PREVALENCE AND RISK FACTORS FOR HYPERTENSIVE RETINOPATHY AT MOI TEACHING AND REFERRAL HOSPITAL, ELDORET, KENYA.

INVESTIGATOR

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A THESIS PRESENTED TO THE SCHOOL OF MEDICINE IN PARTIAL FULFILLMENT FOR THE AWARD OF THE DEGREE OF MASTER OF MEDICINE IN INTERNAL MEDICINE OF MOI UNIVERSITY

DECLARATION

Candidate's Declaration

This thesis is my original work and has not been presented before for the award of a degree or an academic credit in any university. No part of this work may be re-produced without the permission of the author and/or Moi University.

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Supervisors' Declaration

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DEDICATION

This thesis is dedicated to all the Hypertensive patients seeking care in Moi Teaching and Referral Hospital, Eldoret. I would also like to dedicate this thesis to my father, Colonel (Retired) Dr. Peter Okins Rakwach who cultivated my interest in medicine and was my first teacher.

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ACRONYMS

BMI	Body Mass Index
BP	Blood Pressure
DBP	Diastolic Blood Pressure
HDL	High Density Lipoprotein
HTNR	Hypertensive Retinopathy
IREC	Institutional Research and Ethics Committee
LDL	Low Density Lipoprotein
MOPC	Medical Outpatient Clinic
MTRH	Moi Teaching and Referral Hospital
PI	Principal Investigator
SBP	Systolic Blood Pressure
WHO	World Health Organization

DEFINITION OF TERMS

Hypertension – Defined as a measurement of systolic blood pressure of more than 140mmHg and/or a diastolic blood pressure of more than 90mmHg, measured on the upper arm while in a seated position with the cuff applied at the level of the heart OR persons taking antihypertensive medications.

Classification done was using the JNC 8 (Joint National Committee) criteria which classifies hypertension as follows:

Stage 1 - Systolic blood pressure of 140 to 159mmHg and/or a diastolic 90-99mmHg

Stage 2 - Systolic blood pressure of ≥160mmHg systolic **OR** 100 or more diastolic blood pressure.

Blood Pressure Control

Refers to the blood pressure measurement taken on clinic day using a calibrated digital machine and observing the prerequisite guidelines for the accurate measurement of blood pressure as per the AHA guidelines (See Appendix 7).

Uncontrolled blood pressure refers to a blood pressure readings reported to be stage I and stage 2 as per the JNC 8 classification of hypertension.

Hypertensive Retinopathy – Defined as the retinal changes that occur due to hypertension as classified by the Mitchell Wong classification for hypertensive retinopathy. It classifies hypertensive retinopathy into three classes, namely mild, moderate and malignant.

The characteristics of the Mitchell Wong classification are as follows:

Mild (Grade 1) retinopathy - These are retinal arteriolar signs. They include generalized arteriolar narrowing, focal arteriolar narrowing, arteriovenous nicking, opacity (“copper wiring”) of arteriolar wall or any combination of these signs.

Moderate (Grade 2) retinopathy - These are retinopathy like lesions and include retinal hemorrhages (blot-shaped, dot-shaped, or flame-shaped), micro-aneurysms, cotton wool spots, hard exudates or any combination of these signs.

Malignant (Grade 3) retinopathy - These include signs of moderate retinopathy plus optic disc swelling.

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ABSTRACT

Background: Hypertensive retinopathy (HTNR) is a recognized complication of hypertension. Early diagnosis is crucial for the mitigation of more severe complications such as retinal detachment and loss of vision by the timely institution of appropriate management strategies. In addition, HTNR findings are a useful risk stratification tool for acute coronary events and strokes, two leading causes of disability adjusted life years (DALYs) worldwide. Paucity of data exists on the prevalence and associated risk factors for HTNR in Sub Saharan Africa.

Objectives: To determine the prevalence and associated risk factors for HTNR at Moi Teaching and Referral Hospital (MTRH).

Methods: This was a cross-sectional study conducted among patients with hypertension attending the medical out-patient clinic at MTRH between January and April 2018. The study population included 640 patients on follow up for hypertension in this duration. Systematic random sampling was used to select 240 participants. Structured interviewer administered questionnaires were utilized to collect socio-demographic, anthropometric, clinical and laboratory data. Low density lipoproteins-cholesterol (LDL-C) measurement was performed using enzymatic colorimetric method and fundoscopic examination performed using an ophthalmoscope, with all measurements taken on the same visit. Grading of HTNR was done using Mitchell-Wong classification. STATA version 15 was used for analysis and appropriate statistics used to analyse various variables in line with the study objectives. Categorical variables were summarized in frequency tables, percentages and bar graphs. Continuous variables were summarized using means, standard deviations, frequencies, medians and interquartile ranges (IQR). Medians were compared using Wilcoxon-rank sum test. Univariate and multivariate logistic regression models were used to assess associations of the variables with HTNR.

Results: The median age was 59 years (IQR:52,69). The prevalence of HTNR was 23.3% (95%CI: 18.13-29.20) representing 54 participants. Of those with HTNR, 84% (47) had Grade 1, 13% (7) had Grade 2 and 3% (2) had Grade 3. Chi square p values for age (p=0.001), blood pressure control (p=0.004) and duration of hypertension (p=0.017) showed association with the occurrence of HTNR. On multiple logistic regression, age had an Odds Ratio (OR) of 1.3 (95% CI: 1.026-1.086), Stage 2 HTN had OR 3.66 (95%CI: 1.40-9.50) and duration of HTN of more than 15 years had OR 3.69 (95%CI: 1.10-12.28). Body mass index and LDL-C measurements did not show any association with HTNR.

Conclusion: HTNR is a common finding in this population with its mild form (Grade 1) predominating. Longer duration after diagnosis, advanced age and uncontrolled BP were strongly associated with the occurrence of HTNR.

Recommendation: Routine screening of HTNR should be part of the evaluation of patients on follow up for HTN, especially those with other additional risk factors. Prospective studies are required to further evaluate how elevated BP and risk factor control impacts prognosis of both vision and other vascular complications.

CHAPTER ONE: INTRODUCTION

1.1: Background

Hypertensive retinopathy is a recognized complication of systemic hypertension which can result in irreversible loss of vision (Wong & Mitchell, 2004). Hypertension continues to be a major global health issue with approximately one billion people affected worldwide (Grosso, Veglio, Porta, Grignolo, & Wong, 2005) and prevalence projected to be as high as 30% by 2025 (Haldar, 2013).

The prevalence of hypertension will keep rising as life expectancy increases (Kayima, Wanyenze, Katamba, Leontsini, & Nuwaha, 2013). However, challenges in the awareness, management and control means recognition and adequate treatment remains sub optimal. These challenges translate to poor control of blood pressure with a concurrent increased risk for development of complications such as hypertensive retinopathy (Kabedi, Mwanza, Lepira, Kayembe, & Kayembe, 2014), (H. A. Van Leiden et al., 2003).

Hypertensive retinopathy (HTNR) occurrence can also be used in projecting the risk for the development of even more serious complications of hypertension such as strokes, coronary heart diseases and heart failure. This association is because the cerebral and coronary circulation share anatomical and physiological properties with retinal circulation by providing a reflection of this vasculature which is not ordinarily accessible (Akhter et al., 2013).

A diagnosis of hypertensive retinopathy can be reliably made by direct observation of the fundus by use of an ophthalmoscope. An ophthalmoscope is a simple hand held device with a light source which is used to visualize the retina. Numerous studies have also found ophthalmoscopy to be a useful clinical tool in the risk stratification

for the development of strokes and coronary heart disease (Flood, Rochtchina, Wang, Mitchell, & Smith, 2006) and appears in many guidelines for hypertension worldwide (Mancia et al., 2013). Coronary artery disease and stroke represent the top two leading causes of death worldwide and a significant cause of mortality(Haldar, 2013). Hypertension has been identified as one of the major risk factors for the development of these conditions (Hasan, Hussein, & Haji, 2011)(Tien Y Wong & Mitchell, 2004).

The STEPwise survey, which is the WHO recommended surveillance approach for non-communicable diseases that seeks to establish a standard methodology in defining core variables for surveys, surveillance and monitoring instruments especially in low and middle income countries. It aims to achieve data comparability over time and between countries and therefore offering an entry point for these countries to get started in non-communicable disease (NCD) prevention and control activities.

The most recent STEPwise survey in Kenya was conducted in 2015 with 4433 eligible participants being sub-analysed. The overall age-standardized prevalence for hypertension was 24.5% (95% confidence interval (CI) 22.6% to 26.6%). Among individuals with hypertension, only 15.6% (95% CI 12.4% to 18.9%) were aware of their elevated blood pressure. Among those aware only 26.9%; (95% CI 17.1% to 36.4%) were on treatment and 51.7%; (95% CI 33.5% to 69.9%) among those on treatment had achieved blood pressure control. (Mohamed et al., 2018)

The burden of complications will therefore continue to rise as many patients with hypertension remain undiagnosed and those who are diagnosed remain poorly controlled with subsequently increased occurrence of complications. Hypertensive retinopathy is a recognized complication of hypertension associated with reversible

loss of vision, however persistent elevation of blood pressures can cause even more adverse effects with permanent loss of vision through retinal detachment and optic nerve atrophy.

Studies have shown that even for persons with well controlled BPs, the presence of findings of HTNR confers double the risk for occurrence of strokes (Klein, Heiss, Hubbard, & Duncan, 2004)(Tucker et al., 2017). It is therefore crucial that this category of patients undergo regular fundus examination as an add-on to routine monitoring and their risk profiles sufficiently stratified to aid in comprehensive management and to mitigate the occurrence of these catastrophic complications. In addition, early diagnosis of HTNR, especially the proliferative variant of advanced grades of hypertensive retinopathy require urgent referral to an Ophthalmologist to avoid loss of vision (Ong et al., 2013). Primary doctors therefore need to be equipped with these skills to make prompt diagnosis and early referral as needed.

1.2: Problem Statement

Hypertensive retinopathy is a significant cause of retinal and optic nerve disease accounting for 7.7% of the ocular and retinal diseases, as found in a study of 903 hypertensive patients in Nigeria (Oluyeye et al., 2016). The development of retinal changes has also been found to be a predictor for life threatening complications such as strokes and coronary heart disease (Ong et al., 2013).

Hypertension remains a significant healthcare problem whose incidence continues to rise globally (Haldar, 2013). Numerous studies reveal that the levels of blood pressure control remains inadequate, with the reasons for this poorly understood (Asgedom, Gudina, & Desse, 2016)(Addo, Smeeth, & Leon, 2009)(Hasan et al., 2011).

In a study done in Nyeri Level 5 Hospital in 2014, (Mutua et al., 2014) found only 33.4% of the known hypertensives were well controlled on medications. Another study done in Zimbabwe found that BP was not adequately controlled in 67.3% of the respondents (Goverwa et al., 2014). With inadequate blood pressure control, the development of complications such as HTNR significantly increase (Wong, T.W, 2013). A study done among hypertensive patients in Nigeria found that up to 13% of vitreoretinal diseases were associated with hypertension (Falase, Stewart, & Sliwa, 2012).

There is however paucity of data on the prevalence, diagnosis, symptomatology and risk factors for hypertensive retinopathy in Western Kenya, information which can be useful in prevention of adverse ocular complications and also guide in risk stratification and management of hypertensive patients.

1.3: Study Justification

A review of the patient records shows the MOPC clinic in MTRH follows up approximately 100 patients per week, approximately 40% of whom were on follow up for hypertension, representing a significant disease burden. Other specialized clinics such as the Diabetes out-patient clinic have an even higher percentage of hypertensive patients, a study done by Ndege et. al., 2014 found that up to 85% of the diabetics were also hypertensive (Ndege, Diero, Owiti, Anjichi, & Siika, 2014). This study seeks to determine the prevalence and grading of hypertensive retinopathy which has not been done in MTRH despite the large number of patients on follow up for hypertension.

Hypertension is a common cause of morbidity both regionally and worldwide, with recognized complications such as retinopathy, renal failure and cerebrovascular

complications (Haldar, 2013). Development of hypertensive retinopathy, especially in advanced stages represents a significant marker of end organ damage with devastating consequences which can lead to loss of vision through retinal detachment, optic nerve ischaemia and retinal haemorrhages (Grosso et al., 2005).

Routine fundoscopy is a readily available, effective and reliable tool in the diagnosis of HTNR. Vascular changes of HTNR are the common denominator in the development of complications of hypertension. These vascular changes can be first observed by use of a fundoscope (Kabedi et al., 2014).

Early diagnosis of HTNR is therefore useful in preventing more devastating complications of HTNR which can result in loss of vision. In addition, determining the prevalence of HTNR will help in management of hypertensive patients by providing for better risk stratification and closer follow up of patients noted to have developed retinal changes which can be used in predictor for cerebral and coronary complications irrespective of BP control (Ong et al., 2013). This will in turn have a positive impact on reducing the incidence of complications among patients on care for hypertension and early referral for specialized care as appropriate.

1.4: Research Question

What is the prevalence and risk factors for hypertensive retinopathy in the Medical Outpatient clinic in MTRH?

1.5: Objectives

1.5.1 Broad Objective

To determine the prevalence and describe associated risk factors for hypertensive retinopathy among patients attending the MOPC in MTRH.

1.5.2: Specific Objectives

1. To determine the prevalence of hypertensive retinopathy among hypertensive patients attending MOPC in MTRH.

2. To describe the associated risk factors (age, BP measurement, duration of blood pressure, LDL levels and obesity) for the development of hypertensive retinopathy among patients attending MOPC in MTRH.

CHAPTER TWO: LITERATURE REVIEW

Hypertensive retinopathy refers to the spectrum of retinal changes that occur in patients with systemic hypertension. (Ong et al., 2013). These signs include focal and generalized signs occurring consequent to initial physiological auto-regulation of the retinal vasculature. However, they subsequently relate to breakdown of these auto-regulatory pathways due to modulation in the dynamics of perfusion pressure and pre-capillary arterioles by endothelial derived molecules such as endothelins, thromboxane A2, prostaglandins and nitric oxide (Anderson et al., 2006).

Retinal blood vessels differ from other systemic blood vessels in the three ways. Firstly, the retina is devoid of sympathetic nerve supply. Secondly, there is autoregulation of blood flow and finally the presence of the blood-retinal barrier. In the event of increased blood pressure, the effect is transferred directly to the vessels causing vasoconstriction. Additional rise in blood pressure overcomes this mechanism and causes damage to the muscle layer and the endothelium. (Fraser-Bell S et al., 2017)

Retinal changes which can occur in hypertension include retinal arteriolar narrowing, arteriovenous nicking (AVN), retinal hemorrhages, microaneurysms and in severe cases, optic disc and macular edema (Bhargava, Ikram, & Wong, 2012). These signs develop due to acute and chronic elevations in blood pressure. The initial response is diffuse and localized vasospasm of the retinal arterioles with consequent narrowing (generalized arteriolar narrowing and focal arteriolar narrowing (FAN), respectively). Arteriolar narrowing is a defining sign of hypertensive retinopathy and reflects vasoconstriction as an auto-regulatory response, in an attempt to control the volume of blood received by the retinal capillary bed. It is most commonly seen in the early phase of hypertensive retinopathy before the onset of sclerosis can be detected.

Chronic elevation of the blood pressure leads to venule compression owing to the structural changes in the arterioles, resulting in arteriovenous nicking (Addo et al., 2009).

Sustained hypertension leads to progression to an ‘exudative’ stage in which flame-shaped retinal hemorrhages and cotton wool spots are observed. Severe hypertension ultimately causes blood retinal barrier disruption leading to an exudative stages during which flame shaped haemorrhages and cotton wool spots appear. The pathological process of arteriosclerosis sets in and the changes that ensue are generally reversible. Permanent changes cause opacification of the arteriolar wall, sometimes known as ‘silver’ and ‘copper’ wiring. Consequent compression of venules due to artherosclerotic arteriolar changes could also occur leading to arteriovenous nicking. (Erden & Bicakci, 2012)

Higher uncontrolled hypertension leads to a malignant stage with optic disc and macular edema due to raised intracranial pressure. This stage is associated with poor prognosis for survival (Browning, Mengher, Gregson, & Amoaku, 2001). Hypertension also causes damage to the retinal nerves and choroid plexus causing neuropathy and choroidopathy respectively (Oluleye, Olusanya, & Adeoye, 2016).

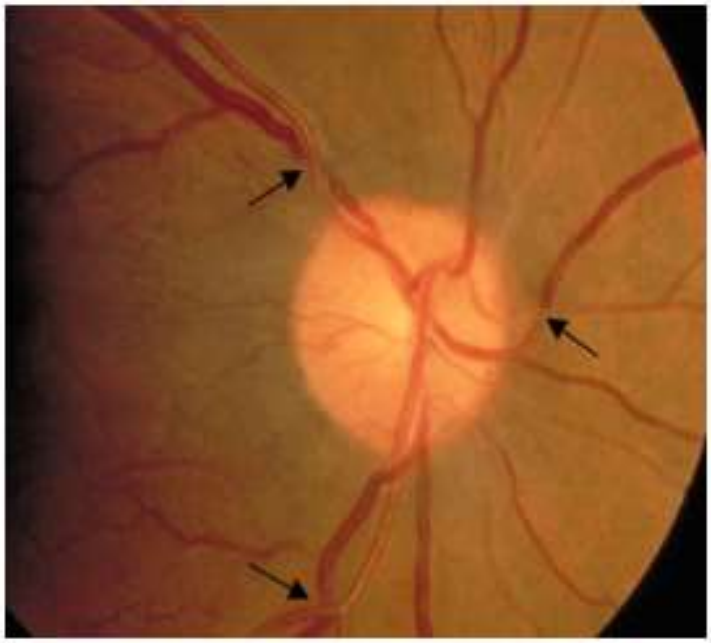
Hypertensive retinopathy has been graded by the Mitchell-Wong classification as follows;

Grade	**Features**
Mild (Retinal arteriolar signs)	Generalized arteriolar narrowing, focal arteriolar narrowing, arteriovenous nicking, opacity (“copper wiring”) of arteriolar wall, or a combination of these signs
Moderate (Retinopathy-like lesions)	Retinal haemorrhages (blot-shaped, dot-shaped, or flame-shaped), micro aneurysms, cotton wool spots, hard exudates, or a combination of these signs
Malignant	Signs of moderate retinopathy plus optic disc swelling

The retinal appearance of the various grades of HTNR are illustrated in the pictures below.

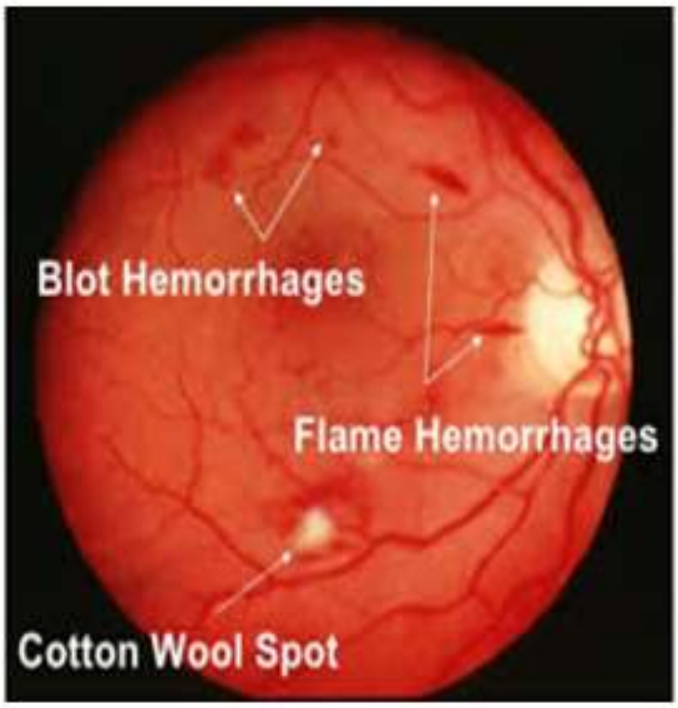
Grade 1 HTNR

Generalized arteriolar narrowing, focal arteriolar narrowing, arteriovenous nicking, opacity ("copper wiring") of arteriolar wall, or a combination of these signs



Grade 2 HTNR

Retinal haemorrhages (blot-shaped, dot-shaped, or flame-shaped), micro aneurysms, cotton wool spots, hard exudates, or a combination of these signs



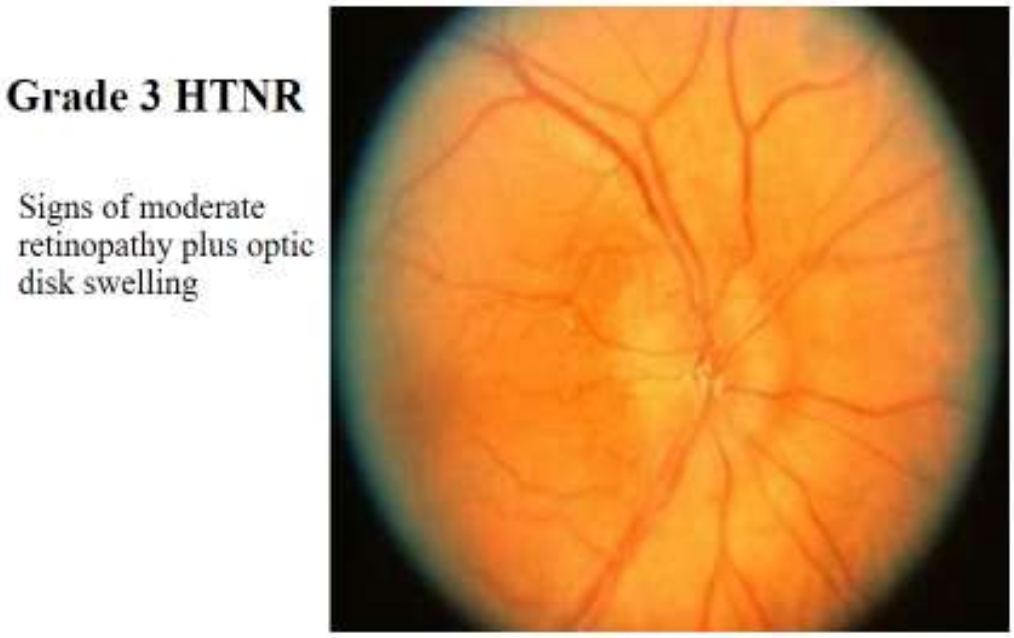


Figure 1: Grading of HTNR (Adapted from *Investigative Ophthalmology and Visual Science*, *48*(9), 4019

An alternative classification system is the Keith Wagener Barker (KWB) classification which has been used in numerous studies on HTNR. It classifies the stages of HTNR as below;

Grade 1 - Mild generalized arteriolar attenuation with broadening of the arteriolar light reflex.

Grade 2 - Marked generalized narrowing and focal attenuation of arterioles associated with deflection of veins at arteriovenous crossings.

Grade 3 - Grade 2 changes plus copper wiring of arterioles, banking of veins distal to arteriovenous crossing, flame-shaped haemorrhages, cotton wool spots and exudates.

Grade 4 - Grade 3 plus silver wiring of arterioles and papilledema.

The Mitchell Wong (MW) classification of HTNR is currently preferred over other the KWB classification as it combines both Grade 1 and Grade 2 HTNR (Aissopou et al, 2015). This provides better clinical predictive value for progression to advanced stages of HTNR and hypertension related organ damage (Mayuri, Bhagvara et al, 2013). Furthermore, there is more intra observer and inter observer variation between the initial two grades of HTNR using the KWB classification making examination findings difficult to standardize as compared to the MW classification. The MW classification thus provides better reliability, reproducibility and accuracy in examination of retinal changes in HTNR. In addition, the Mitchell Wong classification is also more applicable for the stratification of cardiovascular risk of hypertension (Downie et al., 2013).

Table 1: Fundoscopic Findings with Increased Pressure
The table below summarizes the pathophysiological mechanisms, signs and the fundoscopic findings on retinal examination**.**

Pathophysiological Mechanism	Signs	Fundoscopic Findings
Acute hypertension	Vasospasm Increased vascular tone	Generalized arteriolar narrowing
Chronic hypertension	Intimal thickening, media wall hyperplasia, hyaline degeneration of arterioles Compression of venules at their common adventitial crossings.	Diffuse and focal narrowing (‘copper-wiring’) and opacification (‘silver-wiring’) of arteriolar walls ‘Arteriosclerotic stage’: arteriovenous nicking
Severe hypertension	Inner blood–retinal barrier breakdown, necrosis of vascular smooth muscle and endothelial cells. Persistent damage to retinal microvasculature.	Exudative stage’: exudation of blood (retinal hemorrhages) and lipids (hard exudates) Nerve fiber layer ischemia (cotton wool spots)
Accelerated hypertension	Intracranial pressure elevation, fibrinoid necrosis of choroidal arterioles	Hypertensive optic neuropathy/‘malignant retinopathy’Optic nerve ischemia . Optic disc swelling (papilloedema), Hypertensive choroidopathy Infarction of segment of choriocapillaris , Retinal pigment epithelium (RPE) infarcts: Elsching's spots .Linear RPE hyperplasia over infracted choroidal arterioles (Siegrist's streaks) Localized bullous neur

The diagnosis of hypertensive retinopathy can be reliably made by use of dilated fundoscopy which has shown comparable sensitivity and specificity compared to other methods of detecting retinal lesions such as the fundus camera (Figueiredo Neto et al., 2010).

2.1: Associated Factors for the Development of HTNR.

2.1.1: Blood Pressure Control

Sustained elevation of BP is the main driver for the development of hypertension complications such as retinopathy, hypertensive nephropathy, cerebrovascular events and adverse cardiac events such as myocardial infarction. It is the single most important factor in the development of associated complications of hypertension all other factors held constant. Uncontrolled hypertension has been identified as the main cause of accelerated development of hypertensive retinopathy.(Tien Y Wong & Mitchell, 2004). Adequate control of hypertension poses a major challenge, a study done in the US (Kotchen & Hajjar, 2003) revealed that less than 25% had desired control of hypertension. Closer home, a study done in Congo on 159 participants found that only 19.5% of the patients had optimum blood pressure control (Kabedi et al., 2014).

Locally, a study done in health centres in Ruiru sub-county, Kiambu county by (Karonjo, 2016) revealed that only 21% had proper control of hypertension despite being on follow up in the MOPC clinics. A study done in Kenyatta National Hospital by Mongi et al.,2016 had only 35% of the participants with well controlled hypertension, further illustrating that good control of blood pressure remains difficult to achieve (Mongi, Nyamu, Karimi, & Maru, 2016).

Numerous studies have reported a strong association between various hypertensive retinopathy signs and both subclinical and clinical cerebrovascular disease and stroke mortality. (Tien & McIntosh, 2005), (Ong et al., 2013)(Tien Y Wong & Mitchell, 2004). In the Artherosclerotic Risk for Communities (ARIC) study, individuals with retinal haemorrhages, micro-aneurysms and cotton wool spots, as defined from photographs, were two to four times more likely to develop an incident clinical stroke

within 3 years, even when controlling for the effects of blood pressure, cigarette smoking, lipids and other risk factors.

The presence of hypertensive retinopathy can be used to provide additional predictive value for stroke risk in persons with MRI-defined subclinical cerebral disease. Individuals with both MRI-defined white matter lesions and hypertensive retinopathy had 18 times more likelihood [relative risk (RR) 18.1; 95% confidence interval (CI) 5.9–55.4] to suffer from a stroke event as compared to those without either white matter lesions or hypertensive retinopathy (H. A. Van Leiden et al., 2003).

Subclinical and clinical coronary heart disease and congestive heart failure have also been associated with HTNR signs. In the ARIC study, it was found that participants with retinal changes consistent with HTNR changes were twice as likely to develop cardiac failure than those without HTNR after controlling for the other risk factors (RR 1.96; 95% CI 1.52–2.56). The association of HTNR is even stronger in low risk individuals such as those not having diabetes, hypertension or cardiac failure. In this population HTNR changes predicted a 3 fold increase of heart failure (RR 2.97, 95% CI 1.49–5.91). The suggested explanation for this observation is that retinal damage presents microvascular injury which is also occurring in the myocardium from hypertension and other systemic processes (H. A van Leiden et al., 2003).

The three categories of hypertensive retinopathy as per the Mitchell-Wong classification have different predictive values for the development of adverse complications. Grade 1 HTNR has weak association with stroke, coronary heart disease and cardiovascular mortality. Grade 2 HTNR has a strong association with stroke, congestive heart failure, renal dysfunction and cardiovascular mortality.

Grade 3 HTNR is associated with visual loss and mortality mostly from cerebrovascular events (Henderson, Bruce, Newman, & Biousse, 2011).

2.1.2: Body Mass Index (BMI)

Obesity is a known consequence of altered glucose metabolism and causes organ injury such as arteriosclerosis, retinopathy and renal dysfunction through the action of leptin (Uckaya et al., 2000). Leptin is biochemically a peptide hormone produced primarily in the fat cells (adipocytes). This hormone is elevated in the plasma of most of the obese individuals. Due to its impact in metabolic function it causes endothelial cell dysfunction, inflammation, vascular smooth muscle cell proliferation and matrix alteration. As this advances stiffness, loss of elasticity and reduced caliber of luminal vessels is observed. These processes are key in the development of HTNR (Dubey & Hesong, 2006).

Increased occurrence of HTNR in obesity was also observed in the Hoorn Study conducted in Netherlands in 2003 among a diabetic and non-diabetic population of 233 participants. Central obesity was found to be independently related to incidence of retinal haemorrhages, microaneurysms, hard exudates and cotton-wool spots in the non-diabetic general population and revealed an Odds ratio of 8.67 in the highest tertiles of BMI (H. a van Leiden et al., 2003). In the ARIC study, features of HTNR were related to larger waist circumference, a marker of abdominal obesity. (Tien Y Wong & Mitchell, 2004)

Other studies however have not found an association between hypertensive retinopathy and abdominal obesity (Zhang, Zhao, Li, & Wang, 2018). Associations between hypertensive retinopathy signs with other atherosclerosis risk factors have also been investigated with conflicting results (Erden & Bicakci, 2012).

Cross-sectional associations of retinal arteriolar narrowing and AV nicking with biomarkers of inflammation (e.g. white blood cell counts) and endothelial dysfunction (e.g. von Willebrand factor) have been reported in the ARIC study and by other groups. These studies indicate that the signs of hypertensive retinopathy may be related to vascular processes beyond blood pressure control. The study seeks to find any association between BMI and the occurrence of HTNR in our setting.

2.1.3: LDL Levels

LDL levels are key in the pathogenesis of atherosclerosis. Increased LDL levels has been shown to have an association with the development of hypertensive retinopathy. This association was shown in a study carried out on 135 people with hypertension and established an association between high LDL levels and the development of retinopathy.(Adhikari, Gautam, Bekoju, Basnet, & Bhandari, 2018)

In a larger study performed in the Netherlands on 626 participants found that high LDL levels had a significant impact on the occurrence of retinal changes, especially exudative changes which are associated with the damage of the arteriolar wall.(H. A. Van Leiden et al., 2002)

Another study performed by Badhu. B et al, 2003 in India also found a statistically significant correlation between increased levels of LDL and the occurrence of hypertensive retinopathy. Some studies however have found no association of LDL on the occurrence of retinopathy, an example is a study done in Turkey on 655 participants (Erden & Bicakci, 2012). Another study performed in India also found no association between lipids and the occurrence of HTNR (Pai & Hegde, 2019).

In atherosclerosis, modified lipoproteins such as oxidized LDL initiate inflammation in the intima which causes vascular damage through immune and complement

mediated mechanisms in the retinal vasculature (Matsuura, Kobayashi, Tabuchi, & Lopez, 2006). An elevated quantity of free LDL-C causes formation of free radicals which are injurious to the eye and can cause exudative forms of hypertensive retinopathy. This study seeks to determine associations between the development of hypertensive retinopathy and levels of LDL among hypertensive patients on follow up in MTRH.

2.1.4: Age

Increasing age has also been shown to be an associated factor for the development of HTNR in numerous studies.(Kabedi et al., 2014)(Chao et al., 2007) and (Asgedom et al., 2016).

With increasing age there is more visible atherosclerotic changes, which are made worse with the presence of hypertension. Elastin fibres gradually suffer age related degradation and with this associated loss of function. This reduced function leads to load bearing onto stiffer collagen fibrils and increases arterial stiffness (Kohn, Lampi, & Reinhart-King, 2015). In addition, the aging process causes collagen deposition in the arteries increases and results in the shifting of the collagen elastin balance and could explain the association of HTNR with increase in age (Anderson, 2006).

A few studies however have not found an association between age and HTNR. An example of a study which did not show an association between HTNR and age is a study performed in Malawi which had 104 participants enrolled (Kayange et al., 2018).

This study seeks to explore the association of age in the development of hypertensive retinopathy.

CHAPTER THREE: METHODOLOGY

3.1: Study Design

A cross sectional hospital based study was conducted.

3.2: Study Site

The study was conducted in the general medical outpatient clinic at Moi Teaching and Referral Hospital. This hospital is located in Eldoret town, Uasin Gishu County, which is approximately 300 kilometres north-west of Nairobi.

MTRH is a Level 6 facility serving as a teaching hospital for Moi University, School of Medicine. It also serves as the main referral hospital for the western part of Kenya and has a bed capacity of about 990 patients.

3.3: Target Population

Patients attending the general medical outpatient clinic on follow up for hypertension in MTRH.

3.4: Sample Size

The sample size was calculated to be 240 respondents derived from using the Fishers formula shown below using a prevalence of 19.4% derived from a study done by Sunday, Bolutife and Abiodun in Nigeria, carried out on 903 hypertensive patients.

$$\mathbf{n} = \frac{Z^2\ \hat{p}(1-\hat{p})}{\mathbf{e}^2}$$

Where

n=sample size; z=level of confidence (95%); p=prevalence (19.4%); e=acceptable sampling error (5%).

3.5: Sampling Technique

Systematic random sampling was used in this study. On average there are about 40 hypertensive patients who attend the MOPC on a weekly basis. The study period was four months, giving a total of approximately 640 patients on follow up for hypertension during the study period gives a value of 2 for k. Every second eligible patient was enrolled into the study.

3.6: Eligibility Criteria

3.6.1 Inclusion Criteria

Patients above the age of 18 years with hypertension on follow up in the MOPC clinic at MTRH.

3.6.2: Exclusion Criteria

1. Patients with diabetes mellitus as it is likely to confound the retinal findings for HTNR.
2. Patients with conditions precluding fundoscopy such as cataracts or ocular trauma.
3. Patients who are pregnant since Tropicaimide, the mydriatic agent used in this study is a 'Category B' in pregnancy. This category means that animal reproduction studies have failed to demonstrate a risk to the foetus and there are no adequate and well controlled studies in pregnant women or that animal studies have shown adverse effects, but adequate and well - controlled studies in pregnant women have failed to demonstrate a risk to the foetus in any trimester.

3.7: Data Collection

Data Collection Instruments included;

1. Digital blood pressure machine (Omron Healthcare, Inc., 1200 Lakeside Drive, Bannockburn, Illinois 60015).
2. A Welch Allyn™ 3.5V standard ophthalmoscope.
3. Accu-Chek™, Aviva Plus glucometer.
4. Researcher administered questionnaire, designed by the PI (Appendix 1)

3.8: Study Procedure

The Principal investigator was trained for a period of two months, prior to the commencement of the study to the satisfaction of the Consultant in the Ophthalmology department before data collection commenced to ensure quality assurance.

On MOPC clinic days, which take place every Tuesday and Thursday, the PI and the research assistant reviewed the files and screened for those who meet the inclusion criteria. After being identified, the rationale of the study was explained after which informed consent was obtained for participation in the study. A random blood sugar measurement was taken using the Accu-Chek™, Aviva Plus glucometer to exclude diabetes mellitus (DM). As per the American Diabetes Association guidelines (ADA) a random blood glucose reading of more than 11.1 mmol/l was classified as diabetes mellitus or a history of follow up for diabetes.

After screening for DM the research assistant or the principal investigator took the blood pressure measurement and other anthropometric measurements. Measurement of blood pressure was performed using Omron M2 compact upper arm blood pressure monitor (Omron Healthcare, Inc., 1200 Lakeside Drive, Bannockburn, Illinois 60015). The arm cuff position was maintained at the heart level during rest in a seated

position and readings taken after at least 30 minutes of being seated in the waiting area.

Blood pressure measurement was taken by the examiner with the arm on rested on the table. The cuff was wrapped on the arm with the bottom of the cuff one centimetre above the elbow, while allowing for finger breadth allowance on application of the cuff. The machine was switched on, the cuff inflated and the blood pressure reading recorded. Three blood pressure readings were taken at least one minute apart with the average of the last two being recorded as per the American Heart Association recommendation (Muntner et al., 2019). The questionnaire was then administered.

After the primary clinician review, the participants were taken to the Ophthalmology unit. A drop of the mydratic agent, Tropicaimide was instilled in each eye and after fifteen minutes a fundoscopic examination performed on the dilated pupils by the Principal investigator.

A Welch Allyn™ 3.5V standard ophthalmoscope was used for examination. Features of HTNR were examined for and the findings classified as per the Mitchell Wong classification into mild (Grade 1), moderate (Grade 2) and malignant (Grade 3) HTNR and the findings documented for analysis. All fundoscopy examination findings performed in the Ophthalmology unit and were confirmed by either an Ophthalmologist or an ophthalmic clinical officer at the same sitting and the findings recorded in the questionnaire.

A blood sample was then drawn for measurement of LDL levels in the Ampath Reference Laboratory which is an accredited laboratory facility. After verbal consent was obtained, a tourniquet was applied to the arm distal to the elbow. The brachial vein in the ante-cubital fossa was identified and the site cleaned with antiseptic

solution. The vein was punctured gently by a gauge 21 needle at an angle of approximately 30 degrees and 2 ml of venous blood drawn. The needle was then withdrawn from the vein and an adhesive bandage applied at the punctured site to help stop bleeding. The sample was then put in a labelled red top vacutainer and taken to the lab for measurement of LDL. The needle and syringe was then be disposed of safely in a sharps container. Clinical findings were documented in the patients file and parameters requiring intervention were relayed to the primary clinician for the appropriate management to be instituted.

The study procedure is summarized in the schematic diagram below.

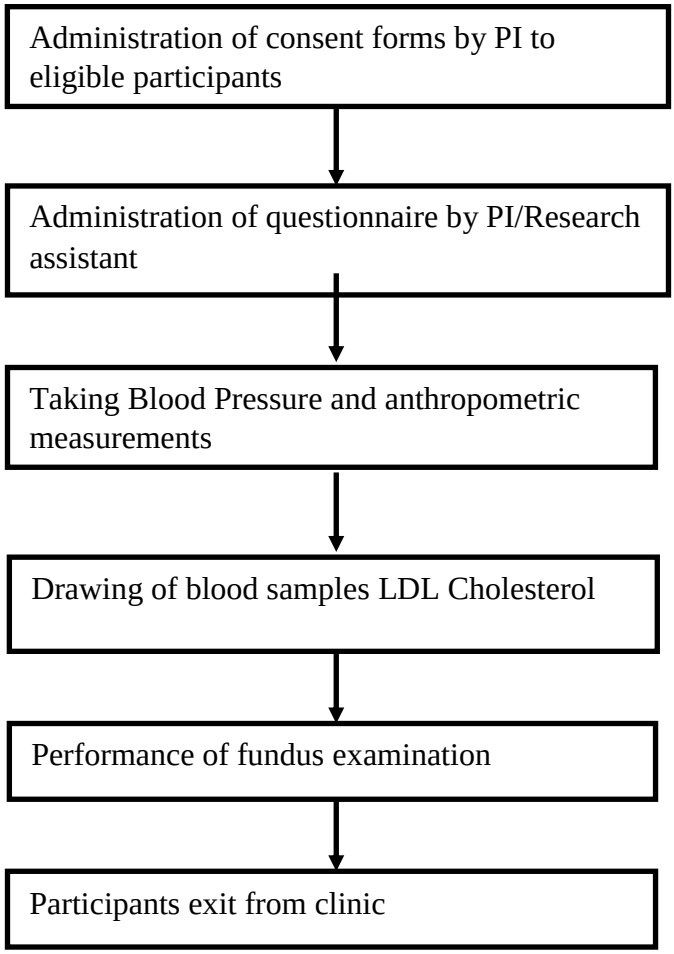


Figure 2: Study Procedure.

3.10 Measures

Independent Variables – Age, BP measurement, duration of hypertension, LDL levels, Body Mass Index (Appendix 10).

Dependent Variable – Hypertensive retinopathy.

3.11 Data Analysis

Validation of the data was done and subsequently entered into the computer for analysis using SPSS Version 24. Descriptive statistics such as the median and corresponding interquartile range were used to summarize continuous variables such as age, BMI, serum and LDL-C levels. Frequencies and the corresponding percentages were used to summarize categorical variables such as gender, level of education, and marital status.

The first objective addressing the prevalence of HTNR was expressed as a percentage of the study population who were diagnosed to have hypertension as per the operational definition. The second objective of the study explored association between hypertensive retinopathy and categorical independent variables assessed using Pearson's Chi Square Test, Fisher's Exact Test and Wilcoxon Rank Sum Test.

Chi- Square Test of Independence was used to compare distribution of hypertensive retinopathy across comparison groups of categorical variables that showed homogeneity in their distribution with a cell size of >20 in all 4 cells of the 2 by 2 table were subjected to this test.

Fisher's Exact Test, a non-parametric alternative to Chi-Square Test was used to test association between categorical variables which violated Chi-Square Test assumptions and had small cell sizes of <20 in any of the 4 cells in the 2 by 2 tables.

Wilcoxon Rank Sum Test, a non-parametric comparing median between two populations was used to determine if the difference in median age between participants with hypertensive retinopathy and those without hypertensive retinopathy was significant.

Logistic regression model was used to assess the variables associated with hypertensive retinopathy. Bivariate logistic regression model was used to calculate the unadjusted odds ratios (OR), and the multivariate logistic regression model was used to calculate the adjusted odds ratios. In the multivariate model, the variables that were significantly associated with hypertensive retinopathy in the bivariate analysis were included.

The univariate analysis that showed significant relationships ($p < 0.20$) between exposure variables and hypertensive retinopathy were included in the multivariate analysis. These variables were age, duration of hypertension and elevated BP reading. Odds ratio and the corresponding 95% confidence intervals were reported. Results were presented using tables, pie charts and bar graphs. The sample size calculated was adequately powered to explore these associations.

3.12 Ethical Considerations.

Ethical clearance was obtained from the Institutional Research and Ethics Committee (IREC) of Moi Teaching and Referral Hospital (MTRH) and Moi University School of Medicine.

A written informed consent was obtained from all the participants and strict confidentiality maintained when recruiting and handling data.

The objectives and purposes of the study were clearly explained to eligible participants in English or Kiswahili prior to inclusion into the study with only the

patients who gave informed consent being enrolled. Patients who declined to participate in this study were not discriminated and continued receiving routine care. The clinician directly managing the patient did not take part in recruitment or in consenting to avoid coercion.

All information for the participants was kept confidential during the conduct of the study and abnormal results were communicated to the participants and the relevant clinician for the appropriate management to be instituted. There was no conflict of interest in this study

The benefits of participating in this study to the patient was that they would get to know their health status as regards to low density cholesterol levels, anthropometric measurements and the presence of hypertensive retinopathy. Patients with conditions precluding fundoscopy such as cataracts were referred to the Ophthalmologist for further management.

There was no known risk for the study to the participants, there was however pain for drawing blood from the antecubital fossa. Only blood samples intended for study were drawn and thereafter discarded after analysis. All data received was entered in a computer and protected using passwords with data for the study participants being placed under lock and key.

CHAPTER FOUR: RESULTS

4.1: Recruitment Schema

There were two hundred and sixty two patients eligible for enrollment in the study from the Medical out-patient clinics which run on Tuesday and Thursday every week. There were 6 participants who were excluded due to Diabetes mellitus and another 6 due to cataracts. Of the remaining 250 who were eligible for enrollment, 10 declined consent leaving 240 participants who were subsequently recruited in the study. The study procedure is illustrated in the schema below.

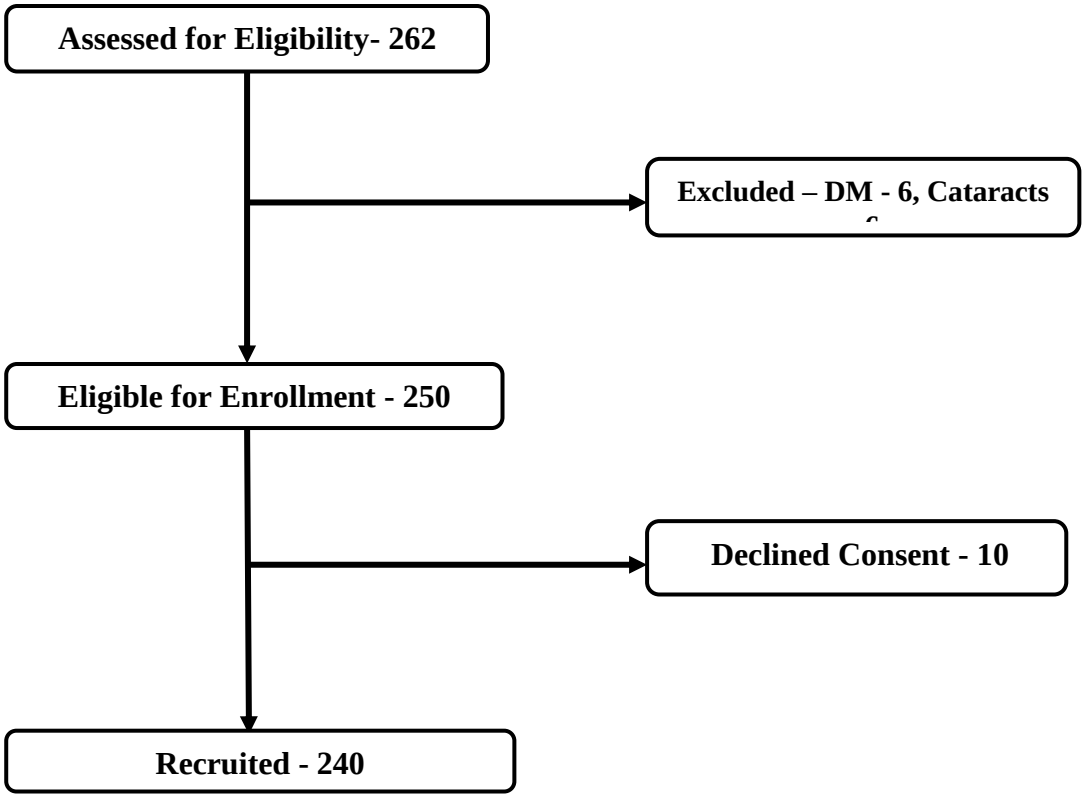


Figure 3: Recruitment Schema

4.2: Demographics.

The median age of the participants was 59 years (IQR:52,69). Of the 240 participants, 185 females representing 77% and 55 males being 23% of the participants.

Most of the participants were of primary level of education at 44.6 % representing 107 participants. Only 7.1% had tertiary level of education representing 17 participants. The socio- demographic characteristics of the participants are expressed in table 2 below.

Table 2: Socio-demographic Characteristics

Variable	**Freq/Median**	**%/ IQR**
Age in years	59	(52,69)
Gender		
Female	185	77 %
Male	55	23 %
Level of Education		
None	50	20.8%
Primary	107	44.6%
Secondary	66	27.8%
Tertiary	17	7.1%

4.3: Duration of Hypertension

Most of the participants had been hypertensive for less than 5 years representing 62.9% of the participants. Only 7.1% of the respondents reported being had been hypertensive for more than 15 years. These findings for the duration of hypertension among the study participants are illustrated in the table 3 below.

Table 3: Table Showing Duration of Hypertension Among Participants

Duration of HTN	Freq	%
Less than 5 years	151	62.90
6-10 years	54	22.50
11- 15 years	18	7.50
More than 15 years	17	7.10

4.4: Anthropometric Characteristics

In this study, 109 (45.4%) of the participants were overweight, defined as a BMI of between 25.0 to 29.9kg/m^2. Obesity which was defined as a BMI of more than 30 kg/m2 was observed in 71 (29.6 %) of the participants, indicating that a total of 75% of the participants were in the overweight and obese categories. A normal BMI of 18-24 kg/m2 was observed in 56 participants (23.3%). These findings are expressed in table 4 below.

Table 4: Table Showing Anthropometric Characteristics

BMI	Freq	%
Underweight	4	1.70
Normal	56	23.30
Overweight	109	45.40
Obese	71	29.60

4.5: Waist Circumference

Abnormal waist circumference was observed in 142 (59.2%) of the participants. Abnormal waist circumference was defined as a circumference of more than 88 centimetres in females and 102 centimetres in males. These findings are illustrated in the pie chart below.

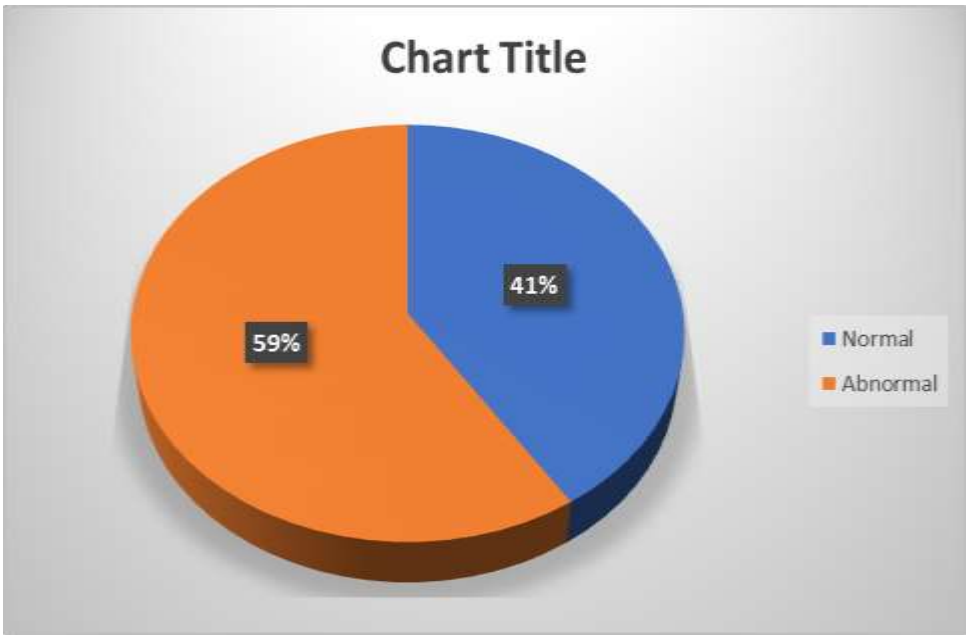


Figure 4: Pie Chart Showing Abdominal Circumference

4.6: Blood Pressure Medications

In this study, 123 (51.2%) of the participants were on two antihypertensive agents, 38 (32.9 %) were on one agent and 38 (15.8%) were on a combination of three agents. CCBs were the most prescribed class of anti-hypertensive with 107 (44.6%) participants on them for hypertension. 58 participants (24.2%) were on ARBs, 44 (18.3%) were on ACEI, 30 (12.5%) were on a thiazide diuretic and 4 (1.7%) were on a beta blocker.

These findings are illustrated in the figure below.

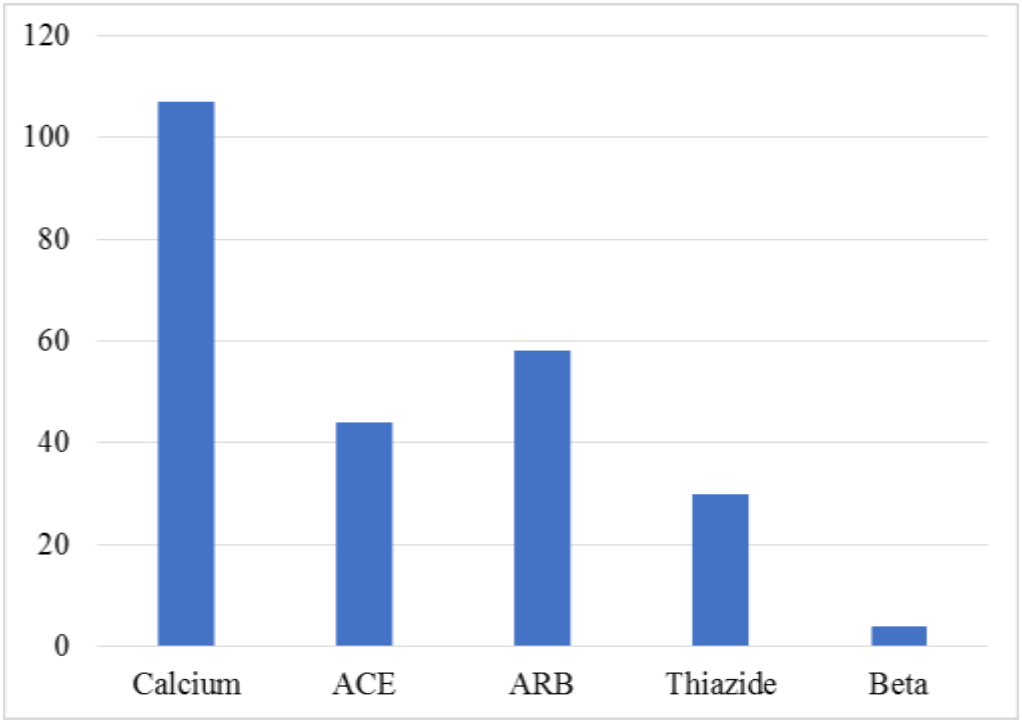


Figure 5: Bar Graph Showing Antihypertensive Agents Used.

CCBs – Calcium channel blockers, ACEI – Angiotensin Converting Inhibitors, ARBs – Angiotensin Receptor Blockers, Beta blockers.

4.7: Levels of LDL among Participants

Of the 240 participants enrolled in the study, 202 participants were found to have normal LDL – C levels with 38 participants having hypercholesterolemia. These findings are illustrated in the pie chart.

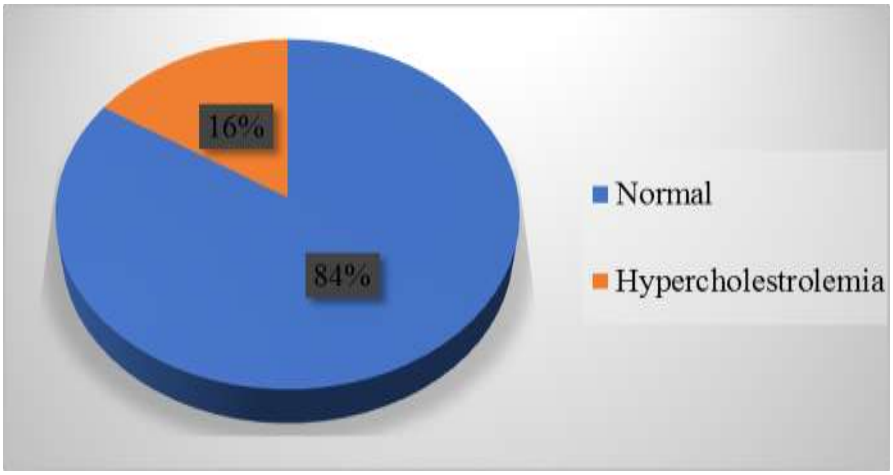


Figure 6: Pie Chart Showing LDL Levels among Participants

4.8: Home BP Monitoring

Home BP monitoring refers to taking blood pressure measurements at home using a personal blood pressure machine. Only 21 patients were performing home monitoring of BPs, while 219 participants did not have a BP machine at home for self-monitoring. These findings are illustrated in the pie chart below.

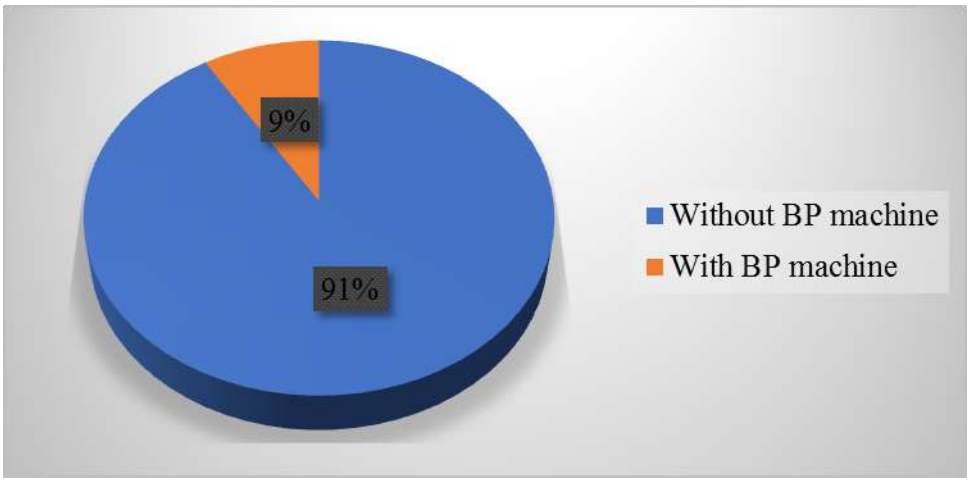


Figure 7: Pie Chart Showing the Participants Performing Home BP Monitoring

4.9: Objective 1: Prevalence of Hypertensive Retinopathy .

The prevalence of hypertensive retinopathy was 23.3% (95%CI: 18.1, 29.2). Of those with grade 1 HTNR, the most common presentation was AV nipping having 40 participants representing 70.37%, arteriolar attenuation was found in 7(12.96%) participants and both features found in 2 (3.7 %) participants. Grade 2 HTNR was found in 7 (12.5%) of those with HTNR. Cotton wool spots were seen in 2(3.5%) participants and 5 (9.0%) participants had retinal haemorrhages.

Grade 3 HTNR was observed in 2 participants representing 3% of participants with HTNR. The findings were optic disc swelling and a macular star.

The occurrence of the various grades are expressed in the pie chart below which depict a high prevalence of grade 1 HTNR.

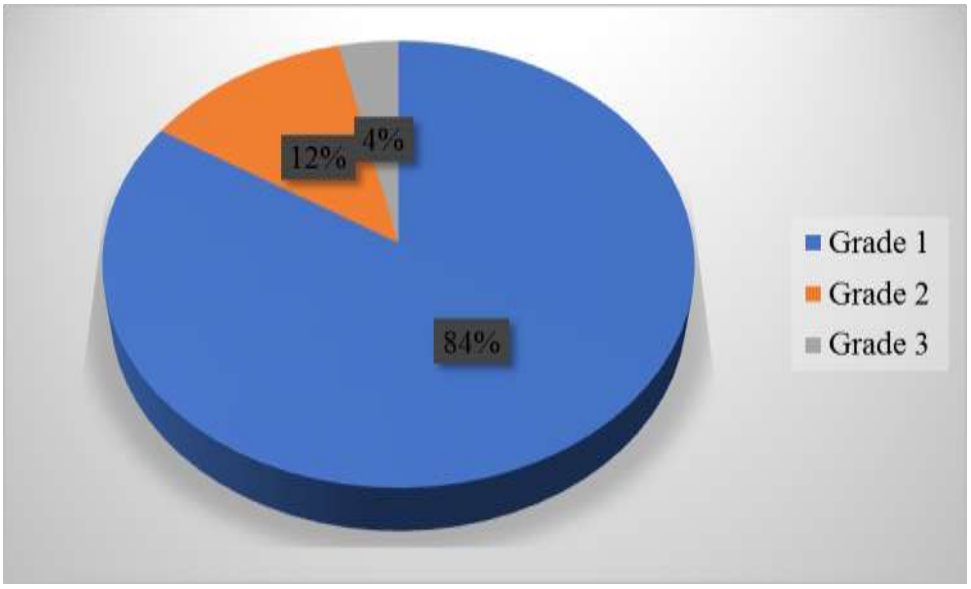


Figure 8 : Pie chart Showing the Grades of HTNR Among Study Participants.

4.10: Objective 2 : Associated Risk Factors for the Development of Hypertensive Retinopathy (Age, Duration of High Blood Pressure, LDL levels and Obesity).

The median age for participants with HTNR was 64 years which was higher than the mean of persons without HTNR at 57 years with a significant p-value of 0.0002. There was no preponderance of sex for the development of HTNR.

The duration of hypertension associated positively with the occurrence of HTNR with a P value of 0.004. BMI and waist circumference did not have an association with the occurence of hypertension. LDL measurements also did not have an association with the occurrence of HTNR. Blood pressure control however had an association with the occurrence of HTNR with a p-value of 0.017.

The variables of interest were subjected to a univariate logistic regression analysis and the findings are represented as below. Variables with a p-value of less than 0.05 were subjected to multiple logistic regression analysis.

These results are illustrated in the table below:

Table 5: Univariate Analysis of the Variables

	HTNR		
	No	**Yes**	
Variable	**Freq (Row%)**	**Freq (Row%)**	**P-value**
Age in categories			
Median (IQR)	57 (50,58)	64 (59,75)	0.0002
Sex			0.431[2]
Female	144 (77.8)	41 (22.2)	
Male	40 (72.7)	15 (27.3)	
Duration of HTN			0.004[3]
Less than 5 years	121 (80.1)	30 (19.9)	
6- 10 years	43 (79.6)	11 (20.4)	
11-15 years	13 (72.2)	5 (27.8)	
More than 15 years	7 (41.2)	10 (58.8)	
BMI			0.162[3]
Underweight	4 (100)	0 (0)	
Normal	42 (75)	14 (25)	
Overweight	89 (81.7)	20 (18.3)	
Obese	49 (69)	22 (31)	
Waist Circumference			0.230[2]
Normal	79 (80.6)	19 (19.4)	
Oversize	105 (73.9)	37 (26.1)	
LDL			0.372[2]
Normal	157 (77.7)	45 (22.3)	
Hypercholestrolemia	27 (71.1)	11 (28.9)	
BP control			0.017[2]
Normal	63 (86.3)	10 (13.7)	
Grade1	74 (77.1)	22 (22.9)	
Grade2	47 (66.2)	24 (33.8)	
Home BP Monitoring			0.612[3]
No	165 (76)	52 (24)	
Yes	17 (81)	4 (19)	

[1] Wilcoxon rank sum test [2]Chisquare test [3] Fishers' exact test

4.11 : Multiple Logistic Regression

Variables of interest which were significant in the univariate analysis being age, duration of hypertension and blood pressure measurement were subjected to multiple logistic regression.

On the multiple regression, age, duration of hypertension of more than 15 years and Grade 2 hypertension remained significant. Significance was assigned for a value of less than 0.05. Grade 2 hypertension is a BP reading of more than 160mmHg systolic and a diastolic BP reading of more than 110mmHg or both.

The results of the multiple logistic regression analysis are expressed in the table below.

Table 6 : Outcomes of Significant Variables on Multiple Logistic Regression Model

Variable	Odds Ratio	P-value	[95% Conf.	Interval]
Age in years	1.056	0.000	1.026	1.086
Duration of HTN				
Less than 5 years	1.000			
6-10 years	1.147	0.751	0.492	2.672
11-15 years	1.356	0.620	0.407	4.511
More than 15 years	4.050	0.020	1.246	13.162
Hypertension control				
Normal				
Grade1	2.195	0.091	0.883	5.456
Grade2	3.961	0.005	1.529	10.262

CHAPTER FIVE: DISCUSSION

This study sought to find the prevalence and associated factors for hypertensive retinopathy (HTNR) among patients attending the Medical Out-patient clinic in Moi Teaching and Referral Hospital, Eldoret.

5.1: Prevalence of HTNR

The prevalence of HTNR was 23.3% representing 56 of the 240 participants. Grade 1 HTNR was the most common among those with HTNR representing 47 participants (83.9%). Grade 2 was found in 7 participants (12.6 %) with Grade 3 found in 2 (3.5%) of the participants.

These findings were similar to the findings of (Oluyeye et al., 2016) conducted in Nigeria which found an overall prevalence of 19.4%. Of these 93.14% were grade 1, 5.7% were grade 2 and 1.1% with Grade 3. Our study findings are also similar to the findings of (Mondal et al., 2017) carried out in India carried out on a sample size of 313 hypertensive patients and found a prevalence of 29.4%. The table below shows the respective occurrence of the grades of HTNR among the study participants.

Table 7 : Comparison of Prevalence of HTNR

Author	**Grade 1(%)**	**Grade 2 (%)**	**Grade 3 (%)**
Rakwach et. al.,2020	**84**	**13**	**3**
Mondal et. al.,2017	79	20	1
Oluyeye et al, 2016	93	6	1

Some studies however found a significantly lower prevalence. A study done by (Akhter et al., 2013) on 836 participants in Bangladesh found a much lower prevalence of 5.4%. This could be attributed to the relatively younger age of the study population, whose mean age was 46 years against 59 years in our study. Studies with

a younger average age also tended to have a lower prevalence of HTNR which would suggest age related changes and possible longer duration of hypertension.

Other studies however have determined a much higher prevalence of HTNR than this study. An example is a study done in rural Malawi by (Kayange et al., 2018) on 108 participants found a prevalence of HTNR of 75%. This relatively higher prevalence in the Malawian study and other studies with relatively higher BP recordings could be attributed to poor control of hypertension, only 17.7% having good control of blood pressure with 82.3% being poorly controlled. Our study found good BP control in only 30% of the participants. The Malawian study cited poor compliance to medications for poor control and attributed it to distance from health facility and frequent stock outs. The prevalence of HTNR findings were also replicated in a study carried out in Ghana on 219 patients with hypertension by (Addo et al., 2009) which found a prevalence of 69.4% for HTNR and only 11.4% had well controlled BPs.

Grade 3 HTNR was consistently an uncommon occurrence with most studies having a prevalence of less than 3% as seen in this study and studies carried out by Mondal et al.2017 in India and Oluyeye et al, 2017 in Nigeria. In the ARIC study which had a sample size of 2907 participants, only one participant had grade 3 HTNR (Ong et al., 2013). The rare occurrence of this advanced grade is probably due to earlier diagnosis and management of hypertension with extremely high blood pressures required for papilledema to occur being rare, in as much as adequate control remains elusive. The eye also has protective mechanisms against adverse effects of hypertension. A breakdown in these adaptive measures and prolonged, extremely elevated pressures are required for Grade 3 HTNR to occur (Grosso et al., 2005)

Studies have found the prevalence of HTNR has been found to be higher in the black race. The occurrence of complications such as HTNR also seems to be disproportionately higher in persons of African origin. After adjusting for age and gender, hypertension status, current and past blood pressure, the black race had a doubling in the incidence of HTNR. (Tien Yin Wong, 2003).

In this study, the entire study population was of the black race and this could in part explain the high prevalence that was found. Differences in the susceptibility to retinal vascular damage from elevated blood pressure may contribute to the higher prevalence of HTNR. Early vascular aging, depressed RAAS mechanisms, genetically determined abnormal sodium handling and elevated vascular reactivity have also been suggested, however the exact mechanisms for racial differences remain unclear (Tien Yin Wong et al., 2003)

5.2: Age

The median age for participants with HTNR was 64 years which was higher than the mean of persons without HTNR at 57 years with a significant p-value of 0.0002, which was significant when subjected to multiple logistic regression. Other studies have found age to be strongly associated with the occurrence of HTNR, similar to the findings of the study carried out by (Kabedi et al., 2014)(Chao et al., 2007) and (Asgedom et al., 2016). In all these studies, the average age of persons with HTNR was significantly higher than the participants found not to have HTNR.

The study performed by (Kayange et al., 2018) however did not find an association of age with the occurrence of HTNR. This is likely due to the distribution of age in this study as the ages between the population of those with HTNR and those without HTNR were similar, 56 years and 57 years respectively. This minimal difference in

the ages may therefore explain the lack of statistical association of age with HTNR that was found.

5.3: Duration & Control of Hypertension

The duration of hypertension was associated with the occurrence of HTNR with a p-value of 0.004 and remained significant when subjected to multiple logistic regressions. This finding was similar to other studies which found that the duration of HTN had a strong association with the occurrence of HTNR. This is thought to result from the prolonged duration of stress on the vasculature from prolonged duration of hypertension (Kabedi et al, 2014), (Mondal et al., 2017).

In the early stages of hypertension, most of the fundus blood vessels are normal. However, with the development of the disease, the formation of atherosclerotic plaques gradually increases the thickness and decreases the diameter of blood vessels, followed by the development of arteriosclerosis and the corresponding retinopathy. (Zhang et al., 2018). Some studies however did not show an association between HTNR with the duration of hypertension (Kayange et al., 2018) found no such association, this is likely because the stratification of duration of hypertension was not long enough to determine it as a factor of the development of HTNR as the categorization was less than 3 years, 3-4 years and more than five years. In addition, a limited sample size of 104 participants may have contributed to the lack of association.

Table 8: Comparison of Duration of Hypertension

Author	Sample Size	< 5 yrs	6 - 10 years (OR)	10-15 years (OR)	> 15 years (OR)	P value
Rakwach et al., 2020 (Kenya)	**240**	**19.9**	**20.4 (1.14)**	**27.8 (1.35)**	**58.8 (4.05)**	**0.004**
Adhikari et al, 2018(India)	135	28.9	58.3	83.3	100	<0.001
Mondal et. al 2017,(India)	313	23.84	30.86	38.27		0

Blood pressure control was associated with the occurrence of HTNR with a p-value of 0.017. When subjected to a multiple logistic regression was found to be statistically significant. This was similar to other studies done which found that control of HTN had a strong correlation with the occurrence of HTNR (Kabedi et al, 2014),(Zhang et al., 2018).

Poorly controlled blood pressure subjects the retinal vasculature to increased arterial wall stress which causes reflex vasoconstriction and subsequent arteriolar attenuation. At higher blood pressures, exudative processes lead to retinal haemorrhages and cotton wool spots. Malignant hypertension (Grade 3) can cause papilledema seen as swelling of the optic disc and is a medical emergency requiring prompt treatment to prevent occurrence of strokes, heart attacks and blindness (Browning et al.,2001).

The study by Kayange et al., 2018 however found no association in the occurrence with the development of HTNR. Up to 83% of the participants however were poorly controlled and this may have weakened the potential association between BP control and development of HTNR. These comparisons are highlighted in the table below.

Table 9: Comparison of Blood Pressure Control

BP Control					
Author	**Sample Size**	**Normal(%)**	**Stage 1 (OR)**	**Stage 2 (OR)**	**P Value**
Rakwach et al., 2018 (Kenya)	**240**	**13.70%**	**22.9% (2.04)**	**33.8 (3.66)**	**0.017**
Chao et al, 2007, USA	4674	4.20%	6.7% (1.5)	18% (4.5)	<0.001
Kayange et.al,2014, Malawi	104	72.20%	77.80%	75.40%	0.68

5.4: Body Mass Index

In this study, BMI was not associated with the occurrence of HTNR. Studies have revealed inconsistent associations between increased BMI and the development of HTNR. Some studies have shown that increased BMI could be associated with HTNR by the action of leptin (Barker, 2016).

Leptin is an endocrine hormone synthesized from adipocytes and its main function glucose and lipid metabolism. Leptin levels are elevated in persons with increased BMI, which in turn increases its associated angiogenic properties on the retina (Al Maskari & Alnaqdy, 2006). Angiogenesis refers to the formation of new blood vessel formation from preexisting ones and plays important roles in many physiological and pathological conditions such as wound healing, retinopathies and atherosclerosis (Tahergorabi Z, 2015)

Additionally, obesity causes microvascular dysfunction associated with increased blood pressure and decreased insulin sensitivity. These findings explain the occurence of impaired microvascular function to the development of obesity-related microangiopathy (De Jongh, Serné, Ijzerman, De Vries, & Stehouwer, 2004). This

study found no association between BMI and HTNR unlike the study by (Adhikari et al., 2018) which probably found an association owing to the higher BMI sample mean of 34 kg/m2. In this study, the sample mean for BMI was 28.2kg/m2.

Studies that found no association between BMI and the occurrence of HTNR seem to have had a lower sample mean and the population were generally leaner. These findings corroborated with the findings of (Chao et al., 2007) which had a sample mean of 23kg/m2 and the Hoorn study carried out in the Netherlands which evaluated BMI as a risk factor with a mean of 25.9kg/m2 (H. A. Van Leiden et al., 2003).

Table 10: Comparison for Body Mass Index

Investigator	Sample Size	BMI < 30	BMI> 30 (OR)	Sample Mean	P value
Rakwach et al., 2020 (Kenya)	**240**	**20.10%**	**30.9% (1.8)**	**28.2**	**0.162**
Chao et al, 2007, USA	4674	5.80%	7.4% (1.3)	23	0.045
Adhikari et al, 2018(India)	135	28.80%	37% (6.08)	34	0.0001

5.5: LDL Levels

LDL was not associated with the occurrence of HTNR. These findings are similar to the findings of the study done by (Zhang et al., 2018) on 228 patients which did not find an association between HTNR and levels of LDL. It has been hypothesized that low-density lipoprotein leads to atherosclerosis or thickening of the arterial walls. This occurs when the LDL seeps into the arterial walls through damaged junctions of the endothelial cells that line the arterial wall. The residual thickening narrows the channel and decreases blood flow through the vessel, which can lead to an infarction and other HTNR changes.

Studies performed by (Akhter et al., 2013) in Bangladesh on 836 participants and (Adhikari et al., 2018) on 240 participants in India both found an association with the occurrence of HTNR. This is likely because in both studies the percentage of the participants with an elevated LDL was 70% and 89% respectively and thus could explain the association with HTNR.

In this study, only 28% of the participants had an elevated LDL and this could explain the lack of association reported. The association between levels of LDL and HTNR have been inconsistent in numerous studies (Erden & Bicakci, 2012).

Table 11: Comparison of LDL

Author	Sample Size	Normal (%)	Abnormal (%)	Sample Mean	P value
Rakwach et al., 2020 (Kenya)	**240**	**22.0%**	**28% (1.21)**	**3.1**	**0.372**
Akhter et al, 2013, Bangladesh	836	30.0%	70% (1.31)	7.2	<0.001
Adhikari et al, 2018(India)	135	54.4%	89.9%(6.69)	4.8	<0.001

5.6: Blood Pressure Control

This study also evaluated the control of hypertension among patients attending MOPC in MTRH. Of the patients attending MOPC at MTRH only 30.4 % were found to be well controlled. 40% were found to have grade I hypertension and 29.5% having grade 2 hypertension.

Good control of hypertension remains a challenge in many clinical units. A study done by (Mohamed et al., 2018) in Kenya found only 51.7 % to be well controlled. The poor BP control in our study could possibly be explained by the high percentage of participants who were obese and overweight, representing 75% of the study population, a factor known to predict poor BP control. Obesity causes sympathetic

nervous system activation which plays a crucial role in the occurrence of hypertension related to obesity. The infinite feedback gain shifts the graph to the right in obese persons due to increase in renal tubular absorption and expansion of extracellular fluid volume thus increased blood pressure. In addition, obesity causes insulin resistance and inflammation resulting in endothelial damage and subsequently development of poorly controlled hypertension (Kotsis, Stabouli, Papakatsika, Rizos, & Parati, 2010)

Poor control of hypertension is frequently associated with non-compliance to medications. Serial surveys show an increasing prevalence of hypertension in developing countries, possibly caused by urbanization, aging of population, changes to dietary habits and social stress. High illiteracy rates, poor access to health facilities, bad dietary habits, poverty and high costs of drugs could also contribute to poor blood pressure control. (Mohsen Ibrahim, 2012). A separate study however will help determine the specific reasons for poor BP control in our set up.

Home monitoring of blood pressure has also been shown to have a pivotal role in the management of hypertension. A meta-analysis of 18 studies concluded that home monitoring translates to better control of hypertension in conjunction with other BP lowering strategies (Tucker et al., 2017). In this study, only 8.75 % had access to home BP monitoring. The likely cause of this poor uptake of home BP monitoring includes financial constraints and a possible lack of knowledge on the benefits of home BP monitoring as an adjunct to better control of BP (Asgedom et al., 2016)(Adhikari et al., 2018).

CHAPTER SIX: CONCLUSION & RECOMMENDATIONS

6.1: Conclusions

HTNR prevalence is high, grade 1 being by far the most common. Poor BP control, increasing age and duration since diagnosis of HTN was associated with the occurrence of HTNR. BMI and LDL were not found to have an association with HTNR.

6.2: Recommendations

Fundoscopy should be done for patients on follow up for hypertension. There is need to have better and more aggressive BP lowering strategies to mitigate the occurrence of HTNR, especially with increasing age and duration of hypertension. We advocate for future prospective studies to further evaluate for development of coronary artery disease and strokes in this population as a risk stratification tool for hard CVD outcomes.

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APPENDICES

Appendix 1: Questionnaire

Prevalence and Associated Risk Factors for Hypertensive Retinopathy in Moi Teaching and Referral Hospital, Eldoret, Kenya.

Name: _____ **Age**: _____ **Sex**: Male Female

Medication:

1. _____ 2. _____

3. _____ 4._____

Weight (Kg):_____ **Height** (Cm): _____ **BMI:**_____ **Abd. Circ:** _____

RBS Measurement _____

Blood Pressure (mmHg) 1st Reading Systolic _____ Diastolic _____

2nd Reading Systolic_____ Diastolic_____

3rd Reading Systolic_____Diastolic _____

Lipid profile (mg/dl): LDL _____

Known duration of hypertension

i. Less than 5 years _____
ii. 6 – 10 years _____
iii. 11-15 years _____
iv. More than 15 years _____

What is your level of education?

i. Primary _____

ii. Secondary_____

iii. Tertiary_____

Do you smoke cigarettes Yes No

Have you had a previous eye check-up: Yes No

Visual acuity: R/E _____ L/E _____

Presence of Hypertensive Retinopathy Yes No

Left Eye	**Right Eye**

Classification of HTNR

- No apparent HTNR ☐
- Mild HTNR ☐
- Moderate HTNR ☐
- Severe HTNR ☐

Comments on Treatment/Referrals/Follow-up:

_____

_____

_____

*Interviewer Signature*_____

Appendix 2: Consent Form.

Preamble

I am Dr. Opolle M .Rakwach, a medical practitioner registered by the Kenya Medical Practitioners and Dentists Board. I am pursuing my Master's degree in Internal Medicine at Moi University.

I would like to enroll you into my study which entails taking your body measurements, BP readings, drawing a blood sample for laboratory examinations and examining your eyes for any changes for hypertension related eye changes using a fundoscope.

Before participating in this research, it is important that you read and understand the information contained in this form. The information provided here will provide information to help you decide whether you wish to participate in this study. In case you need to make any clarifications, please address these concerns to the study personnel, who will be able to answer them. Kindly do not sign this form until you are sure you understand the information in this form.

Purpose of the Research

Hypertension can cause organ damage, including damage to the eyes which is referred to as hypertensive retinopathy. This study aims to find out development of any changes in your eyes caused by hypertension and the risk factors associated with the development of these changes.

Description of the Research

This study will entail collection of basic demographic data such as age, sex. A questionnaire will then be administered by the research assistant/ PI inquiring about information such as duration of hypertension, the medications you have been on. A measurement of your random blood sugar will be taken by pricking your finger and the reading recorded. Body indices such as weight, abdominal circumference, blood pressure will then be taken. After this measurements you will then be taken to the Ophthalmology unit where tests will be done to assess your visual acuity. After this a medication will be administered into your eyes which will help in making your eyes easier to examine by increasing the size of your pupil.

The findings of this examination will then be recorded. A blood sample will then be taken from your arm for a lab test to measure your level of low density lipoproteins (LDL).

Benefits

There will be **NO** direct benefits to you by participating in this study and there will be no money or gifts offered for participation. However the knowledge obtained in this study will be generate useful knowledge in the management of hypertension and the development of eye problems related to hypertension.

Harms

This study poses minimal risk to you. There might be slight pain and discomfort while obtaining blood specimen. There may also be blurring of vision for a short period of time after administration of the drug to your eye, this will resolve within less than 30 minutes.

Alternatives to Participation

You do not need to participate in this study to receive treatment for your condition. If you choose not to participate, you will still receive medical care for hypertension.

Costs to Participation

There are no costs to you should you decide to participate in this study.

Participation and Withdrawal

Participation in research is voluntary. You may refuse to participate or answer any questions, or withdraw from the study at any time. If you elect not to participate, your care will not be interrupted. If you choose to withdraw from the study, the data you provided up to the point of termination (withdrawal) and information about your health status may still be used for analysis.

Study Title: Prevalence and Risk Factors for Hypertensive Retinopathy (HTNR) at Moi Teaching and Referral Hospital (MTRH), Eldoret, Kenya.

The research study has been explained to me, and my questions have been answered to my satisfaction. I have been informed of the alternatives to participation in this study. I have the right not to participate and the right to withdraw without affecting the quality of medical care at MTRH. As well, the potential harms and benefits of participating in this research study have been explained to me. I have been told that I have not waived my legal rights nor released the investigators or involved institution from their legal and professional responsibilities.

I know that I may ask now, or in the future, any questions I have about the study. I have been told that records relating to me and my care will be kept confidential and that no information will be disclosed without my permission unless required by law. I have been given sufficient time to read the above information.

_____ _____ _____

Name of Participant Signature of Participant Date/Time

I have explained to the above Participant the nature and purpose, the potential benefits, and possible risks associated with participation in this research study. I have answered all questions that have been raised.

_____ _____ _____

Name of Person Obtaining Consent Signature of Person Obtaining Consent Date/Time

I am the Principal Investigator responsible for the conduct of this study at MTRH and I have delegated the explanation of this study to this participant to _____ (Name of person conducting the consent discussion).

_____ _____ _____

Name of Investigator Signature of Investigator Date

This study has been approved by the Institutional Research and Ethics Committee (IREC) of Moi University/Moi Teaching and Referral Hospital.

For further clarifications please contact IREC using the address below.

The Chairman IREC,

Moi Teaching and Referral Hospital,

PO Box 3,

Eldoret.

Tel: 33471/2/3

My cell phone number is: 0721374353

B. Kiswahili

Jina langu ni Daktari Opolle Rakwach.

Nimehitimu udaktari na nimesajiliwa na bodi ya madaktari ya Kenya (Kenya Medical Practitioners and Dentists Board). Mimi ni msomi wa shahada ya pili (Masters) ya udaktari katika chuo kikuu cha Moi. Utafiti wangu unahusu mabadiliko ya macho yanayosababishwa na ugonjwa wa shinikizo la damu.

Utafiti huu pia utahitaji kutoa damu ili ipimwe katika maabara,

Matatizo ya Shinikizo la Damu

Shinikizo la damu yaweza kusababisha madhara machoni. Uchunguzi wa macho na matibabu kwa wakati unaofaa yanaweza kuzuia uharibifu huu.

Katika utafiti huu, sampuli ya damu itatolewa kwa minajili ya uchunguzi katika maabara. Uchunguzi utajaribu kuidhinisha vipimo vinavyoweza kusababisha kudhorora kwa macho katika ugonjwa wa shinikizo la damu.

Matokeo yatasalimishwa na kuwekwa siri. Utapata matibabu bila kubaguliwa bila kuzingatia uweko wako katika uchunguzi huu na utaelezwa kuhusu vipimo.

Uchunguzi huu umehidhinishwa na kamati ya kusimamia utafiti (Institutional Research and Ethics Committee-IREC) katika chuo kikuu cha Moi na hospitali ya rufaa ya Moi

Iwapo unahitaji maelezo zaidi tafadhali wasiliana na IREC kwa kutumia anwani ifuatayo.

Mwenyekiti IREC,

Moi Teaching and Referral Hospital,

S. L. P. 3,

Eldoret.

Simu: 33471/2/3

Nambari yangu ya rununu ni: 0721374353.

Hidhini Yako

Walio na miaka 18 na zaidi

Nimeelezwa kwamba ninashiriki katika utafiti wa kuchunguza uharibifu wa macho katika ugonjwa wa shinikizo la damu.

Mchunguzi amenihakikishia kuwa matibabu yangu yataendelea bila hitilafu bila kuzingatia kushiriki kwangu katika utafiti huu.

Aidha nafahamu kuwa hamna gharama kwangu katika utafiti huu.

Sahihi: _____

Jina: _____

Tarehe:_____

Appendix 3 : Procedure for drawing Venous blood

Venous blood was drawn for a lipid profile. The procedure was explained to the participant and the verbal consent obtained. Universal safety procedures were observed. Venous blood was drawn from the median cubital vein in the antecubital fossa of the less dominant upper limb.

Below is an overview of the steps that were followed;

1. Arm was selected and tourniquet placed on the arm above the draw site. The median cubital vein was selected.
2. Site was cleansed with a sterile alcohol/ methylated spirit in the preparation pad.
3. A needle was inserted into the vein and the collection tube engaged.
4. Two millilitres of blood was obtained in the plain Vacutainer (Red top)
5. Tourniquet was removed once the quantity of blood required is obtained.
6. A small band aid was placed on the venous draw site.
7. The blood collection tube was labelled with the patients' information.
8. Blood collection tubes was batched in groups and taken to the accredited lab for analysis.

Appendix 4: Procedure for Measuring Height

The height of participants was taken to calculate the body mass index (BMI), which is weight relative to height. The height was measured with a mechanical roll up measuring tape (Seca 260) with wall attachment in the observation room.

Height was measured using the procedure below;

1. The participant was asked to remove their footwear (shoes, slippers, sandals, etc) and headgear (hat, cap, hairbows, comb ribbons etc). However, those with a scarf or veil were not asked to remove them (Measurement taken over light fabric)
2. Participant was asked to stand next to the measuring board/ wall facing the research assistant/ investigator.
3. Participant was asked to stand with feet together, heels against the measuring board/ wall, knees straight.
4. Participant was asked to look straight ahead and not tilt their head up.
5. The research assistant/ investigator makes sure the eyes are at the same level as the ears.
6. The measure arm was moved gently down onto the head of the participant and he/ she was be asked to breath in and stand tall
7. The height was read in centimetres at the exact point.
8. The participant was asked to step away from the measuring board/ wall.
9. The height measurement in centimetres was recorded in the recording form.

Appendix 5: Procedure for Measuring Body Weight

The weight of the participant was taken to calculate the body mass index (BMI) which is the weight relative to the height. The weight was measured using the 762 dial scale at the Observation room.

The steps for measuring weight were as below

1. The scale was placed on a firm, flat surface.
2. Participant was asked to remove their footwear(Shoes, slippers, sandals etc)
3. The participant was asked to step on the scale with one foot on each side of the scale.
4. Participant was asked to stand still, face forward, place arms on the side and wait until they were asked to step off.
5. The weight in kilograms was recorded in the participant data sheet.
6. The participant was be asked to step off the scale.

Appendix 6: Procedure for Measuring Waist Circumference

Waist circumference measurements was taken to provide additional information on overweight and obesity. A constant tension tape was used to take this measurement. A private area was necessary for this procedure.

Below were the steps to be followed in measuring waist circumference.

1.The measurement was to be taken over light clothing.

2.Standing on the side of the participant, the investigator/ research assistant was to locate the last palpable rib and the top of the hip bone. The participant was asked to assist in locating these points.

3.The participant was asked to wrap the tension tape around them and then position the tape at the midpoint of the last palpable rib and the top of the hip bone, making sure to wrap the tape over the same spot on the opposite side.

4.The research assistant/ investigator was then to check that the tape is horizontal across the back and front of the participant and as parallel to the floor as possible.

5.Measurement was to be taken at the end of normal expiration with the arm relaxed at the sides, at the midpoint between the lower margin of the last palpable rib and the top of the iliac crest(hip bone)

6.The waist circumference was then be measured, The measurement shall be read at the level of the tape to the nearest 0.1cm, making sure to the keep the measuring tape snug but not tight enough to cause compression of the skin.

7.The measurement was the recorded in the participant's data sheet.

Appendix 7: Procedure for Measuring Blood Pressure

Blood pressure was measured using an Omron M2 compact upper arm blood pressure monitor (Omron Healthcare, Inc., 1200 Lakeside Drive, Bannockburn, Illinois 60015). The patients was required to have had at least 15 minutes rest in a relaxed sitting position with no tight fitting cloth on the upper arm, or any thick clothing such as sweater.

The steps were as illustrated below;

1. Participant was to be seated upright with the back straight and the right arm placed on the table so that the cuff was at the same level with the heart.
2. Cuff was to be wrapped on the arm so that the bottom of the cuff was at least 1cm above the elbow, with the cuff fastened snugly.
3. Start button was pressed and the cuff would automatically inflate and take the blood pressure reading,
4. Blood pressure and pulse rates results were displayed on the screen of the machine.
5. Blood pressure readings were to be recorded in the participant data sheet.
6. Should an error occur, the cuff was to be deflated and the process repeated.

Appendix 8: Procedure for Drawing Finger Stick Blood

Finger stick blood was drawn for random blood sugar. The procedure was to be explained to the participants and verbal consent obtained. Universal safety procedures were observed. Finger stick blood was drawn from the second and third finger of the less dominant hand.

The steps that were used are as below.

1. Finger and site selected.
2. Finger cleaned with alcohol/ methylated spirit and allowed to air dry to decrease haemolysis and not alter glucose results.
3. Spring activated lancet lightly applied on the finger to get a puncture.
4. First drop of blood will be wiped away.
5. Approximately 2 drops of blood is drawn using the capillary tube.
6. An adhesive bandage is placed on the small puncture.
7. Using the capillary tube, the whole blood is transferred into the glucose electrode of the Accu-Chek™, Aviva Plus glucometer.

Appendix 9: Procedure for Eye examination

The eye examination took place in the Ophthalmology unit. The procedure for eye examination was explained to the participant before the commencement of the examination. The following steps were followed in the examination.

i. Measurement of Visual Acuity

The participant was to stand six metres away from the Snellen chart which is affixed on the wall in a well illuminated room. The participant was then requested to occlude one eye and start reading the Snellen chart. For every line in the Snellen chart three letters will be read. After correct reading of every line the research assistant was to point the next line. This was done until the line which the participant was not able to read. The same procedure was then be followed for the contralateral eye. Visual acuity was defined as number of letters read correctly without glasses if the participant did not have glasses or with glasses if they had them. If a participant's vision was too poor to read any letter on the chart at 6 metres, then she/he was to be tested at 1M, then counting fingers, hand movement, light perception and no light perception in this sequence.

ii. Procedure for Fundoscopy

The participant was seated in a dark room at the Ophthalmology unit. The patient details were then confirmed and a drop of Tropicamide 1% installed in each eye. The participant was then asked to close both eyes for a period of ten minutes to allow the mydriatic effect of Tropicaimide to set in. The macula, retinal vasculature and peripheral retina were then examined independently for features of hypertensive retinopathy. The Mitchell Wong classification was used to classify the various grades of HTNR which has three grades, Grade 1, 2 and 3. These findings were then entered in the questionnaire for analysis. In the event that both eyes do not have congruent findings, the more adverse findings will be used in the classification of HTNR

Appendix 10 : Description of Study Variables.

LDL-C levels.

LDL-C levels were defined as normal if ≤ 4.14 mmol/l, while > 4.14 mmol/l was abnormal as per the Adult Treatment Panel IV (National Cholesterol Education Program/ American Heart Association guidelines).

Body Mass Index (BMI)

BMI was calculated in kilograms per metre square (kg/m2) were categorized using clinically acceptable limits as follows; Underweight <18.5 kg/m2; Normal 18.5-24.9 kg/m2, Overweight 25.0 to 29.9 kg/m2; Obese ≥30.0 kg/m2 as per the National Institute for Health & Care Excellence (NICE guidelines, 2014).

Waist Circumference

A normal waist circumference was defined as a circumference of less than 88 centimetres in females and 102 centimetres for males. Waist measurements above these were defined as abnormal as per the European Patient-Centred Guidelines for Adult Obesity Management, 2017.

Duration of Hypertension

Duration of hypertension was defined as the self-reported period for which a patient has been known to be hypertensive, or the duration that one has been on anti-hypertensive medications.

Appendix 11: IREC Approval

INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

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

MOI UNIVERSITY
COLLEGE OF HEALTH SCIENCES
P.O. BOX 4606
ELDORET

Reference: IREC/2017/130
Approval Number: 0001941

8th September, 2017

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
08 SEP 2017
APPROVED
P. O. Box 4606-30100 ELDORET

Dr. Rakwach Moses Opolle,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

Dear Dr. Rakwach,

RE: FORMAL APPROVAL

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

"Prevalence and Risk Factors for Hypertensive Retinopathy at Moi Teaching and Referral Hospital, Eldoret, Kenya".

Your proposal has been granted a Formal Approval Number: ***FAN: IREC 1941*** on 8th September, 2017. You are therefore permitted to begin your investigations.

Note that this approval is for 1 year; it will thus expire on 7th September, 2018. 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 CEO - MTRH Dean - SOP Dean - SOM
Principal - CHS Dean - SON Dean - SOD

Appendix 12: MTRH Approval

MOI TEACHING AND REFERRAL HOSPITAL

Telephone: 2033471/2/3/4
Fax: 61749
Email: ceo@mtrh.go.ke
P. O. Box 3
ELDORET

Ref: ELD/MTRH/R&P/10/2/V.2/2010

18th September, 2017

Dr. Rakwach Moses Opolle,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

APPROVAL TO CONDUCT RESEARCH AT MTRH

Upon obtaining approval from the Institutional Research and Ethics Committee (IREC) to conduct your research proposal titled:-

"Prevalence and Risk Factors for Hypertensive Retinopathy at Moi Teaching and Referral Hospital, Eldoret, Kenya".

You are hereby permitted to commence your investigation at Moi Teaching and Referral Hospital.

18/09/2017

DR. WILSON K. ARUASA
CHIEF EXECUTIVE OFFICER
MOI TEACHING AND REFERRAL HOSPITAL

CC - DCEO, (CS)
- Director of Nursing Services (DNS)
- HOD, HRISM