of renal artery stenosis. This evidence will inform policy that will consequently benefit patients.

Ethical clearance was sought from IREC before the commencement of data collection. A consent form explaining the rationale and benefits of the study to the public health system was used to seek informed consent from potential interviewees. Participation in the study was on a voluntary basis, the participants were at liberty to withdraw from the study at any stage without being penalized. There were no incentives for participating. The interviews were conducted in a confidential manner; participant names were not recorded. No study participant was identified by name in any report or publication derived from information collected for the study. Data collected was stored in lockable cabinets; databases created were password protected to avoid unauthorized access.

3.12 Dissemination of Information

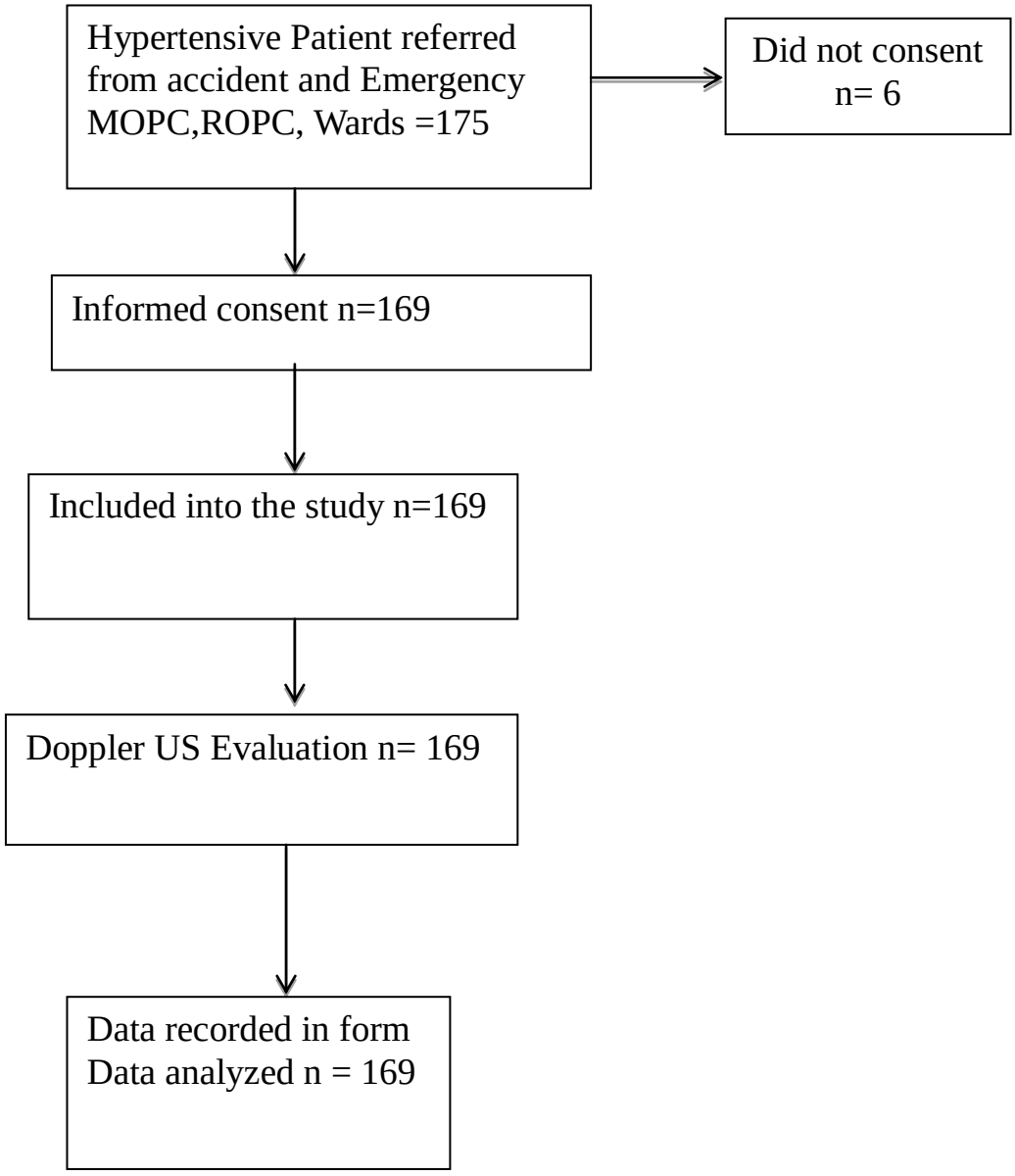
The information from the ultrasound examination and the laboratory was shared with the patient's primary physician in the form of a written report and images which were printed out and a copy filed in the patient's hospital file as well as verbally with the physician. The patients were also given a copy after explanation of the findings.

In cases where any pathology was identified in the Duplex Doppler examination, the patient was linked up with the appropriate caregiver- either a surgeon for correction or an Interventional Radiologist for further evaluation and planning of the necessary corrective measure.

3.13 Study Time Frame

The study was carried out within a period of two years, with data collection taking place over a period of one year.

3.14 Study Flow Chart



CHAPTER FOUR

RESULTS

4.1 Socio- Demographic Characteristics

A total of 169 hypertensive patients aged between 18-86 years and presenting with clinical features suggestive of renal artery stenosis participated in the study.

62.1% of the participants were females.

46% were self-employed, 42.9% unemployed and 11.1% were formally employed.

50.9% of the respondents were from Uasin Gishu county, 13.2%from Nandi , 10.2% from Bungoma ,4.8% from Kericho , 4.3% from Kakamega among others as shown in Table 1

Table 1: Demographic Characteristics

Variable	Categories	Frequency	Percentage (%)
Age (n=169)	<30 years	38	22.5
	30-55 years	56	33.1
	>55 years	75	44.4
Gender (n=169)	Female	105	62.1
	Male	64	37.9
Occupation (n=163)	Employed (teacher, casual, mining)	18	11.1
	Self Employed (business, farmer)	75	46.0
	Unemployed (student, housewife, retired)	70	42.9
Residence (n= 167)	UasinGishu	85	50.9
County	Nandi	22	13.17
	Bungoma	17	10.18
	Kericho	8	4.79
	ElgeyoMarakwet	6	3.59
	Kisii	6	3.59
	Kakamega	7	4.19
	Kisumu	5	2.99
	Trans-Nzoia	5	2.99
	Turkana	2	1.2
	Baringo	2	1.2
	Homabay	2	1.2

The age of respondents showed a multimodal distribution as shown in Figure 1 below. The median age of respondents was 46 years with an inter-quartile range (IQR) of 30 years.

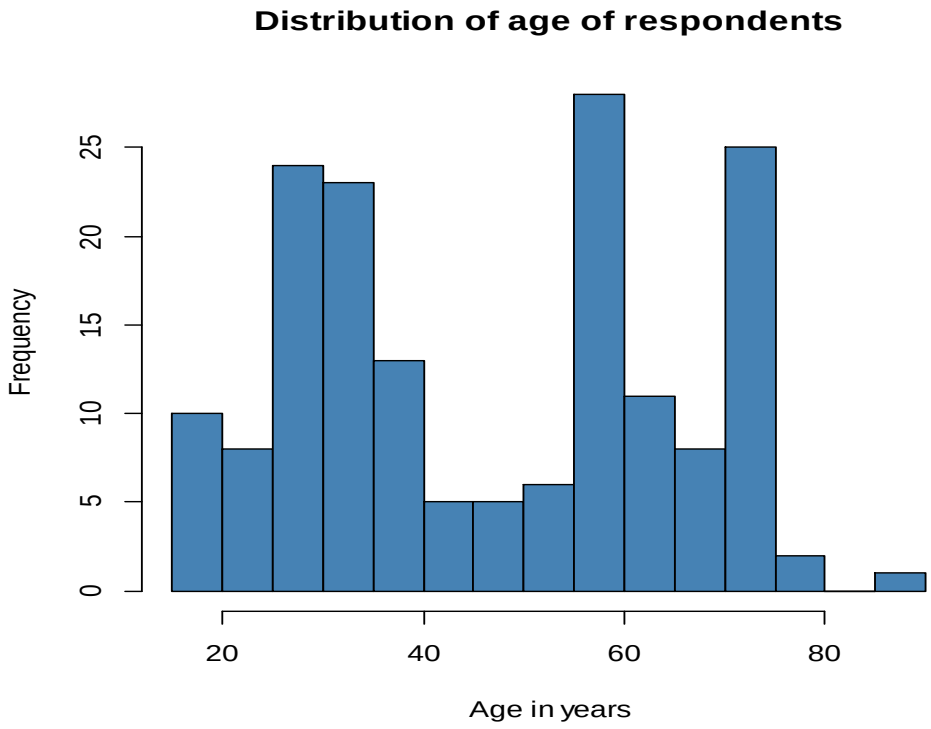


Figure 5: Histogram Showing The Distribution of Age of Respondents

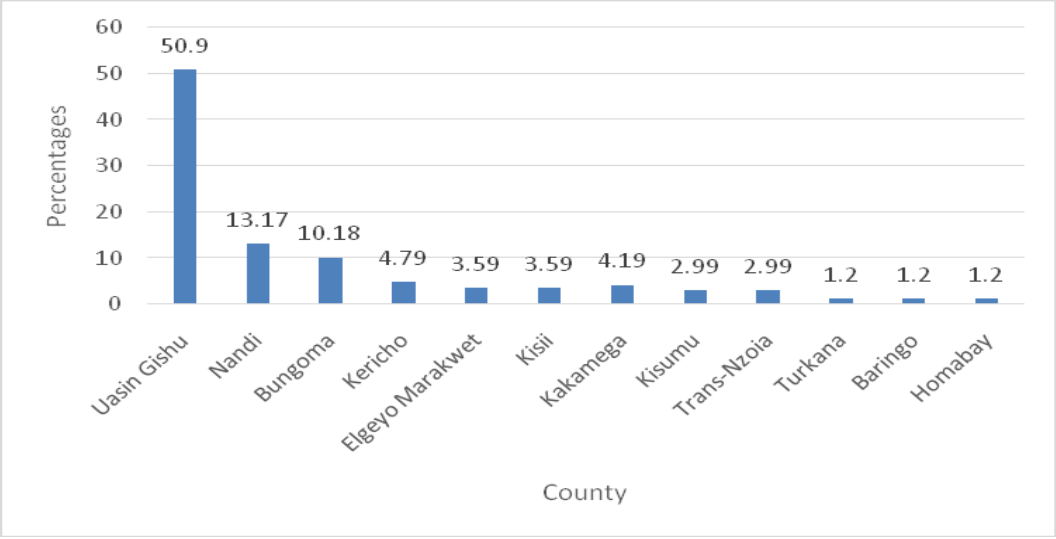


Figure 6: Distribution Of Respondents By County Of Residence

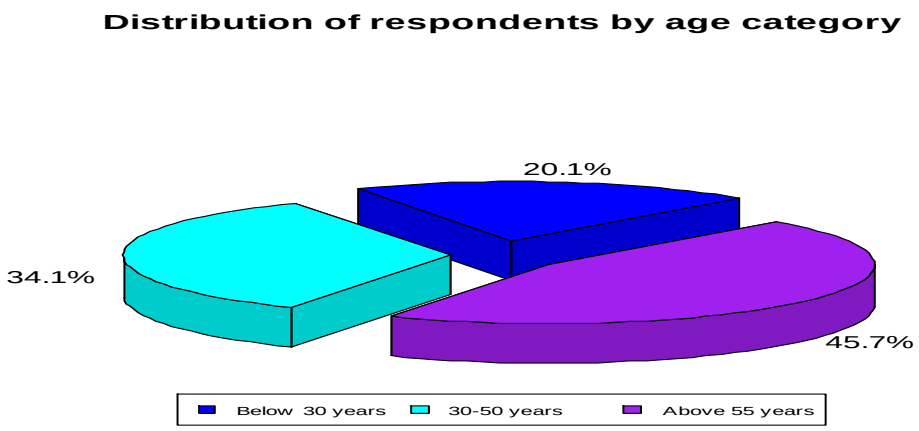


Figure 7: Distribution of Respondents By Age Category

4.2 Clinical Findings

Table 2: Summary of Clinical Findings

Variable	Categories	Frequency	Percentage (%)
BMI (n=157)	Underweight (<18.5)	4	2.5
	Normal (18.5-24.9)	21	13.4
	Overweight (25-29.9)	59	37.6
	Obese (≥30)	73	46.5
Blood Pressure	Pre-hypertension	16	9.7
(Hypertension)	Stage 1 hypertension	55	33.3
(n=165)	Stage 2 hypertension	94	57.0
Onset of Hypertension	<30 years	88	52.1
(n=169)	>55 years	81	47.9

As shown in table 2, a majority (86.6%) of the respondents had an abnormal weight for their height; 46.5% were obese, 37.6% overweight and 2.5% underweight. Respondents with normal weight constituted of 13.4% of the respondents.

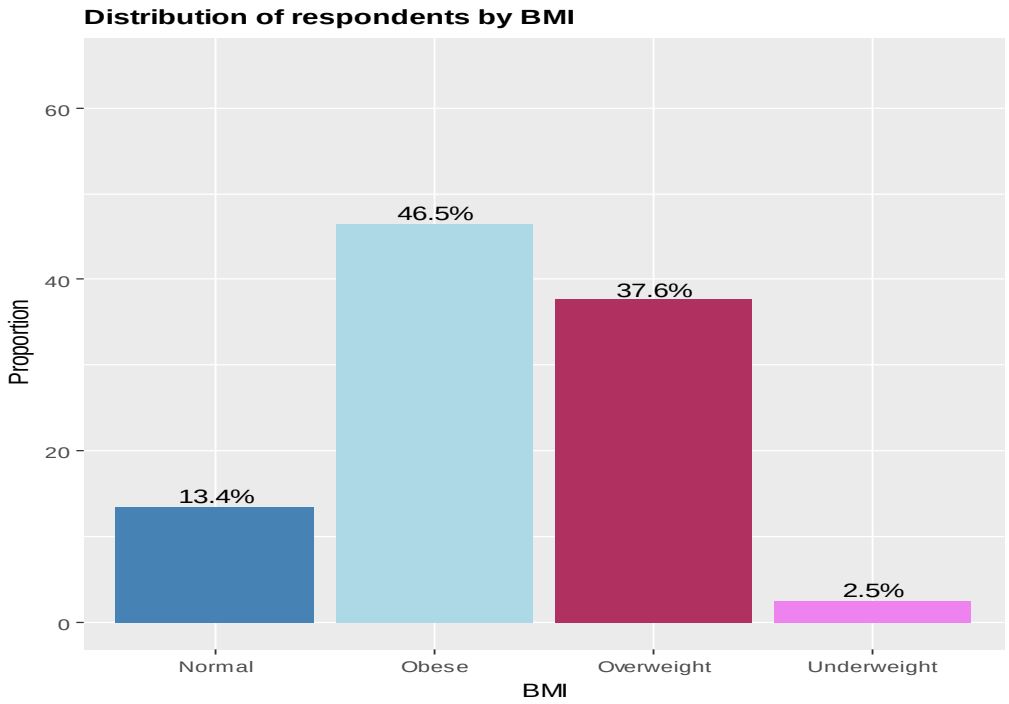


Figure 8: Barplot Showing Distribution Of participants By BMI

4.3 Renal Duplex Doppler Ultrasound Findings

The mean peak systolic velocity in participants found to have renal artery stenosis was 47cm/ sec in both the right and left renal arteries, the mean End diastolic velocity was 12.5cm/sec in the right renal artery and 14.5cm/sec in the left renal artery. The systolic renal to aortic velocity ratio was 3.48 in the right renal artery and 3.23 in the left renal artery whereas the resistive index was 0.6 in both the right and left renal arteries.

The kidney lengths were 7.64cm and 7.20 cm for the right and left kidneys respectively, width 3.77cm for both right and left kidneys and depth was 3.84cm and 3.85cm for the right and left kidneys respectively. Renal cortical thickness was 1.42cm and 1.24 cm for the right and left kidneys respectively.

Table 3: Summary Of Renal Duplex Doppler Ultrasound Findings in those found to have RAS

Renal characteristic	Kidney	Mean	SD	Median	IQR	Min	Max
Peak systolic velocity	Right (n=48)	47.31	14.49	29.20	11.30	6.60	78.30
	Left (n=57)	47.67	20.59	35.70	27.30	12.60	107.00
End diastolic velocity	Right (n=48)	12.55	6.57	12.55	6.10	2.30	35.60
	Left (n=57)	14.59	9.25	15.10	12.37	1.08	47.20
Systolic renal/ aortic ratio (RAR)	Right (n=46)	3.48	1.26	2.70	0.95	1.03	7.20
	Left (n=56)	3.23	0.69	2.62	1.05	1.64	4.25
	Right (n=48)	0.68	0.11	0.61	0.14	0.38	0.86
Resistive Index (RI)	Left (n=57)	0.65	0.11	0.60	0.15	0.39	0.97
Systolic / diastolic (SD) ratio	Right (n=42)	0.89	0.67	0.77	0.49	0.16	3.50
	Left (n=47)	1.05	0.90	0.80	0.68	0.20	3.87
Length (cm)	Right (n=57)	7.64	1.40	8.25	2.38	5.0	9.80
	Left (n=57)	7.20	1.30	8.27	2.12	5.78	10.0
width (cm)	Right (n=57)	3.77	0.76	3.79	1.03	2.30	5.51
	Left (n=57)	3.77	0.56	3.60	0.62	2.76	5.10
depth (cm)	Right (n=55)	3.84	1.04	3.93	1.18	1.45	6.96
	Left (n=55)	3.85	0.76	3.71	0.71	2.50	5.70
Renal cortical thickness	Right (n=43)	1.42	0.36	1.36	0.45	0.60	2.10
	Left (n=48)	1.24	0.33	1.22	0.43	0.12	1.81

In the participants who did not have renal arteries stenosis as shown in the table below; the mean peak systolic velocity was 32.9cm/ sec and 37.81cm/sec in the right and left renal arteries respectively. The mean End diastolic velocity was 14.74cm/sec in the right renal artery and 17.82cm/sec in the left renal artery. The systolic renal to aortic velocity ratio was 2.93 in the right renal artery and 2.80 in the left renal artery whereas the resistive index was 0.6 in both the right and left renal arteries.

The kidney lengths were 8.57cm and 8.66 cm for the right and left kidneys respectively, width 4.48cm for the right kidney and 4.22cm for the left kidney and depth was 4.34cm

and 4.36cm for the right and left kidneys respectively. Renal cortical thickness was 1.27cm and 1.26 cm for the right and left kidneys respectively.

Table 4: Summary Of Renal Duplex DopplerUltrasound Findings In Those With No RAS

Renal characteristic	Kidney	Mean	SD	Median	IQR	Min	Max
Peak systolic velocity	Right (n=108)	32.91	15.82	47.60	21.60	19.20	84.00
	Left (n=112)	37.81	13.71	46.50	16.20	25.90	81.10
End diastolic velocity	Right (n=108)	14.74	5.07	16.20	6.40	0.64	24.90
	Left (n=112)	17.82	11.12	14.00	9.15	0.64	51.90
Systolic renal/ aortic ratio (RAR)	Right (n=94)	2.93	1.37	3.05	1.72	1.74	8.50
	Left (n=97)	2.80	1.31	2.83	1.74	1.49	7.67
Resistive index(RI)	Right (n=108)	0.62	0.12	0.66	0.13	0.40	0.98
	Left (n=112)	0.61	0.14	0.64	0.16	0.33	0.98
Systolic/ diastolic (SD) ratio	Right (n=98)	1.04	0.40	1.00	0.46	0.25	2.92
	Left (n=102)	0.98	0.37	0.95	0.43	0.41	2.71
Length (cm)	Right (n=108)	8.57	1.08	8.77	1.46	5.53	11.40
	Left (n=112)	8.66	1.31	8.79	1.26	4.58	12.10
width(cm)	Right (n=108)	4.48	1.13	4.43	1.28	2.83	8.36
	Left (n=112)	4.22	0.69	4.21	1.03	2.60	6.39
depth (cm)	Right (n=105)	4.34	1.24	4.70	1.46	1.37	6.33
	Left (n=105)	4.36	1.13	4.18	1.70	2.50	6.88
Renal cortical thickness	Right (n=82)	1.27	0.40	1.30	0.45	0.12	2.01
	Left (n=83)	1.26	0.31	1.23	0.34	0.14	2.09

Table 5: Summary Of Renal Doppler Wave Characteristics in All Patients

Variable	Category	Frequency	Percent (%)
Areas of aliasing (n=166)	No	161	96.4
	Yes	6	3.6
Presence of localized perivascular tissue vibration (n=164)	No	164	100
	Yes	0	0
Presence of venous collaterals (n=164)	No	164	100
	Yes	0	0
Presence of post stenotic turbulence (n=169)	No	152	89.9
	Yes	17	10.1
Thickening and calcification of arterial wall (n=167)	No	165	98.8
	Yes	2	1.2
Presence of a beaded appearance (n=167)	No	167	100
	Yes	0	0
Presence of filling defect (n=164)	No	164	100
	Yes	0	0

The above table shows the Doppler wave characteristics in all participants. 3.6% had areas of aliasing, 10.1% had post stenotic turbulence and 1.2% had thickened arterial walls.**:**

Doppler wave characteristics in patients found to have renal artery stenosis.

Post stenotic turbulence and areas of aliasing were the most common Doppler wave characteristics seen in those with renal artery stenosis. Post stenotic turbulence was seen in 24.6% and areas of aliasing in 37.5% of patients with RAS. Thickening and calcification of arterial wall was seen in 2% of patients with renal artery stenosis.

Table 6: Summary of Renal Spectral Flow Pattern in All Patients

Renal spectral flow pattern	Kidney	Frequency	Percent (%)
Normal	Right (n=165)	112	67.9
	Left (n=169)	120	71.0
High Resistant	Right (n=165)	3	1.8
	Left (n=169)	0	0
Low	Right (n=165)	6	3.6
	Left (n=169)	9	5.3
Absent	Right (n=165)	5	3.0
	Left (n=169)	0	0
Reversed	Right (n=165)	5	3.0
	Left (n=169)	0	0
Tardus Parvus	Right (n=165)	32	19.4
	Left (n=169)	37	21.9
Turbulent	Right (n=165)	7	4.2
	Left (n=169)	1	0.6

A majority of the respondents had normal right (67.9%) and left (71.0%) renal spectral flow patterns. High resistant (1.8%), low (3.6%), absent (3.0%) and reversed (3.0%) renal spectral patterns were observed in a few respondents, where the right kidneys were the only ones affected. Tardus- parvus pattern was seen on the right in 19.4% of the participants and on the left in 21.9% of the participants.

Table 7: Association between RAS status and Renal spectral flow pattern

variable	category	RAS status		p-value
		No RAS n (%)	RAS n (%)	
Normal right	no	6(5.6)	47(82.5)	<0.001**
	yes	102(94.6)	10(17.5)	
Normal left	no	2(1.8)	47(82.5)	<0.001**
	yes	110(98.2)	10(17.5)	
High resistant right	no	107(99.1)	55(96.5)	0.274*
	yes	1(0.9)	2(3.5)	
Low right	no	106(98.1)	53(93.0)	0.183*
	yes	2(1.9)	4(7.0)	
Low left	no	110(98.2)	50(87.7)	0.007*
	yes	2(1.8)	7(12.3)	
Absent right	no	108(100.0)	52(91.2)	
	yes	0(0.0)	5(8.8)	
Reversed right	no	105(97.2)	55(96.5)	>0.999*
	yes	3(2.8)	2(3.5)	
Parvus-Tardus right	no	108(100.0)	25(43.9)	
	yes	0(0.0)	32(66.1)	
Parvus-Tardus left	no	112(100.0)	20(35.1)	
	yes	0(0.0)	37(64.9)	
* Fisher's exact test ** Chi square				

4.4 Gray-scale renal ultrasound findings and RAS status

4.4.1 Echogenicity and corticomedullary differentiation

In the participants found to have renal artery stenosis, 43.9% of them had echogenic kidneys, whereas 26.3% of them had loss of corticomedullary differentiation,though both these associations were not statisticaly significant (p = 0.814 and 0.262).This is shown in the table below.

Table 8: Association between RAS status and other U/S findings

variable	category	RAS status		p-value
		No RAS n(%)	RAS n(%)	
Echogenicity	no	65(58.0)	32(56.1)	0.814
	yes	47(42.0)	25(43.9)	
Loss of cortico-medullary difference	no	73(65.2)	42(73.7)	0.262
	yes	39(34.8)	15(26.3)	
Chi square test				

4.4.2 Kidney volumes

Comparison of the kidney volumes was done between the participants who had renal artery stenosis and those without using Mann- Whitney U test. Those with renal artery stenosis had a right mean kidney volume of 63.3cm3 and a left mean kidney volume of 59.8cm3 whereas those without renal artery stenosis had a right mean kidney volume of 85.3cm3and a left mean kidney volume of 59.8cm3. The association was statistically significant.

Table 9 :Association between kidney volume and RAS status

Kidney	**RAS status**	**Median**	**IQR**	**Min**	**Max**	**p-value**
Right	No RAS (n=105)	85.3	68.7	20.7	187.5	0.0003
	RAS (n=55)	63.3	51.4	8.7	143.8	
Left	No RAS (n=105)	81.6	62.6	30.4	225.3	0.0031
	RAS (n=55)	59.8	31.1	22.4	143.1	

Mann-Whitney U test comparing medians

4.5 Sonographic prevalence of Renal artery stenosis.

Table 10: Sonographic Prevalence of RAS

	Frequency	Percent
No RAS	112	66.3
RAS	57	33.7
Total	169	100.0

The sonographic prevalence of RAS was 33.7 % (57 cases); those who did not have renal artery stenosis were 66.3% (112).

Renal artery stenosis was further sub-classified into two i.e. Partial stenosis (52) and occlusion (5); this is shown in the table below.

Table 11: Sub classification of Renal Artery Stenosis

	Frequency	Percent
Partial stenosis	52	91.2
Occlusion	5	8.8
Total	57	100.0

4.4 Association Between covariates And RAS Status

Chi-square and fishers' exact tests were used to evaluate the association between demographic characteristics, clinical findings, laboratory findings and final diagnosis (Renal artery stenosis status) at alpha level of significance, 0.05.

Table 12: Association between RAS status and demographic characteristics

variable	category	RAS status		p-value
		No RAS n(%)	RAS n(%)	
sex	Female	69(61.6)	36(63.2)	0.844
	Male	43(38.4)	21(36.8)	
Age	<30 years	20(17.9)	18(31.6)	0.079
	30-55 years	42(37.5)	14(24.6)	
	>55 years	50(44.6)	25(43.8)	
Chi square test				

More females (63.2%) than males had RAS, though this was not statistically significant (P = 0.844). Majority (43.8%) of those with RAS were above 55 years; 31.6% were below 30 years and 24.6% were between 30-55 years. This association between age and presence RAS was also not statistically significant (P = 0.079).

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Table 13: Association between renal function tests and RAS status

		RAS status		
Variable	**Categories**	No RAS n(%)	RAS n(%)	p-value
Urea	< 8.3mmol/l	60(55.1)	15(26.3)	<0.001
	> 8.3mmol/l	49(44.9)	42(73.7)	
Creatinine	0 -80 µmol/l	63(57.8)	10(17.5)	<0.001
	>80µmol/l	46(42.2)	47(82.5)	
Sodium	136 -145mmol/l	66(61.1)	36(65.5)	0.588
	<136, >145mmol/l	42(38.9)	19(35.5)	
Potassium	3.5 – 5.1 mmol/l	83(76.2)	16(28.1)	<0.001
	> 5.1 mmol/l	26(23.8)	41(71.9)	

Urea, creatinine and potassium were significantly associated with RAS status (p<0.001). Among those with RAS, 73.7% had elevated urea level compared to 44.9% of those with no RAS. Among those with RAS 82.5% had elevated creatinine levels compared to 42.2% among with those with no RAS. Among those with RAS 71.9% had elevated potassium levels compared to 23.8% among those with no RAS.

Table 14:Association between lipids profile and RAS status

		RAS status		
Variable	**Categories**	No RAS n(%)	RAS n(%)	p-value
Total Cholesterol	<5.2 mmol/l(n)	86(76.8)	26(45.6)	<0.001
	>5.2 mmol/l(↑)	26(23.2)	31(54.4)	
LDL	<2.50mmol/l(n)	73(65.2)	18(31.6)	<0.001
	>2.50 mmol/l(↑)	39(34.8)	39(68.4)	
HDL	>1.68 mmol/l(n)	81(72.3)	31(54.4)	0.020
	<1.68 mmol/l(↓)	31(27.7)	26(45.6)	
Triglycerides	<2.3 mmol/l(n)	90(80.4)	31(54.4)	<0.001
	>2.3mmol/l(↑)	22(19.6)	26(45.6)	

Elevated Total cholesterol, LDL and triglycerides were significantly associated with RAS status (p<0.05). More patients with RAS had elevated total cholesterol (54.4%), LDL

(68.4%), and triglycerides (45.6%) compared to those without RAS Total cholesterol (23.2%), LDL (34.8%) and triglycerides (19.6%).

Table 15: Association between RAS status and BMI

Variable	Category	RAS status		p-value
		No RAS n(%)	RAS n(%)	
BMI	Underweight	4(3.8)	0(0)	
	Normal	18(17.1)	3(15.8)	
	Overweight	32(30.5)	27(51.9)	
	Obese	51(48.6)	22(42.3)	
*Chi square				

42.3% of those with RAS were obese as shown in the table above.

Sample Images

The following are some of the images that were obtained from Duplex Doppler renal scans of some of the participants with renal artery stenosis. The images demonstrate the various imaging findings in renal artery stenosis.

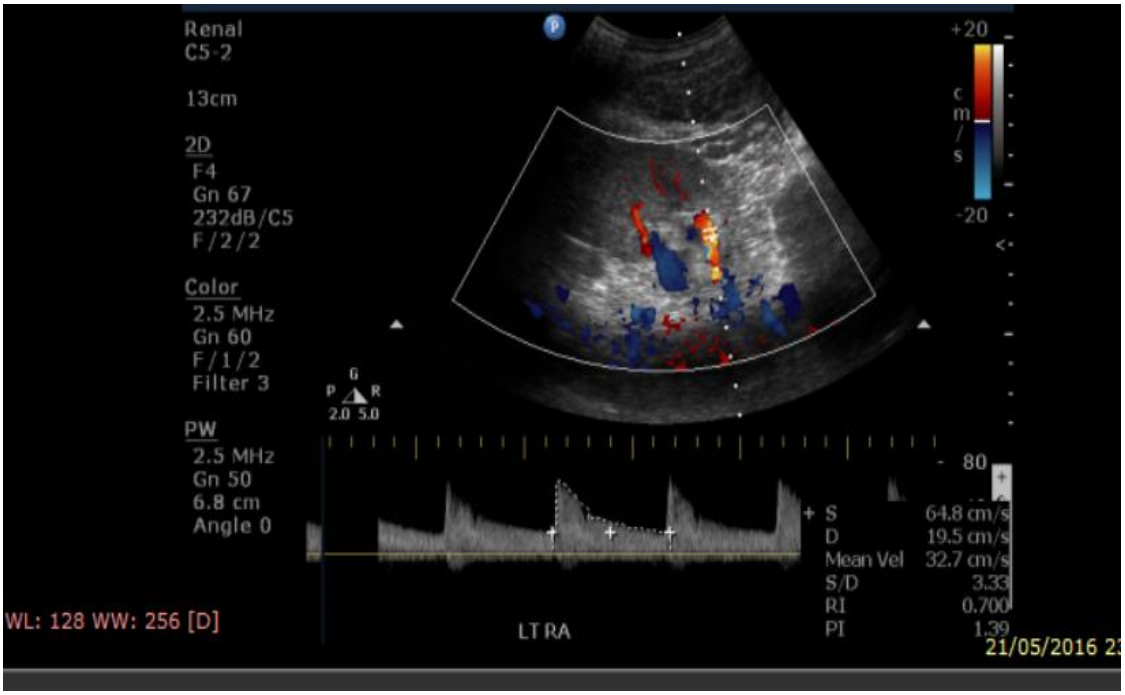

Figure 9: Normal renal artery waveform pattern showing the normal sharp peak systole.

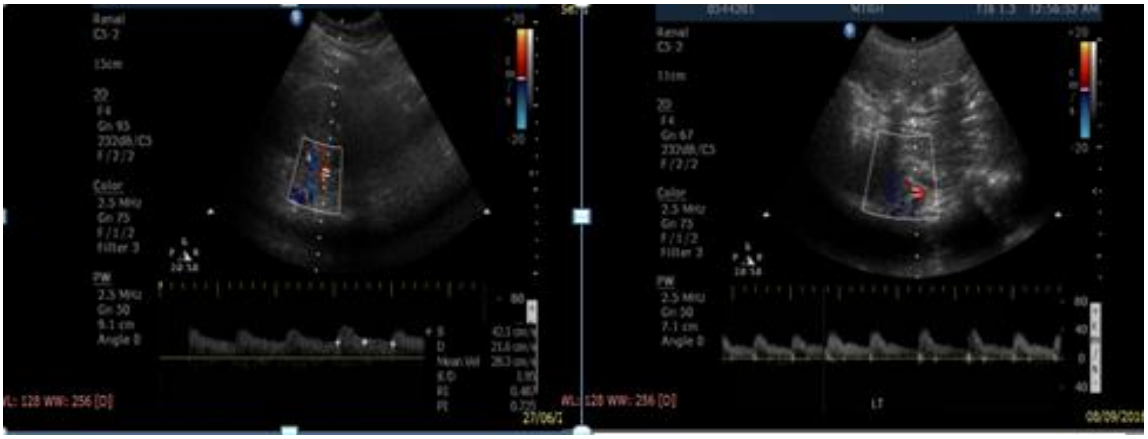

Figure 10: Bilateral Parvus – Tardus waveform pattern in a 21 year old girl with uncontrolled hypertension.

Parvus- Tardus is a peak systole that is slowed and reduced in amplitude

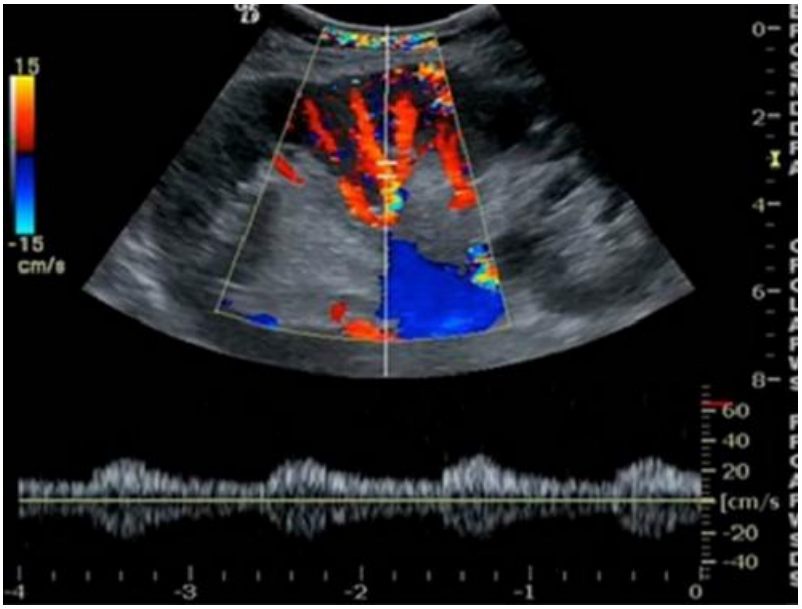

Figure 11: Severe parvus- tardus waveform pattern of the right renal artery post stenosis.

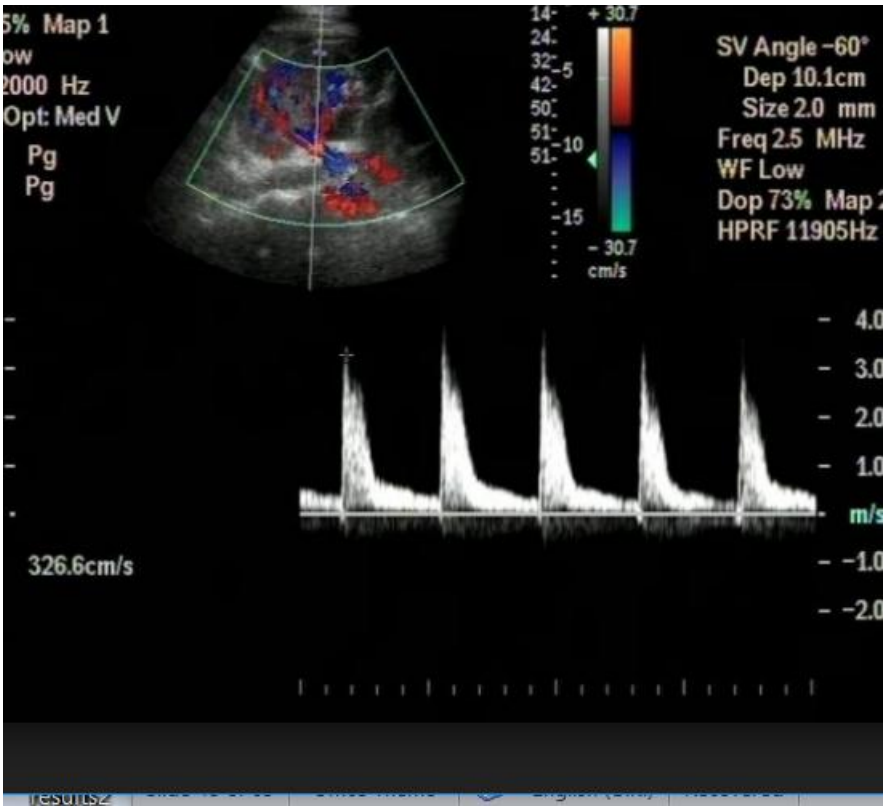

Figure 12: Showing high PSV at a Stenotic Region.

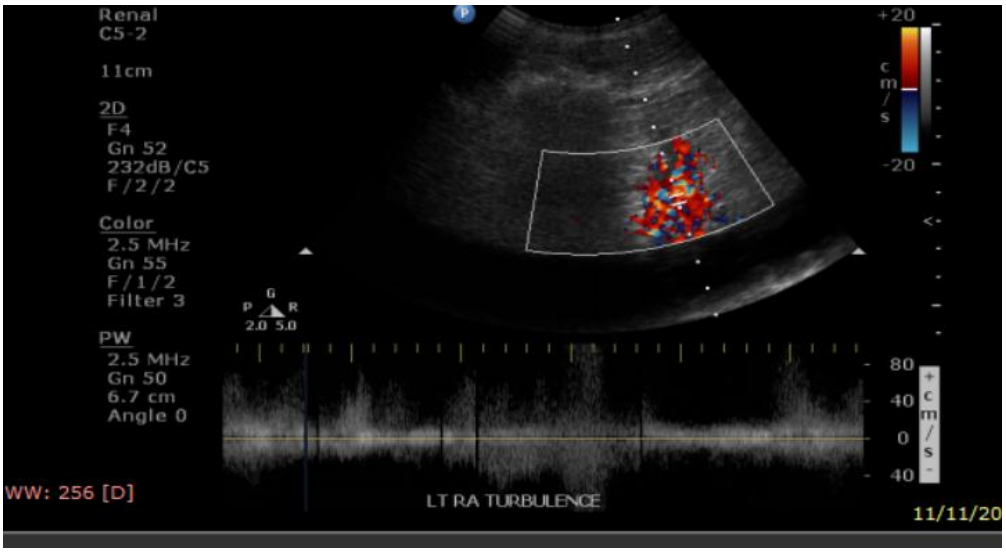

Figure 13: Turbulent waveform pattern post stenosis

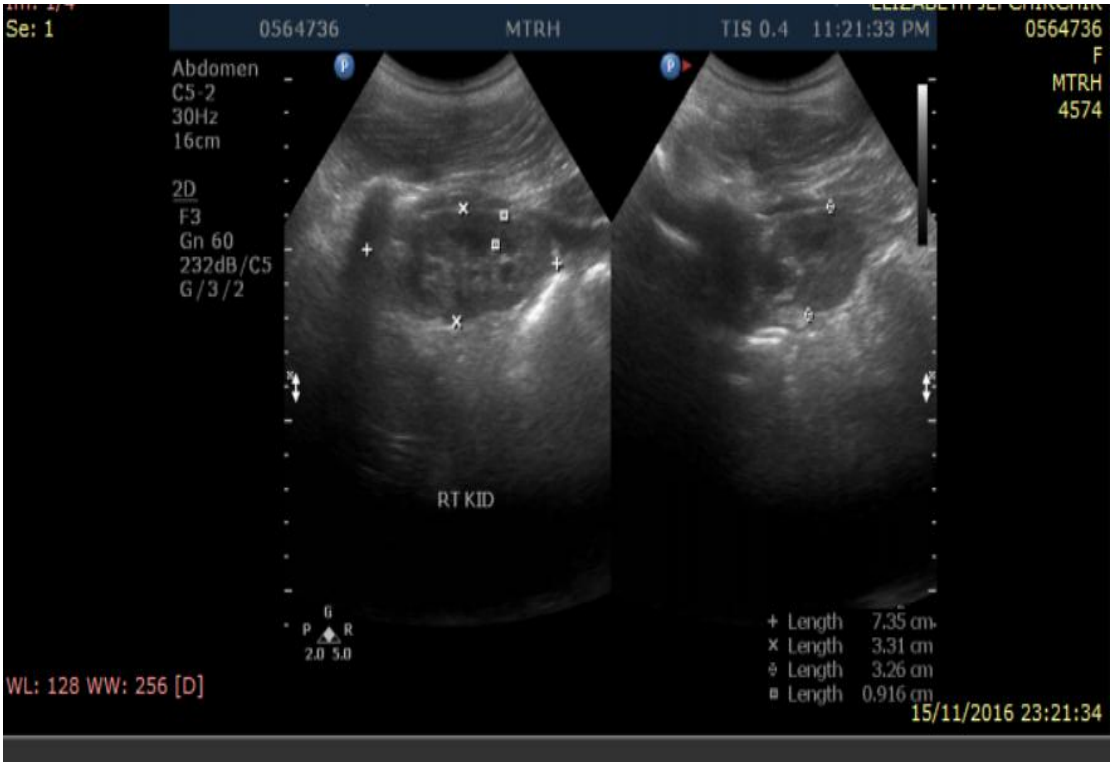

Figure 14 : Bilateral Echogenic Shrunken Kidneys in a Patient with Bilateral Renal Artery Stenosis.

CHAPTER FIVE

DISCUSSION

5.1 Sonographic fndings in adult hypertensive patients with clinical features of RAS

5.1.1 Doppler Parameters

The mean Peak systolic velocity (PSV) in those found to have renal artery stenosis was 47 cm/s in both the right and left renal arteries while in those without renal artery stenosis the mean was 32.9cm/s and 37.8cm/s in the right and left renal arteries respectively. Similarly Missouris *et al,* (1996) also found a peak systolic velocity of 37.7cm /s in their study of non- invasive screening for RAS using ultrasound contrast enhancement done in London. This finding could be attributed to the fact that in both studies a combination of both direct and indirect criteria was used to make the diagnosis of renal artery stenosis, so despite having a normal PSV value the patient could have had other features in the Doppler wave pattern that qualified for stenosis.

Harding *et al,* (1992) in the Cardiovascular Health Study found a mean PSV of 264cm / sec in patients who had renal artery stenosis. This is because they used only the Direct criteria and used only a PSV of above 200cm/sec to make the diagnosis of RAS.

The Renal to Aortic ratio (RAR) in those with renal artery stenosis was found to be 3.48 and 3.23 in the right and left renal arteries respectively. House *et al,* (1999) in their study of 63 patients using Doppler sonography to evaluate the optimal imaging parameters for renal artery stenosis in the United States found a mean of 3.0 . Both studies combined both direct and indirect criteria for evaluating renal artery stenosis.

The resistive index (RI) was found to be 0.68 and 0.65 in the right and left kidneys respectively in those with renal artery stenosis and 0.62 and 0.61 in the right and left kidneys respectively in those without renal artery stenosis. Similarly Patriquin *et al*, (1992) in Sainte- Justine Hospital in Montreal, Canada also found lower resistive Indices of 0.43-0.54 in kidneys with stenotic arteries as compared with healthy subjects. In cases of Renal artery stenosis resistive index will be elevated if measured upstream from the stenosis. The lower RI values could be because the measurements were taken downstream from the stenosis.

5.1.2 Doppler Wave Characteristics and Spectral Flow Patterns

Parvus – Tardus waveform pattern was seen in 66.1% and 64.9% in the left and right renal arteries respectively in patients with renal artery stenosis. This was similar to findings of Stavros *et al*, (1992) at the Swedish Medical Centre in Washington who found 61% in both right and left renal arteries and Carroll, (1994) at Duke University Medical Centre North Carolina who found 60% and 62% in the right and left renal arteries respectively. This finding is because the flow downstream to a significant stenosis is damped and will show a slow rise to peak systole with low height (amplitude) of the wave. Due to its high sensitivity and specificity it is one of the indirect methods highly recommended for evaluation of renal artery stenosis.

Post stenotic turbulence and areas of aliasing were the most common Doppler wave characteristics seen in those with renal artery stenosis. Post stenotic turbulence was seen in 24.6% and areas of aliasing in 37.5% in patients with RAS.

Zoller *et al*, (1990) also found turbulence to be a valuable sign of a hemodynamically significant stenosis.

The findings could be attributed to the fact that spectral sampling was done at the point of the stenosis where the velocities were high .

5.1.3 Grey- scale Ultrasound Findings

In this study the mean kidney lengths for those with renal artery stenosis was reduced ;7.64cm and 7.20 cm for the right and left kidneys respectively compared to those without renal artery stenosis which was 8.57cm and 8.66cm for the right and left kidneys respectively.

The kidney volumes were also reduced in patients with renal artery stenosis 63.3 cm^3 and 59.8 cm^3 in the right and left kidneys respectively, compared to 85.3 cm^3 on the right and 81.6 cm^3 on the left in those without renal artery stenosis.

These findings compare well with a study by Musa, (2014) in Aseer region, Abha ,Saudi Arabia where he used ultrasound to evaluate renal changes in hypertensive patients in a high altitude area . He found a mean kidney length of 8.8 cm for both kidneys and renal volumes of 57.2 cm3 in the right and 55.3 cm3 in the left in patients with renal artery stenosis. These parameters were reduced compared to those without renal artery stenosis.

The reduced kidney lengths and volumes in patients with renal artery stenosis could be due to the fact that atherosclerosis which causes stenosis of the renal arteries causes deficiency of blood flow to the kidneys which leads to atrophy.

Adedeji *et al,* (2015) in South Western Nigeria found normal kidney volumes in patients with hypertension (114cm^3 and 123 cm^3 in the right and left kidneys respectively).

The difference in findings could be because they studied hypertensive patients with normal renal functions hence no renal compromise. In our study some of the patients had elevated urea and creatinine levels which denotes some underlying renal compromise. Hypertension tends affect renal volumes when there is a severe underlying renal parenchymal damage or compromise.

5.2 Sonographic Prevalence of RAS in Adult Hypertensive Patients with Suggestive Clinical Features.

This study included 169 participants with clinical features suggestive of Renal artery stenosis, this is because the prevalence of renovascular hypertension rises in selected groups of hypertensive patients (Karasch & Rubin, 1998).

The sonographic prevalence of renal artery stenosis was found to be 33.7%. This is comparable to findings of Watchtell et al (1996) in Denmark . He studied patients with hypertension and risk factors for peripheral arterial disease. The reason why a high prevalence was found in both studies is because patients with risk factors for renal artery stenosis were studied.

Harding *et al,* (1992) at Duke University Medical Centre found a prevalence of 30% which is almost similar to the findings of this study, this is because he studied patients with cardiovascular risk factors which is also a risk factor for RAS (Harding et al., 1992).

Benjamin *et al*, (2014) at Bayer Heart and vascular Hospital (USA) found a prevalence of 24.2%. The difference could be attributed to the fact that they used conventional angiography which is a different tool from what we used.

5.3 Relationship between presence of RAS and Gender, Age, Renal Functions, Lipid Profile and Body Mass Index (BMI).

5.3.1 Gender

Amongst the adult hypertensive patients with clinical features of renal artery stenosis seen in Moi Teaching and Referral Hospital during the study period more females (63.2%) than males were found to have renal artery stenosis. This was an interesting finding since women are commonly not felt to have a high association with atherosclerotic disease. The higher prevalence in females could be because the number of female participants recruited was twice that of males as this was a census study carried out in a period of one year and more females could have come to hospital during that period as compared to males.

Similarly Harding *et al*, (1992) in their study of 1,302 patients with cardiovascular risk factors at Duke University Medical Centre found more females had significant renal artery stenosis.

It is well established that women have a higher incidence of fibromascular disease than men; furthermore, atheromatous lesions can develop in patients with hypertension and fibromascular dysplasia. It is therefore speculative that fibromascular renovascular disease could have accelerated coexistent atherosclerotic disease in the females.

Edwards *et al*, (2005) in the Cardiovascular Health Study found RAS to be present in twice as many men (9.1%) as women (5.5%).

5.3.2 Age

Majority (43.8%) of those with RAS were above 55 years; 31.6% were below 30 years and 24.6% were between 30-55 years. This is similar to the findings of Harding *et al*, (1992) and Edwards *et al*, (2005) in the Cardiovascular Health study where they also found the presence of renovascular disease was associated with increasing age. This is because generally incidence of artherosclerotic disease increases with age.

5.3.3 Urea and Creatinine Levels

There was a significant association between RAS status and elevated serum creatinine levels. This compares to a prospective study by Caps et al, (1998) who examined the natural history of renal artery stenosis using Duplex ultrasonography. They found out the severity of renal artery stenosis was associated with worsening renal functions and kidney atrophy.

Similarly Kuroda *et al* in, (2000) in a study of autopsy patients with renal artery stenosis in Japan, found a mean creatinine level of 221µmol/l in those who had renal artery stenosis whereas in those with normal renal arteries the mean was 124µmol/l.

This was however different from Harding *et al*, (1992) who found elevated creatinine not to be an important predictor of RAS. This could be because unilateral RAS may not cause elevated creatinine if contralateral kidney functions properly.

5.3.4 Lipid profile

Elevated Total cholesterol, LDL and triglycerides were significantly associated with RAS status ($p<0.05$). More patients with RAS had elevated total cholesterol (54.4%), LDL (68.4%), and triglycerides (45.6%) compared to those without RAS; total cholesterol

(23.2%), LDL (34.8%) and triglycerides (19.6%). Similarly Harding *et al,* (1992) in a study of RAS in patients undergoing routine cardiac catheterisation at Duke Medical Centre found majority (53%) of the patients with RAS had elevated cholesterol levels (mean of 11mmol/l). This could be explained by the fact that hyperlipidaemia is one of the risk factors for atherosclerosis which is the leading cause of RAS.

In the Cardiovascular Health study Edwards *et al,* (2005) found majority of the participants had lower lipids (especially High Density Lipoproteins). This could be because their participants were selected on the basis of having Cardiovascular Risk factors such as myocardial Infarction and could have been put on lipid lowering agents.

5.3.5 Body Mass Index

Majority of the patients with RAS (42.3%) were obese. Similarly Postma *et al,* (2012) in a study done to find out the prevalence of RAS among patients with diabetes found 33% of their patients were obese. This is because obesity is linked to hyperlipidaemia which is a risk factor for atherosclerosis hence RAS.

In the cardiovascular health study, Hansen *et al,* (2002) found only 29.4% of those with RAS were obese. This could be because the patients in the study had cardiovascular disease hence had been advised to maintain a lower BMI.

CHAPTER SIX

CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusions

1. The commonest waveform pattern seen in those with renal artery stenosis was Parvus-Tardus, and it showed a statistically significant association with presence of RAS.
2. The sonographic prevalence of renal artery stenosis was 33.7%.
3. There was an association between presence of renal artery stenosis and elevated levels of urea, creatinine, potassium, total cholesterol, triglycerides and low density lipoproteins.

6.2 Recommendations

1. A high index of suspicion for renal artery stenosis whenever parvus- tardus waveform pattern is encountered during a renal Duplex Doppler ultrasound study of the kidneys.

2. Future longitudinal study to further evaluate the magnitude and direction of the associations found.

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APPENDICES

Appendix I: Consent Form
English Version

Investigator: My name is Dr. ALUNG'AT Miriam Omasete. I am a qualified doctor, registered with the Medical Practitioners and Dentists Board of Kenya. I am currently pursuing a Masters degree in Radiology and Imaging at Moi University. I would like to recruit you into my research which is to study the Renal Doppler ultrasound findings in hypertensive patients attending the medical and renal outpatient clinics and medical wards.

Purpose: This study will seek to determine the renal Doppler ultrasound findings in hypertensive patients attending medical and renal outpatient clinics and medical wards.

Procedure: Adult hypertensive patients with clinical features suggestive of renal artery stenosis for whom consent has been given will undergo renal Doppler evaluation. Demographic data will be obtained and the patients subjected to a physical examination. Both the clinical and radiologic data will be collected on data collection forms. Data collecting material will be kept in a locked cabinet during the study period.

Benefits: There will be no direct benefits of participating in this study. Study subjects will be accorded same quality of management as non-study subjects

Risks: There are no anticipated risks to the participants attributable to this study.

Confidentiality: All information obtained in this study will be treated with utmost confidentiality and shall not be divulged to any unauthorized person.

Rights to Refuse: Participation in this study is voluntary, there is freedom to refuse to take part or withdraw at any time. This study has been approved by the Institutional Research and Ethics Committee (IREC) of Moi University/Moi Teaching and Referral Hospital.

Sign or make a mark if you agree to take part in the study

Parent/Guardian: …… Investigator: ……Date: ……

Kiswahili Version

Mpelelezi: jina langu ni Dr ALUNG'AT Miriam Omasete. Mimi ni daktari aliyehitimu na kusajiliwa na bodi ya Kenya ya Madaktari na Madaktari wa meno. Kwa sasa natafuta shahada ya uzamili katika Radiology na Imaging katika Chuo Kikuu cha Moi. Ningependa kukusajili katika utafiti wangu ambao ni wa kuangalia matokeo ya figo doppler ultrasound kwa wagonjwa wa shinikizo la damu wanaohudhuria matibabu katika medical outpatient kliniki, kliniki ya figo na wodi za matibabu.

Kusudi: Utafiti huu utajaribu kueleza namna magonjwa mbalimbali ya mishipa ya figo yataonekana kwenye picha ya Ultrasound.

Utaratibu: Wagonjwa wote ambao wana makala kukisia ateri stenosis ya figo , watashirikishwa kwenye utafiti huu ikiwa watakubali. Data zitakusanywa kwenye fomu za ukusanyaji data. Hifadhi zitakazo tumika katika ukusanyaji wa data zitawekwa katika kabati iliyofungwa katika chumba cha mpelelezi mkuu kwa kipindi cha utafiti.

Faida: Kutakuwa hakuna faida moja kwa moja ya kushiriki katika utafiti huu.Wanaofanyiwa utafiti watakuwa na haki ya kupewa matibabu sawa na wale ambao hawatahusishwa kwenye utafiti huu.

Hatari: Hakuna hatari ya kutarajia kwa washiriki kutokana na utafiti huu.

Usiri: habari zote zilizopatikana katika utafiti huu wa kutibiwa zitawekwa kwa usiri mkubwa na wala haitatolewa kwa mtu yeyote asiye husika na utafiti.

Haki ya kukataa: Kushiriki katika utafiti huu ni hiari yako, kuna uhuru wa kukataa kushiriki au kujiondoa wakati wowote. Utafiti huu umepitishwa na Utafiti wa Taasisi na Kamati ya Maadili (IREC) ya Chuo Kikuu cha Moi na Hospitali ya Rufaa.

Weka sahihi au alama kama umekubali kushiriki katika utafiti

Mzazi / Mlezi: ..... Mpelelezi: .....

Tarehe: .....

Appendix II : Recruitment Protocol

Guidelines regarding who to investigate for RAS as per the American College of Cardiology /American Heart Association in 2005 (Hirsch et al., 2006).

They recommend screening anyone with the following;

- Onset of hypertension before age of 30 years or severe hypertension after age 55years.
- Accelerated, resistant or malignant hypertension.
- Development of new azotemia or worsening renal function after administration of an ACE Inhibitor or ARB.
- Unexplained atrophic kidneys or size discrepancy > 1.5cm between kidneys.
- Sudden, unexplained pulmonary edema.
- Unexplained renal dysfunction, including patients starting renal replacement therapy.
- Multivessel coronary artery disease or peripheral arterial disease.
- Unexplained congestive heart failure or refractory angina.

Appendix II1: Data Collection Form

SOCIO-DEMOGRAPHICS

Date: ……. Medical Record Number: ……

Serial Number…….

Age……

Gender……Male ☐ Female ☐

County of residence.....

Occupation ……..

Clinical Findings

a) weight_____ kgs BMI_____

b) Height _____Mtrs

c) Blood Pressure

Categorization of BP

	Systolic	**Diastolic**	
Normal	<120	<80	
Pre-hypertension	120-139	80-89	
Stage1	140-159	90-99	
Stage 2	>160	>100	

Clinical Findings

Onset of HPTN **<30 years** **>55yrs**

Resistant / malignant HPTN Yes ☐ No ☐
(>180/120) ☐ ☐

1. Presence of cold feet or Yes No
   Darkening of feet or hands ☐ ☐
   or chronic wound in the lower limb

2. Presence of lower limb swelling Yes No
   ☐ ☐

3. History of unexplained dyspnoea Yes No
   or chest pain ☐ ☐

4. Family History of Hypertension Yes No.
   ☐ ☐

5. Family history of diabetes Yes No.
   ☐ ☐

6. a) Are you diabetic? Yes No
   ☐ ☐

   b) If , Yes, was onset of hypertension before diabetes Yes No
   ☐ ☐

7. History of reduced urine output Yes No
   ☐ ☐

8. History of passing dark urine Yes No
   ☐ ☐

9. History of passing frothy urine Yes ☐ No ☐

10. History of abdominal trauma Yes ☐ No ☐

11. If female, are you pregnant? Yes ☐ No ☐

12. History of steroids use? Yes ☐ No ☐

13. Use of oral contraceptives Yes ☐ No ☐

14. Use of anticoagulants Yes ☐ No ☐

15. History of surgery Yes ☐ No ☐

16. History of central line catheterisation Yes ☐ No ☐

17. Presence of abdominal murmur Yes ☐ No ☐

18. Presence of flank pain/ tenderness Yes ☐ No ☐

Renal Duplex ultrasound findings

	Right Kidney	**Left Kidney**
Peak Systolic Velocity (PSV)		
End diastolic Velocity (EDV)		
Acceleration Index		
Systolic/ diastolic (S/D) Ratio		
Resistive index (R.I) a)Upper b) Mid c) Lower		
Systolic Renal / Aortic ratio (RAR)		
Kidney measurements a) length(cm) b) width (cm) c) depth (cm)		
Renal cortical thickness		

2) Doppler wave characteristics.

a) Areas of aliasing Yes ☐ No ☐

b) Presence of localized perivascular tissue vibration Yes ☐ No ☐

c) Presence of Venus collaterals Yes ☐ No ☐

d) Presence of post stenotic turbulence Yes ☐ No ☐

e) Thickening and calcification of arterial wall Yes ☐ No ☐

f) Beaded appearance of arterial wall Yes ☐ No ☐

g) Presence of a filling defect Yes ☐ No ☐

h) Renal spectral flow pattern

☐ Normal

☐ High Resistant

☐ Low

☐ Absent

☐ Reversed

3. Other ultrasound findings

a) Echogenicity Yes ☐ No ☐

b) Loss of cortico- medullary differentiation Yes ☐ No ☐

c) Other findings (specify)……

Final Diagnosis

1. Renal Artery Stenosis (RAS)
    i. Normal ☐
    ii. <60% ☐
    iii. ≥ 60%–99% ☐
    iv. Occlusion ☐
a) Atherosclerosis ☐
b) Fibromuscular dysplasia ☐

1. Renal Artery thrombosis ☐
2. Renal Artery aneurysm ☐
3. Renal vein Thombosis ☐

Laboratory Findings

U/E/Cs	Urea Creatinine Sodium Potassium
Lipid profile	Total Cholesterol LDH LDL Triglycerides
Urinalysis	Protein Red Blood cells
Full haemogram	HB

Appendix III: Time Schedule

Activity	May –Jul 2015	Aug 2015	Sept -Oct 2015	Nov 2015	Dec 2015	Jan-Mar 2016	April -July 2016	Aug -Sep 2016	Oct-Dec 2016	Jan / Feb 2016	March -Dec 2017
Contact with supervisors											
Proposal development											
Submit proposal and obtain IREC approval											
Pretest data collection tools											
Data collection											
Data entry, cleaning											
Data analysis											
Report writing and dissemination											
Thesis completion and submission											

Appendix IV: Estimated Project Budget

ITEM	**QUANTITY**	**UNIT PRICE(ksh)**	**TOTAL(Ksh)**
Laptop computer	1	50,000	50,000
Printer and photocopier	1	10000	10000
Renal Doppler Cost	169	1800	304,200
U/E/Cs	169	1500	253,500
Lipid profile	169	1500	253,500
Urinalysis	169	150	25,350
Stationery	-	-	5,000
CDs (US Image storage)	169	20	3,380
Statistical consultation	-	-	25,000
Internet services and communication	-	-	4,000
Miscellaneous	-	-	10,000
GRAND TOTAL	**-**	**-**	**943,930**

Appendix V: 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

Reference: IREC/2015/140
Approval Number: 0001468

20th August, 2015

Dr. Alung'at Omasete Miriam,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
20 AUG 2015
APPROVED
P. O. Box 4606-30100 ELDORET

Dear Dr. Alung'at,

RE: FORMAL APPROVAL

The Institutional Research and Ethics Committee has reviewed your research proposal titled:-

"Renal Doppler Ultrasound Findings in Adult Hypertensive Patients in Moi Teaching and Referral Hospital, Eldoret, Kenya.".

Your proposal has been granted a Formal Approval Number: ***FAN: IREC 1468*** on 20th August, 2015. You are therefore permitted to begin your investigations.

Note that this approval is for 1 year; it will thus expire on 19th August, 2016. If it is necessary to continue with this research beyond the expiry date, a request for continuation should be made in writing to IREC Secretariat two months prior to the expiry date.

You are required to submit progress report(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,

PROF. E. WERE
CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc Director - MTRH Dean - SOP Dean - SOM
Principal - CHS Dean - SON Dean - SOD

Appendix VI: Hospital 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
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Sincerely,

PROF. E. WERE
CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc Director - MTRH Dean - SOP Dean - SOM
Principal - CHS Dean - SON Dean - SOD