

**PATTERN AND ASSOCIATED FACTORS FOR RETINAL VEIN
OCCLUSION AT MUHIMBILI NATIONAL HOSPITAL**

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**Mmed (Ophthalmology) Dissertation
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**PATTERN AND ASSOCIATED FACTORS FOR RETINAL VEIN
OCCLUSION AT MUHIMBILI NATIONAL HOSPITAL**

By

Peter Christian Mlundwa

**A Dissertation Submitted in Partial Fulfillment of the Requirements for Degree
of Master of Medicine (Ophthalmology) of
Muhimbili University of Health and Allied Sciences**

October, 2021

CERTIFICATION

The undersigned certify that they have read and hereby recommend for acceptance by Muhimbili University of Health and Allied Science a dissertation entitled: “*Pattern and associated factors for retinal vein occlusion at Muhimbili National Hospital*”, in (partial) fulfillment of the requirement for the degree of Master of Medicine (Ophthalmology) of the Muhimbili University of Health and Allied Science.

Prof. Milka Mafwiri

(Supervisor)

Date _____

Dr. Celina Mhina

(Co-supervisor)

Date _____

DECLARATION AND COPYRIGHT

I, **Dr. Peter Mlundwa**, declare that this **dissertation** is my own original work and that it has not been presented and will not be presented to any other university for a similar or any other degree award

Signature..... Date.....

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DEDICATION

To my loving wife, Epifania Assey and our children Kasele and Kagusa, for their endless love and support. Also to my parents Dr Christian Mlundwa and Mrs Rose Mlundwa for the encouragement and prayers.

ABSTRACT

Background: Retina vein occlusion (RVO) is among the common causes of visual impairment and blindness especially in middle age and elderly individuals, after diabetic retinopathy. Impaired vision can impact on the ability to carry out everyday tasks, the ability to work, the ability to lead an active social life. RVO is associated with systemic diseases such as hypertension, hyperlipidemia, diabetes mellitus and cardiovascular diseases. Other associated factors include increasing age, glaucoma, peripheral vascular disease, and active cigarette smoking. Knowing the pattern of RVO and associated factors in our setting aids in prompt diagnosis of treatable causes of visual morbidity.

Aim: The aim of this study was to assess the pattern and associated factors for RVO, in patient with RVO attending the retina clinic at Muhimbili National Hospital.

Methodology: A hospital based descriptive cross-sectional study was conducted at the Retina clinic, Muhimbili National Hospital, from June to December 2020. A total of 73 adults aged 18 years and above were enrolled into the study. A detailed history, ophthalmic and systemic examinations, laboratory investigation and optic coherence tomography were performed.

Results: A total of 73 participants with 76 eyes were analyzed. Age ranged from 18 to 85 years with mean age of 60.87 ± 22.3 years. The proportion of RVO was 7.9%. The proportion of retinal vein occlusion increased with increasing age, with more than half (56.1%) of participants being in the age group of 61 years and above. There were more males than females. Majority of the eyes 39(51.3%) had central retinal vein occlusion, 33(43.4%) eyes had branch retinal vein occlusion, and 4 (5.3%) eyes had hemi retinal vein occlusion. Ischemic retinal vein occlusion was seen in 2(6.1%) eyes with branch retinal vein occlusion and 18(46.1%) eyes with central retinal vein occlusion. The common comorbidity were hypertension sixty five (89.0%), hyperlipidemia fifty three (72.6%), diabetes mellitus 46 (49.3%) and glaucoma 15 (20.6%). Thirty (41%) patients with retinal vein occlusion, actively smoked cigarette. Severe visual impairment and blindness were seen in more than

half of the eyes 40(52.6%) and 34(87.2%) eyes were due to CRVO.

Conclusion: Retinal Vein Occlusion is a significant cause of visual impairment and blindness. The highest proportion of RVO was seen in patients with hypertension, hyperlipidemia and increasing age. Therefore early identification of the associated factors for RVO and prompt treatment to reduce the incidence of RVO and the complications is recommended.

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LIST OF ABBREVIATIONS

BRVO	Branch Retinal Vein Occlusion
CBC	Complete Blood Count
CRVO	Central Retinal Vein Occlusion
DM	Diabetes Mellitus
FBS	Fasting Blood Sugar
HBA1C	Glycated Hemoglobin
HDL	High-density lipoprotein
HRVO	Hemi Retinal Vein Occlusion
IOP	Intraocular Pressure
ISCH	Ischemic
LDL	Low-density lipoprotein
LE	Left eye
ME	Macular edema
MNH	Muhimbili National Hospital
MUHAS	Muhimbili University of Health and Allied sciences
NISCH	Non-ischemic
NV	Neovascularization
NVD	Disc neovascularization
NVG	Neovascular Glaucoma
NVI	Iris neovascularization
OCT	Optical Coherence Tomography
PVA	Presenting visual acuity
RAPD	Relative Afferent Pupillary Defect
RE	Right Eye
RVO	Retinal Vein Occlusion
VA	Visual Acuity
VEGF	Vascular Endothelial Growth Factor
WHO	World health organization

DEFINITION OF TERMS

Anterior segment: Anterior third of the eye that includes the structures in front of the vitreous humor; the cornea, anterior chamber, iris, ciliary body and crystalline lens.

Blindness: is defined as visual acuity of less than 3/60, or a corresponding visual field loss to less than 10°, in the better eye with the best possible correction

Branch retinal vein occlusion (BRVO) is a venous occlusion at any branch of the central retinal vein. BRVO is further divided into Major BRVO and Macular BRVO.

Central Retinal Vein Occlusion (CRVO): obstruction of the central retinal vein at the optic nerve head, therefore occurring at or posterior to the lamina cribrosa.

Hemi retinal vein occlusions (HRVO): a rare form of occlusion which occurs when one half of the retina supplied by a major branch of the central retinal vein becomes occluded at or near the optic nerve.

Ophthalmoscope: An instrument used to view the posterior segment of the eye.

Posterior segment: Posterior two-thirds of the eye that includes the anterior hyaloid membrane and all of the optical structures behind it; the vitreous humor, retina, choroid and optic nerve.

Retinal Vein Occlusion (RVO): is the common vascular disorder of the retina, where there is an occlusion to the venous drainage of the retina.

Snellen chart: An eye chart used to measure visual acuity at a definite distance.

Slit-lamp: An instrument consisting of a high-intensity light source and biomicroscope that can be used to examine the lids and anterior segment of the eye.

Visual acuity: Sharpness of vision, measured by the ability to discern letters or numbers at a given distance according to a fixed standard.

Visual impairment: Visual impairment is often defined as a best-corrected visual acuity of worse than either 6/12 mild, 6/18 moderate and 6/60 severe.

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background

Retinal Vein Occlusion (RVO) is the most common retinal vascular occlusive disorder, where there is an occlusion to the venous drainage of the retina. It is among the common causes of visual impairment and blindness especially in middle age and elderly individuals, after diabetic retinopathy. Impaired vision can impact on the ability to carry out everyday tasks, the ability to work, the ability to lead an active social life as well as reduced quality of life. Additionally, it leads to increase social isolation, depression, and anxiety disorders. Pooled data of population studies in the United States, Europe, Asia, and Australia, show an overall prevalence of 16.4 million adults with RVO. Incidence of RVO increases with age, therefore as the life expectancy increases, the number of affected people will also increase (1)(2)(3).

The risk factors for retinal vein occlusion include increasing age; changes in lifestyle habits such as active smoking and obesity. Systemic risk factors include, hypertension, hyperlipidemia, diabetes mellitus, cardiovascular diseases, peripheral vascular disease, hypercoagulable disorders (such as activated protein C resistance, factor V Leiden, protein C and S deficiency) and antiphospholipid syndrome. Ophthalmic risk factors for RVO are ocular hypertension and glaucoma, lower ocular perfusion pressure and congenital as well as acquired changes in retinal arteries (4) (5).

The exact etiopathogenesis of all types of RVO remains unclear. The etiopathogenesis is multifactorial and thus no single factor alone causes the occlusion. RVO is due to occlusion of a portion of the venous circulation that drains the retina. Intraluminal thrombus formation in RVO is associated with venous stasis, endothelial injury, and hypercoagulability (6)(7).

Widely acceptable cause of retinal vein occlusion is external compression by atherosclerotic artery or disease of the venous wall, which causes blockage of venous

circulation, resulting in pressure build-up within the capillaries leading to hemorrhage and leakage of fluid and blood in the macular causing macular edema. Non-perfusion of the retina causes increase demand for oxygen and liberation of Vascular endothelial growth factor (VEGF) leading to abnormal growth of new vessels in the anterior and posterior segment. Neovascularization of the iris and anterior chamber angle may progress to neovascular glaucoma. Subsequently neovascularization in the retina leads to vitreous hemorrhage and retinal detachment. Visual morbidity and blindness is due to macular edema, retina hemorrhage, macula ischemia, and neovascular glaucoma (5)(7)(8).

Occlusion of the retinal venous system, have been classified into central retinal vein occlusion (CRVO), branch retinal vein occlusion (BRVO) and Hemi retinal vein occlusion (HRVO). In BRVO there is occlusion of a branch of the retinal vein system, which is further divided into Major BRVO and Macular BRVO. HRVO, which is a rare form of occlusion occurs when one half of the retina supplied by a major branch of the central retinal vein becomes occluded at or near the optic nerve (6)(7).

In CRVO, the occlusion is at or proximal to the lamina cribrosa of the optic nerve, where the central retinal vein exits the eye. CRVO is further divided into Non-ischemic (perfused) CRVO and Ischemic (non-perfused) CRVO. Non-ischemic CRVO is also known as venous stasis retinopathy and is due to circulatory stasis and stagnation thrombosis. The site of occlusion is further back from the lamina cribrosa or in the adjacent retro laminar region. Patients present with mild to moderate loss of acuity, usually 6/60 or better, and an absent or mild relative afferent pupillary defect (RAPD). Ischemic CRVO is also known as hemorrhagic retinopathy the occlusion is at lamina cribrosa or immediately posterior to that and is characterized by rapid onset venous obstruction resulting in decreased retinal perfusion, capillary closure, and retinal hypoxia. It leads to severe visual loss, usually less than 6/60; a marked afferent pupillary defect, extensive deep blot and flame-shaped hemorrhages, severe disc edema and hyperemia. This may lead to profound vascular leakage, rubeosis iridis and raised intraocular pressure with subsequent neovascular glaucoma (4)(6)(7)(8).

Clinical features of RVO may be variable depending on the type of occlusion. Branch retinal vein occlusion (BRVO) may be asymptomatic, patients may complain of relative scotoma or areas of blurred vision, classically worsening over hours to days. (4)(5).

Patients with CRVO are symptomatic as a rule, classically presenting with sudden painless monocular vision loss or dense central scotoma. The non-ischemic type is often the more subtle whereas the ischemic type is sudden and dramatic. Examination findings of the retina may reveal varying degrees of dilated and tortuous retinal veins, intraretinal hemorrhages, retinal edema, exudates, and cotton wool spots as well as retinal neovascularization (8).

RVO diagnosis is often based on the retinal examination findings of intraretinal hemorrhages, dilated veins, and cotton wool spots often described as a "blood and thunder appearance" as well as macular edema may be present. Extensive laboratory workup for retinal vein occlusion is only indicated in unusual case presentations or bilateral CRVO and in younger patients (4)(10).

RVO evaluation includes a detailed medical and ocular history to determine the associated factors. Physical examination includes blood pressure assessment, as well as ocular examination with slit-lamp. Laboratory investigations i.e. complete blood count, and assessment of erythrocyte sedimentation rate, fasting serum glucose, lipid profile, serum protein electrophoresis, C-reactive protein, homocysteine, serum viscosity, and thrombophilic screening (factor V Leiden mutation, protein C or S deficiency, antithrombin III deficiency, antiphospholipid antibodies). Imaging studies such as fluorescein angiography and optical coherence tomography (OCT) supplement clinical decision making. Fluorescein angiography is useful for determining the degree of ischemia present. OCT is useful for monitoring macular edema and retina thickness (4)(5).

Currently, there is scarce evidence on treatment to reverse the acute phase of retinal vein occlusion either the use of antithrombotic or thrombotic medication has limited or no benefit on retinal vein occlusion. However, some late complications, such as persistent macular edema in patients with RVO may be treated with intravitreal Anti-vascular endothelial growth factors (anti-VEGF) and/or intravitreal steroids, while neovascularization in patients with RVO may be treated with laser photocoagulation (5).

The complications of RVO depend upon duration, location and degree of ischemia. The presentation of decreased vision in RVO is the primary concern and may be due to multiple factors such as cystoid macular edema, retinal ischemia, retinal hemorrhage, vitreous hemorrhage, retinal detachment, and neovascular glaucoma, all these results to visual impairment and blindness (7)(8).

The retina clinic at the Muhimbili National Hospital (MNH) attends more than 45 patients each clinic day, with an average of four patients with Retinal Vein occlusion. The mainstay of treatment of RVO at MNH is intravitreal injection with Anti-vascular endothelial growth factors (anti-VEGF) often bevacizumab injection and laser photocoagulation for BRVO associated with macular edema and intact foveal vasculature. Despite having many patients presenting to the retina clinic with RVO, no studies have been conducted on the pattern and associated risk factors for retinal vein occlusion among patients attending the retina clinic at MNH.

1.2 Problem statement

Retina vein occlusion is among the common causes of visual impairment and blindness especially in middle age and elderly individuals, after diabetic retinopathy. Impaired vision due to RVO has a significant impact on the ability to carry out everyday tasks, the ability to work, the ability to lead an active social life. This has direct impact on the quality of life of an individual and may lead to increased social isolation, depression and anxiety disorders. Studies have found a twofold higher risk for the incidence of cardiovascular and cerebrovascular morbidity and mortality in patients with RVO compared to controls. This is likely due to the fact that RVOs affect the ocular blood vessels, which form part of the cerebrovascular system and the associated atherosclerosis risk (1)(2). The retina clinic at the Muhimbili National Hospital (MNH) attends more than 45 patients each clinic day, with an average of four patients with Retinal Vein occlusion who receive treatment. Despite having many patients presenting to the retina clinic with RVO, no studies have been conducted on the pattern and associated risk factors for RVO. Such knowledge would help to identify those patients that are at high risk of cardiovascular and cerebrovascular morbidity and mortality and refer them for care accordingly. The study aimed to determine the pattern and associated factors for RVO in patient with the retinal vein occlusion attending the retina clinic at Muhimbili National Hospital.

1.3 Conceptual Framework

The increasing prevalence of hypertension, diabetes mellitus hyperlipidemia, active smoking as well as lifestyle change among Tanzanian societies, it is expected to have a corresponding increase in the prevalence of RVO.

In Tanzania patients with hypertension and diabetes mellitus are frequently treated at various clinical levels, from clinical officers to consultant physicians, but rarely an eye examination or consultation to eye care is offered. This may be due to poor awareness of both the healthcare giver and patients or poor management protocol. To some extent attributes to the late presentation of patients with RVO to Ophthalmic evaluation.

This study will reveal the pattern, associated factors and complications of RVO among adult patients attending the retina clinic. The study will provide baseline data for future studies on patients with RVO attending the retina clinic at MNH and in Tanzania.

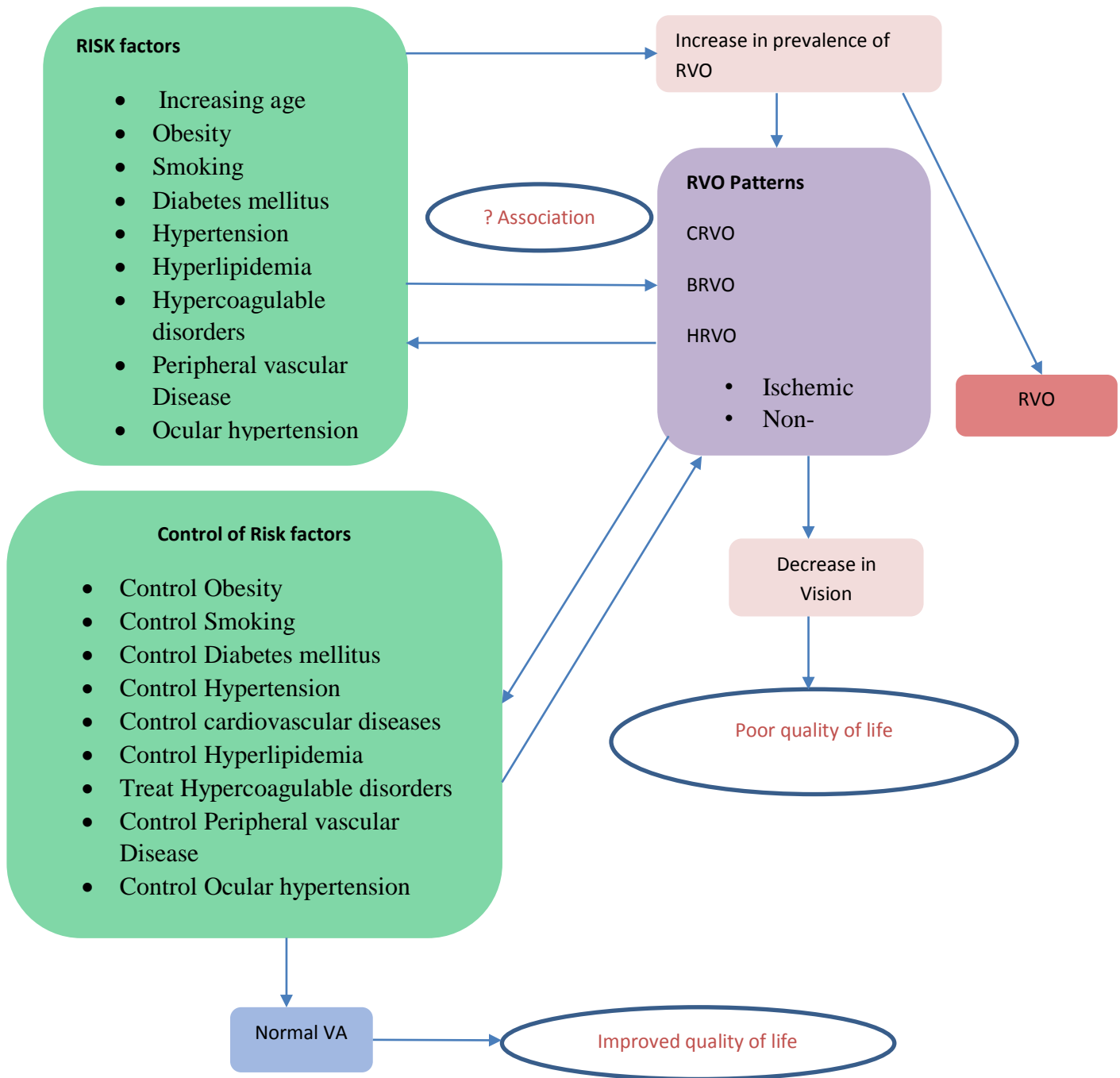


Figure 1: Conceptual Framework

1.4 Rationale

Findings from this study provide baseline information on the pattern and associated factors for RVO at MNH. The known pattern of RVO fills the knowledge gap and increase awareness of RVO in our setting and enables prompt diagnosis and interventions for better management outcomes.

The results of the study would be used to sensitize health care workers about RVO and planning for comprehensive multispecialty care and prevention of RVO.

This results would also be used for the establishment of institutional management protocols and guidelines for patients with RVO. Additionally, this results would be used as baseline reference for future studies on RVO.

1.5 Research Questions

1. What is the proportion of patient with retinal vein occlusion among patients attending the retina clinic at MNH during the study period?
2. What are the common types of retinal vein occlusion among patients attending the retina clinic at MNH during the study period?
3. What are the factors associated with retinal vein occlusion in patients attending the retina clinic at MNH during the study period?

1.6 Objectives

1.6.1 Broad Objective:

To assess the pattern and associated factors for retinal vein occlusion among patients attending the retina clinic at Muhimbili National Hospital.

1.6.2 Specific Objectives:

1. To determine the proportion of patients with retinal vein occlusion presenting to the retina clinic at MNH.
2. To determine the types of retinal vein occlusion among patient attending the retina clinic at MNH.
3. To determine factors associated with retinal vein occlusion in patients presenting to the retina clinic at MNH.

1.7 Literature review

1.7.1 Proportion of retina vein occlusion

Reports on the prevalence of retina vein occlusion from different studies across the world show variations. A recent pooled analysis of patients in the United States, Europe, Asia, and Australia estimated an overall prevalence of 5.20 per 1000 adults with RVO. Of these 4.42 per 1000 for BRVO, and 0.80 per 1000 for CRVO (3).

Studies conducted in the Caucasian population aged from 40 years and above have shown similar prevalence for branch BRVO and CRVO ranges between 0.6% - 1.1% and 0.1–0.4% respectively (11)(12)(13).

However, a study from the University Medical Center of the Johannes Gutenberg Germany, (the Gutenberg Health Study) on the prevalence and risk factors for retinal vein occlusion, the prevalence was 0.4%, for RVO, 0.08% for CRVO, and 0.32% for BRVO (10).

In Beaver Dam Wisconsin, United States, the Beaver Dam Eye Study on the epidemiology of RVO reported the prevalence of 0.7 % for RVO, 0.6% for retinal BRVO with a small proportion of 0.1% for CRVO (12).

In the multi-ethnic Asian population study, the Singapore epidemiology of eye disease study found an overall crude prevalence of RVO 0.72%. The crude prevalence of RVO was similar among study participants (Chinese, Indian and Malay) (14).

In a population-based cross-sectional study on the prevalence, pattern and risk factors for RVO in the elderly population (60 to 95 years) of Nepal, the Bhaktapur retina study the overall population prevalence for RVO was 2.95%, BRVO 2.74% and CRVO 0.21% (15).

Few studies on RVO have been reported in Africa and they show varying but comparatively higher prevalence. A study from West Africa, Nigeria at the University of Port Harcourt Teaching Hospital, on the prevalence and risk factors for retinal vein occlusion of the 364 patients seen at the retina clinic during the study period, 27 (7.4%) had RVO, 20 (74%) had CRVO and 7 (26%) had BRVO (6). These levels are significantly higher than those found in the Caucasian population. These data was reported to signify the impact of changing economies, and unhealthy lifestyle changes (unhealthy diet, increase in smoking, alcohol consumption, stress and physical inactivity). Such life style factors lead

to an increase in the prevalence of hypertension, hyperlipidemia and diabetes in developing societies, and a corresponding increase in RVO.

1.7.2 Types of RVO

Occlusion of the retinal venous system, have been classified into central retinal vein occlusion. (CRVO), branch retinal vein occlusion (major and macular BRVO) and hemi retinal vein occlusion (HRVO). CRVO may be further classified as ischemic and non-ischemic (4) (6) (8) (7).

In Branch retinal vein occlusion (BRVO) there is occlusion of a branch of retinal vein system. BRVO is further divided to Major BRVO and Macular BRVO. BRVO is more than twice as common as CRVO and more than 10 times as common as HRVO. In the Beaver dam eye study the prevalence of BRVO was found to be 0.6% and it was commoner than CRVO. The overall incidence of BRVO in the Blue Mountain Eye was 1.1% and was strongly associated with age (12).

Central Retinal Vein Occlusion (CRVO) occurs when the obstruction is at the optic nerve head, at or posterior to the lamina cribrosa and can result in four quadrants of retinal hemorrhages. Broadly can be divided into ischemic (there is significant enough pressure on the capillary system to result in areas without blood flow) which is usually severe and non-ischemic(4)(6)(8).

Hemi retinal vein occlusion (HRVO) is a rare form of occlusion that occurs when one half of the retina supplied by a major branch of the central retinal vein becomes occluded at or near the optic nerve (4).

1.7.3 Factors associated with RVO

Age

The Incidence of RVO increases with age where more than half of all cases occur in patients older than 65 years; this is likely due to the association of age with atherosclerosis. The Beaver Dam Eye Study reported the association between increasing age and RVO where there were 2.9 % BRVO and 1.3% CRVO in patients aged 65 to 74 years or older at

baseline. Persons aged 75 years or older at baseline were 4.6 times as likely to develop a BRVO compared to those aged 43 to 54 years (12).

In a large population-based German cohort which included 15 010 participants (aged 35–74 years) from the Gutenberg Health Study, the prevalence of RVO was 0.2% in participants aged 35–44 and 45–54 years, respectively, 0.48% in those aged 55–64 years, and 0.92% in those aged 65–74 years (16). Data from the Blue Mountain Eye Study in Australia suggest that the prevalence of RVO is 0.7% for those younger than 60 years, 1.2% for those 60 – 69 years, 2.1% for those 70 – 79 years and it increases to 4.6% in people aged 80 years or above (11).

A study from India, on the evaluation of various risk factors of retinal vein occlusion it was found that 2% of patient in 25-35 years, 18% patients in 35-45 years, 28% patients in 46-55 years, 16% patients in 66-75 years, while 4% patients are in >75 years (17).

Gender

Multiple studies have suggested that men may be at increased risk of CRVO compared with women a fact related to this frequent exposure of men to risk factors such as active smoking, and changes in lifestyle. The Beaver Dam Eye Study on the epidemiology of RVO reported similar prevalence of BRVO and RVO between men and women (1.5% vs 2.1%, respectively for BRVO and 0.5% vs 0.6%, respectively for CRVO) (12). However, The Gutenberg Health Study reported that men were 1.7 times more frequently affected by RVO than were women (16). A study on the evaluation of various risk factors of RVO done in India found a higher incidence in males 26 (52%) than females 24 (48%) (17).

Ethnicity

Data about the ethnicity predisposition to RVO is not consistent, with most of the studies being done on a single race depending on the geographical location of the study done. Some studies suggest the prevalence of any type of RVO to be similar across races. One recent study found a 58% increased risk in black patients compared with white patients after adjusting for common risk factors (8)(7)(18).

A large 2010 study reported the prevalence of BRVO to be 2.8 per 1000 in whites, 3.5 in blacks, 5.0 in Asians, and 6.0 in Hispanics and the prevalence of CRVO to be 0.88 per 1000 in whites, 0.37 in blacks, 0.74 in Asians, and 1.0 in Hispanics (3)(19).

Systemic factors

Several systemic factors have been implicated in the development of RVO; an essential risk factor for RVO is advancing age. Other risk factors include systemic conditions like hypertension, arteriosclerosis, diabetes mellitus, hyperlipidemia, vascular cerebral stroke, blood hyper viscosity, and thrombophilia. A strong risk factor for RVO is the metabolic syndrome which is made up of a combination of hypertension, diabetes mellitus, and hyperlipidemia. Cigarette smoking also increases the risk of RVO as do systemic inflammatory conditions like vasculitis and Behcet disease. Ophthalmic risk factors for RVO are ocular hypertension and glaucoma, higher ocular perfusion pressure, and changes in the retinal arteries (20).

Hypertension

In Hypertension, arteries are vulnerable to the narrowing and plaque buildup associated with atherosclerosis. Atherosclerosis is implicated in the etiopathogenesis of RVO. In a meta-analysis of published studies on the association between RVO and traditional risk factors for atherosclerosis: the authors reviewed all studies on RVO published between January 1985 and July 2007. A total of 21 studies that included 2916 cases and 28,646 controls were found. Hypertension (odds ratio [OR] 3.5) was found to be significantly associated with RVO. RVO was attributed to hypertension in 47.9% of cases (21). Hypertension was also found to be an Independent risk factor associated with RVO (odds ratio [OR] 2.06 (18) in a Multi-Ethnic Study of Atherosclerosis on traditional risk factors. In the Beaver dam eye study on the epidemiology of retinal vein occlusion and associated risk factors, hypertension showed a higher odds ratio OR 5.42 compared to other factors (10) . Similarly, hypertension was found to be a risk factor for RVO among an elderly population in Nepal (Bhaktapur retina study). About 45% of the study subjects were hypertensive (15).

Among the few studies in Africa, a study done in West Africa, Onitsha Nigeria, on Risk Factors for RVO found that 55.6% of patients had hypertension which was significantly higher compared to other associated factors (22).

Hyperlipidemia

Studies suggest that disorders in lipoprotein metabolism may contribute to the etiology of RVOs. In a meta-analysis of published studies that investigated the association between RVO and traditional risk factors for atherosclerosis, on the Low-density lipoprotein triglycerides and lipoprotein (a) as risk factors for RVO, showed significantly higher levels compared to control, of LDL-cholesterol (3.82 ± 1.06 , 3.59 ± 0.90 and 3.07 ± 0.83 mmol/L), LDL-triglycerides (0.39 ± 0.14 , 0.40 ± 0.12 and 0.35 ± 0.14 mmol/L) and apolipoprotein B (1.06 ± 0.27 , 1.05 ± 0.26 and 0.84 ± 0.21 g/L) in the LDL fraction. Again hyperlipidemia (OR 2.5) was significantly associated with RVO (21).

Diabetes mellitus

Diabetic Mellitus associations with RVO are related to the raised risk of atherosclerosis, which is a culprit of thrombus formation and hence the development of RVO. Data analyzed from one Meta-analysis of published studies on the association between RVO and risk factors for atherosclerosis showed diabetes mellitus OR 1.5 to have a higher risk compared to other risk factors(21). In the beaver dam eye study diabetes mellitus with OR 2.43 ranked 4th among the risk factors (12). Additionally, the study from Onitsha Nigeria on the Pattern and Risk Factors for RVO showed that 10 (22.2%) patients with RVO had diabetes Mellitus (22).

Cigarette smoking

Cigarette smoking is a major modifiable risk factor for cardiovascular disease. However the microcirculatory effect of cigarette smoking remains partially understood. A systematic review on the long term effect of smoking on retinal microvasculature in the population of older persons, observed cross-sectional associations of cigarette smoking with wider venular caliber and to a lesser extent, widening of arteriolar caliber. These findings were

even persistent after five years of follow up (23). Similarly, tobacco use affected 28% of study participants and ranked three among the risk factors for RVO in a study done in India (17).

Ocular risk factors

Ophthalmic risk factors for RVO are ocular hypertension, higher ocular perfusion and changes in the retinal arteries. The relationship between ocular hypertension and RVO has always been the subject of controversy despite the number of studies still there are uncertainties about its course (8)(11)(12)(17)(21)(24)(25).

Glaucoma

Open-angle glaucoma is the most frequent local alteration predisposing to RVO as it compromises venous outflow by increasing intraocular pressure. It is postulated that high intraocular pressure causes external compression of the central retinal vein as it passes through the lamina cribrosa resulting in turbulent blood flow distal to the constriction and subsequent thrombus formation. RVO is detected in 4–4.5% of eyes with primary open-angle glaucoma, and primary open-angle glaucoma or ocular hypertension in 4–43% of patients with RVO (25).

In the Gutenberg Health Study, 5.1% of persons with RVO had glaucoma compared to 2.2% of patients with glaucoma in participants without RVO (16).

The Onitsha Nigeria study on the prevalence of ocular risk factors for RVO found that 23.2% of patients with RVO were due to glaucoma (22). Likewise, The study at the University of Port Harcourt Teaching Hospital, showed 33.3% of patients with CRVO had glaucoma while 7.4% with BRVO had glaucoma (6).

CHAPTER TWO

2.0 METHODOLOGY

2.1 Study design

A hospital based descriptive cross-sectional study.

2.2 Study period

June to December 2020.

2.3 Study area

The study was conducted at Muhimbili National (MNH). The hospital is located in Dar-es-Salaam city, Ilala region in Upanga along United Nations road. Muhimbili National Hospital is a tertiary hospital that receives patients from all over the country. It is also a teaching hospital for Muhimbili University of Health and Allied Sciences (MUHAS). The retina clinic is under the department of ophthalmology. It is a specialized clinic for patients with retinal conditions including RVO. The clinic runs on Wednesdays and Thursdays, with an average of 40 to 60 patients per clinic day. Nearly 10% of the patients attending the retina clinic have RVO. The clinic is equipped with all necessary investigations tools including OCT and Fundus photography.



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Figure 2: Map of Dar es Salaam, showing location of Muhimbili National hospital

2.4 Target population

All adult patients attending the retina clinic at Muhimbili National Hospital.

2.5 Study population

All adult patients with RVO attending the retina clinic at Muhimbili National Hospital

2.6 Sampling technique

A consecutive sampling technique was used to select study participants. All patients who presented to the retina clinic and who met the inclusion criteria and agreed to participate in the study during the study period were recruited until the sample size was reached.

Inclusion criteria

1. All patients aged 18 years old and above diagnosed with RVO at the retina clinic between June to December 2020.

Exclusion criteria

1. Patients with ocular conditions that impaired fundal view for example dense cataract, vitreous hemorrhage and corneal opacity.
2. Very ill patients and physically incapacitated who failed to sit still for an eye examination

2.7 Sample size estimation

The sample size was estimated using the calculation of sample size for prevalence studies as follows:

$$n = [z^2 P (100\% - P)] / d^2$$

Where

n = required sample size

z= statistic value for the level of confidence (1.96)

P= expected prevalence in percentage

d= margin of error

From the study conducted at the University of Port Harcourt Teaching Hospital, Port Harcourt, Nigeria, the prevalence of retinal vein occlusion was 7.4% (6)

z = 1.96,

d = 7%

$$\frac{[1.96^2 \times 7.4 \times (100 - 7.4)]}{7^2}$$

Thus the minimum sample size required was 73 patients.

2.8 Variables

The independent variables were social demographics i.e., (age, sex, and race, level of education, occupation, residence, and contacts) and factors associated with RVO i.e. Age, hypertension, hyperlipidemia, diabetes mellitus, glaucoma and smoking cigarette.

The outcome variables were the proportion of RVO and types of RVO i.e. (CRVO, BRVO and HRVO).

Age categories were 18-40, 41-60 and 61+

Sex categories were Males and Females

Race categories were African, Asian, and Caucasian

Occupations was categorized as peasants, Public servants, Trading, Technicians
Unemployed

Residence was categorized as Rural or urban

Proportion of RVO was obtained as the number of patient diagnosed with RVO over the total number of patients who attended the retina clinic during the study period.

BRVO was defined by presence of a focal occlusion of retina vein, presence of dilatation and tortuosity of affected venous quadrant and at arterio-venous crossing point.

CRVO was defined by presence of marked dilation and tortuosity of the retinal veins, extensive retinal edema, superficial and deep retinal hemorrhages radiating outward from the optic disk in all quadrants, cotton-wool spots, and optic disk swelling.

HRVO was defined as an occlusion of the superior or inferior branch of the central retinal vein, (hemi-retinal involvement in the distribution of the involved occluded vein).

Ischemic CRVO was defined by presence of marked relative afferent pupillary defect and one or more of the following characteristics, poor visual acuity of worse than 6/60, extensive deep blot and flame-shaped hemorrhages involving the peripheral retina and posterior pole, presence of multiple cotton wool spots, severe retinal vein dilatation and tortuosity as well as severe disc edema.

Non-ischemic CRVO was defined by minimal or absent relative pupillary defect, mild to moderate loss of visual acuity better than 6/60, mild tortuosity and dilatation of retinal veins, dot/blot and flame-shaped hemorrhages in the periphery, and optic disc and macular edema.

2.09 Data collection tools

- i. Snellen's chart/ E chart for visual acuity testing
- ii. Rebound tonometer-hand held icare-TA01i for intraocular pressure measurement assessment.
- iii. Pen torch to test for pupillary light reflex
- iv. Slit-lamp Haag-Streit BD 900, for the anterior segment and posterior segment examinations.
- v. Indirect ophthalmoscopy (head mount-Appassamy) for posterior segment examinations
- vi. Optical Coherence Tomography Topcon 3D OCT-1 maestro for measurement of distinctive layers of the retina and fundus photos.
- vii. 2.5% phenyl epinephrine and 1% tropicamide for dilatation of the pupil.
- viii. A semi-structured questionnaire containing three sections was used to record the information. Part one was on baseline information i.e. patients demographic data, part two patients ocular history and part three were for patients examinations findings including laboratory results as well as imaging results.

2.10 Data collection procedure

On every clinic day (Wednesday and Thursday), the investigator, visited the retina clinic, selected and informed eligible patients about the study. After agreement to participate eligible patients signed an informed consent and were recruited in the study. The investigator also informed other doctors in the ophthalmology clinic about his study on RVO and left his contacts and was notified once a patient with RVO was diagnosed at the clinic. Patients were interviewed to collect information on demographic data, ocular history related to poor vision, systemic and ocular risk factors for RVO and possible

complications. Then a general examination of the vital signs of the patient i.e. pulse rate, respiratory rate, blood pressure measurement for those who are not known to be hypertensive.

Hypertension was defined as blood pressure of $\geq 140/90$ millimeters of mercury (mmHg) taken two readings on six hours apart and on two separate days or patient had diagnosis of hypertension. Diabetes mellitus was defined as glycated hemoglobin (Hb1Ac) of $\geq 6.5\%$. Or the patient is taking hypoglycemic medication.

The ocular examination commenced with the assessment of visual acuity using the Snellen acuity chart. The visual acuity was taken for every study subject, both with and without pinhole. For patients whose vision did not improve with pinhole, their visual acuity was recorded. The patients whose vision improved with pinhole were then refracted and the final visual acuity recorded. Levels of visual acuity were recorded according to the WHO, International Classification of Diseases 11 (2018) where visual impairment for distance was defined as mild visual impairment when the presenting visual acuity was 6/12 to 6/18, moderate visual impairment= visual acuity worse than 6/18 to 6/60, Severe visual impairment=visual acuity worse than 6/60 to 3/60 and Blindness =visual acuity worse than 3/60.

Assessment of a relative afferent pupillary defect (RAPD) was done using a swinging flash light for both eyes. The RAPD test was used to differentiate between patients with ischemic and non-ischemic RVO. The intraocular pressure was assessed by rebound tonometer-hand held icare-TA01i. An IOP of more than 21mmhg was regarded as high after an average of six reading.

Patients were then examined using a Slit-lamp to assess for: iris neovascularization and clarity of the media. The dilatation of the pupil was done using one drop of 2.5% phenyl epinephrine and 1% tropicamide instilled twice or thrice in the conjunctival sac at an interval of 10 to 15 minutes. After pupillary dilatation, an indirect ophthalmoscope was done using a slit-lamp with a 78D and 90D retinal lens to assess for retinal signs of RVO: optic disc changes, damage, cup to disc ratio, optic disc edema and new vessels on the disc.

Intra-retinal hemorrhages, retinal edema, dilated tortuous retinal vasculature, exudates, as well as cotton-wool spots ("blood and thunder appearance").

Then patients underwent Optical Coherence Tomography imaging to confirm macular edema, epiretinal membrane and sub retinal fluid accumulation. Macular edema was defined as retina thickening within the macular area and central macular thickness of more than 255 μm .

2.11 Laboratory procedures

Performed laboratory procedure included: complete blood count and erythrocyte sedimentation rate (ESR). ESR of more than 15 mm/hr for males and 20 mm/hr for females was regarded higher. A lipid profile was done to detect the presence of hyperlipidemia. Hyperlipidemia was defined as S. cholesterol > 5.17 mmol/L, S. triglycerides > 1.69 mmol/L, HDL cholesterol > 1.55 mmol/L, and LDL cholesterol > 3.34 mmol/L.

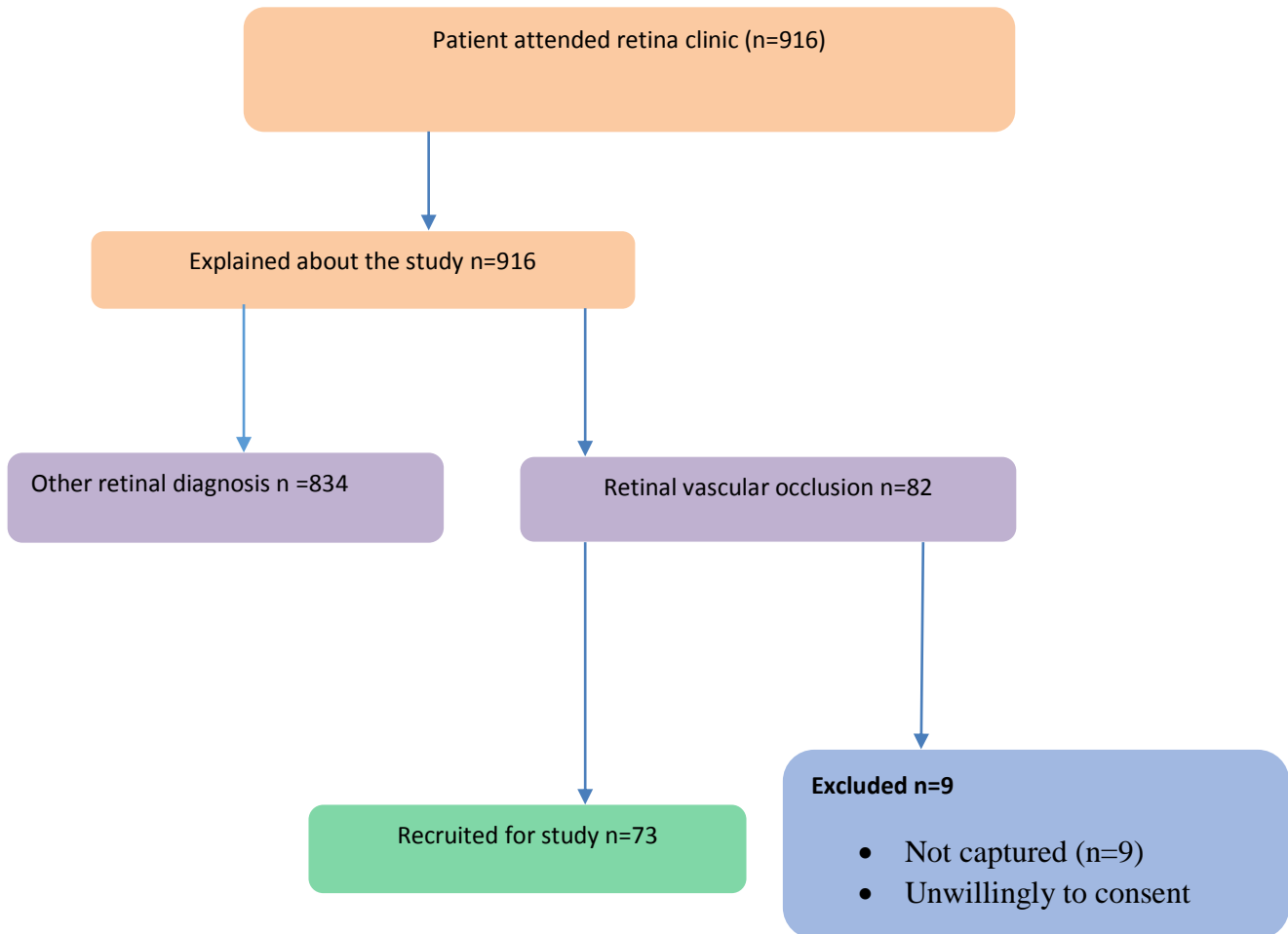
All collected information was recorded on a structured questionnaire.

2.12 Data Analysis

Data was transferred from the hand-written data forms into a data spreadsheet and analyzed with Statistical Package for the Social Science computer software (SPSS) version 22.0. Descriptive statistics were analyzed by frequency distribution tables for social demographics, visual impairment level, associated factors (systemic and ocular) as well as complication of RVO and pie chart.

2.13 Ethical clearance and consideration

Ethical approval to carry out this study was obtained from the SENATE Research and Publication Committee of MUHAS. Permission to conduct the study was obtained from the Executive Director of MNH. All eligible patients were informed about the study and those who agreed signed an informed consent before participation. All data collected were treated with strict confidentiality and stored in locked cabinets and coded computers.

CHAPTER THREE**Figure 3: Flow diagram**

3.0 RESULTS

A total 916 participants attended the retina clinic during the study period, of which 73 participants presented with RVO. Three (4.1%) patients had bilateral involvement giving a total of 76 eyes. Most participants were aged more than 60 years with a mean age of 60.87 ± 22.3 years. Only one participant was aged less than 40 years and had RVO. There were 44 (60.3%) males and 29 (39.7%) females, with a male to female ratio of 1.5:1. (Table 1)

Table 1: The Socio-demographic characteristics of the study population (N=73 participants)

Characteristics	Frequency (n)	Percentage (%)
Age group (years)		
18-40	1	1.4
41-60	31	42.5
61 and above	41	56.1
Sex		
Male	44	60.3
Female	29	39.7
Level of education		
No formal education	5	6.9
Primary education	20	27.4
Secondary education	24	32.9
College	24	32.9
Occupation		
Unemployed	4	5.5
Peasant	11	15.1
Public servant	34	46.7
Businessman	24	32.8
Residence		
Dar-es-Salaam	50	68.5
Other regions	23	31.5

**other regions includes Zanzibar, Morogoro, Mtwara, Dodoma, Singida Iringa, Mbeya. Tanga, Kilimanjaro Arusha, Tabora and Katavi.*

The proportion of retinal vein occlusion was 7.9 % (figure 4).

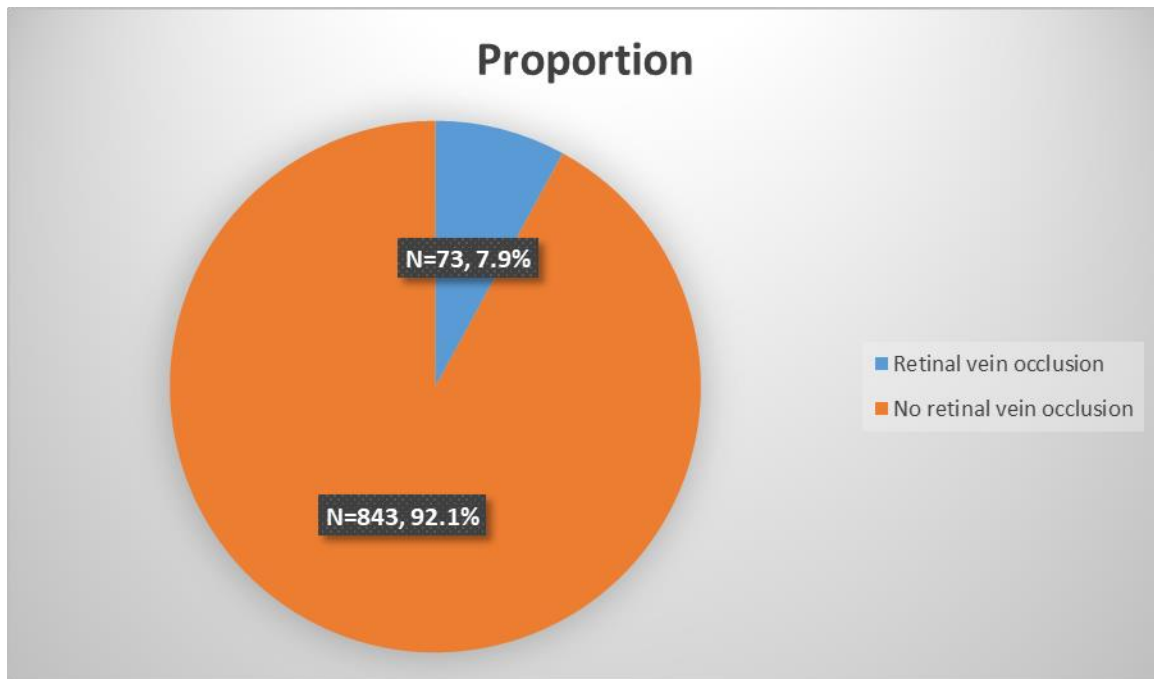


Figure 4: Proportion of participants with retinal vein occlusion at the retina clinic at MNH

Table 2: The distribution of visual impairment and blindness by type of RVO (N=76 eyes).

Visual Acuity (BCVA)	RVO type			Total No (%)
	BRVO No (%)	CRVO No (%)	HRVO No (%)	
6/4—6/9	0(0.0)	0(0.0)	0(0.0)	0(0.0)
6/12--6/18	11 (100)	0(0.0)	0(0.0)	11 (14.5)
6/18--6/60	18(72.0)	5(20.0)	2(8.0)	25(32.9)
6/60--3/60	4(22.2)	13(72.2)	1(5.6)	18 (23.7)
<3/60—NPL	0(0.0)	21(95.5)	1(5.5)	22(28.9)
Total	33	39	4	76(100)

BCVA-best corrected visual acuity

Eleven (14.5%) eyes had mild visual impairment while 22 (28.9%) eyes were blind. Majority of the eyes with CRVO had severe visual impairment and blind while most eyes with BRVO had moderate visual impairment 18(72.0%) (Table 2).

Table 3: Distribution of types of RVO in affected eyes by laterality. (N=76 eyes)

	BRVO	CRVO	HRVO	Total
	No (%)	No (%)	No (%)	No (%)
RE	16(48.5)	27(69.2)	3(75)	46(60.5)
LE	17(51.5)	12(30.8)	1(25)	30(39.5)
TOTAL	33(43.4)	39(51.3.0)	4(5.3)	76(100)

Right eyes 46(60.5%) were commonly affected than left eyes 30 (39.5%). (Table 3)

Table 4: Description of the eyes by ischemic status according types of RVO (N=76 eyes)

Type of occlusion	Clinical type		
	ISCH	NISCH	Total
	No (%)	No (%)	No (%)
BRVO	2(6.1)	31(93.9)	33(43.4)
CRVO	18(46.2)	21(53.8)	39(51.3)
HRVO	0(0.0)	4(100)	4(5.3)
TOTAL	20 (26.3%)	56(73.7)	76(100)

ISCH=ischemic RVO, NISCH=non-ischemic RVO

The commonest clinical type of RVO was non-ischemic which affected 56(73.7%) eyes. The majority of the eyes with ischemia were affected by CRVO. (Table 4)

Table 5: Factors associated with retinal vein occlusion at MNH (N=73 participants).

Associated factors	Frequency (n)	Percentage (%)
Age group (years)		
18-40	1	1.4
41-60	31	42.5
61 and above	41	56.1
Hypertension		
Yes	65	89
No	8	11
Hyperlipidemia		
Yes	53	72.6
No	20	27.4
Diabetes mellitus		
Yes	36	49.3
No	37	50.7
Cigarette smoking		
Yes	30	41.1
No	43	58.9
Alcohol use		
Yes	18	24.7
No	55	75.3
Glaucoma		
Yes	15	20.6
No	58	79.4

Systemic hypertension affected a high proportion of the participants with RVO 65(89%), followed by hyperlipidemia 53 (72.6%) and older age. The low proportion of RVO was seen among patients with alcohol use 18 (24.7) and glaucoma 15 (20.6%). (Table 5)

Table 6: The Association between lipid profile and types of RVO (N=73 participants)

Lipid profile	Type of vein occlusion				P-value
	BRVO	CRVO	HMRVO	TOTAL	
Total cholesterol					
Normal	29 (90.6)	21 (56.8)	2 (50.0)	52 (71.2)	0.003
Raised	3 (9.4)	16 (43.2)	2 (50.0)	21 (28.8)	
HDL					
Normal	26 (81.3)	17 (46.0)	2 (50.0)	45 (61.6)	0.005
Raised	6 (18.8)	20 (54.0)	2 (50.0)	28 (38.4)	
LDL					
Normal	18 (56.3)	5 (13.5)	0 (0)	23 (31.5)	<0.001
Raised	14 (43.8)	32 (86.5)	4 (100)	50 (68.5)	
Triglyceride					
Normal	24 (75.0)	25 (67.6)	3 (75.0)	52 (71.2)	0.829
Raised	8 (25.0)	12 (32.4)	1 (25.0)	21 (28.8)	

* Fisher's exact $P=0.05$ BRVO=branch retinal vein occlusion, CRVO=central retinal vein

The association between LDL, total cholesterol, HDL and types of occlusion, was found to be statistically significant. For the difference in the proportion of patients with RVO and high triglyceride the different types of occlusion was not statistically significant (Fischer exact $P=0.519$). (Table 6)

Table 7: Description of the eyes by ocular complication according to types of RVO (N=68 eyes)

Type of occlusion	Complications				
	VH	NVI	NVD	ME	TOTAL
	No (%)	No (%)	No (%)	No (%)	No (%)
BRVO	2(22.2)	1(20)	1(16.7)	8(16.7)	12(17.6)
CRVO	7(77.8)	4(80)	5(83.3)	36(75.0)	52(76.5)
HRVO	0(0)	0(0)	0(0)	4(8.3)	4(5.9)
TOTAL	9(100)	5(100)	6(100)	48(100)	68(100)

VH=vitreous hemorrhage, NVI=iris Neovascularisation, ME=macular edema, NVD=disc neovascularisation,

The leading complications were: macular edema 48(70.6%), followed by vitreous hemorrhage, iris and disc neovascularization. The complications were more in patient with CRVO (Table 7).

CHAPTER FOUR

4.0 DISCUSSION

The present study assessed the pattern and factors associated with retinal vein occlusion among 73 participants (76 eyes). The proportion of retinal vein occlusion in this study was 7.9 %. This finding correlates with that of Port Harcourt and Ekiti State in Nigeria, where the prevalence of retinal vein occlusion were 7.4% and 9.3% respectively (6)(26). Our findings contrast with most population-based studies done across the world that reported a much lower incidence of RVO. Elsewhere the incidence of RVO ranged from 0.6% to 2.9% (3)(11)(12)(13)(14)(15)(24). The high proportion of RVO in our environment may reflect changing economies reflected by the increase in unhealthy lifestyles (unhealthy diet, increase in smoking, alcohol consumption, stress and physical inactivity). An unhealthy lifestyle is associated with the increase in the prevalence of hypertension, hyperlipidemia, and diabetes mellitus and therefore rise in the incidence of RVO. Again the variations in study design may also explain a high occurrence of RVO among our participants. Therefore a population-based study is required to determine the true incidence or prevalence of RVO in our environment.

In this study, increasing age was found to be an important factor associated with retinal vein occlusion. The mean age in this series was 60.87 ± 22.3 years. The proportion of participants afflicted by RVO increased with the increasing age of the participants, 56.1% of the participants with RVO were from the 61 and above age group. This finding is in keeping with studies done in USA, Europe Australia, Asia and Africa (6)(11)(12)(15)(16)(17)(22)(26)(27)(28). These results also reflect the increase in life expectancy of Tanzania, according to the United National world population prospect in 2021. The increasing age is associated with an increased rate of atherosclerosis, hypertension and cardiovascular diseases. These are factors associated with development of RVO. Therefore RVO is a disease of the older population, afflicting individuals with more than 50 years.

Finding from this study indicate a higher preponderance of males with RVO compared to females. This could be related to the fact that more men are engaged in risky lifestyles including smoking and alcohol consumption. Therefore increases their predisposition to the disease. On the other hand, the high proportion of RVO in men attending hospital may be explained by the fact that the majority of men in our environment are economically better off and therefore are able to attend to hospital for their ailments compared to females. This finding is similar to most studies (12)(16)(17)(29). Our findings contrast with those from Nigeria at Onitsha ,Port Harcourt and Ekiti State, where the proportion of RVO was higher among women compared to men (6)(22)(26).

Our findings show that most eyes were affected by CRVO 39(51.3%), followed by BRVO 33(43.4%), and HRVO was at least 4(5.3%). This trend was also observed in hospital-based studies in Onitsha, Port Harcourt, Benin city and Ekiti State Nigeria as well as in India (6)(17) (22)(26)(28). Findings from population based studies done in, USA, Australia and Asia, showed different trend in the incidence of RVO. In those studies the incidence of BRVO was reported to be higher than CRVO (3)(12)(13)(14)(15)(16)(18). The higher proportion of CRVO in our setting may reflect variations in the genetics, ethnicity, diet, and environment that may play a role in the occurrence of RVO. Furthermore, the pathogenesis of RVO has been established to be different among the types of occlusion, this was demonstrated by Hayreh and colleagues (4). Thus, CRVO is strongly associated with hypertension and glaucoma whereas BRVO is mainly due to Artherosclerosis, which tend to be higher in the western world as compared to developing countries. Again, the high number of CRVO participants in our study may correlate to the reported high predisposition of CRVO in the African race compared to others, Stem et al (30).

In this study, the vision loss in relation to RVO was assessed and WHO international classification of diseases 11(2018) was used to categorize the visual acuities in the eyes with RVO. Severe visual impairment and blindness was seen in more than half 40(52.6%) of affected eyes and the highest proportion of vision loss was found in eyes affected by CRVO 34(87.2%). Mild and Moderate visual impairment was seen in majority of patients with BRVO 29(87.9%).

These findings correlate with the Onitsha study in Nigeria where blindness was seen in 54.2% of the eyes with RVO. Also, the Port Harcourt and Ekiti State study in Nigeria reported a high proportion of visual impairment in the eyes with CRVO (22)(6)(26). Similarly, Prajapati et al, reported severe visual impairment in the eyes with CRVO and more so in ischemic CRVO. Our findings also are in keeping with other population-based studies in the World (15)(17)(30). The visual loss that occurs from RVO may be reduced by modifying known associated factors and early institution of appropriate therapy for complications that occur.

In the current study, the factors which were examined for association with RVO, included age, active cigarette smoking, hypertension, hyperlipidemia, diabetes mellitus, and glaucoma. In the previous studies these factors have shown relationship with RVO. In this study, the high proportion of participants with RVO also suffered from hypertension, hyperlipidemia, and had advanced age. Almost half the patients were suffering from diabetes mellitus and more than a third from glaucoma and were cigarette smokers. These findings are consistent with findings from previous studies, where increasing age, hypertension, and hyperlipidemia showed a highest proportion among RVO patients.

Sixty five (89.0%) participants with RVO had systemic hypertension. This finding correlates with hospital-based studies such as the Onitsha, Benin City, Port Harcourt and Ekiti State study in Nigeria where they recorded the highest proportion of RVO patients among hypertensive (6)(22)(26)(28). Studies done in India by Prajapat et al and Sharma R et al observed hypertension to be the major risk factor associated with RVO. Similarly, population-based studies done across the world showed a strong association between hypertension and RVO (3) (11)(14)(29). The higher occurrence of RVO among hypertensive in our environment may be reflected by an increasing trend of hypertension in Tanzania as noted by Muhihi A.J et al (31). On the other hand, the rising incidence of non-communicable diseases such as hypertension in our environment may result in a corresponding increase in the occurrence of RVO. It is therefore important to control the risk factors associated with RVO like hypertension in order to reduce the prevalence of RVO.

Fifty-three (72.6%) participants with RVO had elevated levels of lipids, other previous studies recorded similar findings where hyperlipidemia was seen in their series. Other studies also found hyperlipidemia to be an independent risk factor for RVO (6)(13)(17)(21)(28)(29). Thus, there is a need to raise awareness on the factors associated with RVO, especially modifiable factors such as unhealthy lifestyles and unhealthy diets in our society.

In our study diabetes mellitus was found to afflict 49.3% of the participants with vein occlusion. This finding correlates with hospital based studies in Nigeria, India and other population based studies across the world. However, most of the previous studies have found a weak association between diabetes mellitus and RVO (6)(12)(17)(21)(22)(28)(29). The increasing burden of non-communicable diseases such as diabetes mellitus, hypertension, and dyslipidemia in our environment poses an alarming challenge and may be associated with the rising incidence of RVO. Therefore, controlling of Diabetes Mellitus should be emphasized in order to avoid complications such as RVO.

Glaucoma is the only ocular risk factor recorded in this study where 20.6% of our participants also had glaucoma. We also found that glaucoma was more in CRVO 23.1% than BRVO 15.2%. This study is in keeping with studies done in Onitsha, Port Harcourt and Benin City Nigeria, where glaucoma was found in 23.2%, 33.3% and 22.7% respectively (6)(22)(28). The study done in Ekiti state Nigeria is contrary to our report on glaucoma, as they reported a higher percentage of RVO patients with glaucoma 51.3% (26). Previous studies done across the world reported a slightly lower incidence of glaucoma, this could be due to the high prevalence of primary open-angle glaucoma in the African race as opposed to other populations in the world (16)(20)(29). Control of glaucoma therefore would help to reduce the risk of developing RVO.

Thirty (41.1%) of our participants had a history of cigarette smoking. Smoking predisposes smokers to vein occlusion, however, we found no association between a history of smoking and RVO. Our finding is in keeping with other studies done in Australia, Asia, Europe and America (11)(13)(14)(16)(17)(23)(27). Therefore, lifestyle modification that includes

smoking cessation, eating a healthy diet, and regular excises is crucial to reducing the incidence of RVO.

Alcohol consumption was lower in the factors associated with RVO 18(24.7) participants with RVO took alcohol. This finding is keeping with others studies done across the world, whereby previous studies have establishes that moderate alcohol consumption has a protective effect on the development of RVO (15)(17)(21)(32).

In this study, macular edema was the most ocular complication leading to vision loss, followed by vitreous hemorrhage. In this study, macular edema was the most ocular complication leading to vision loss, followed by vitreous hemorrhage. These findings correlate with the Port Harcourt and Benin city studies of Nigeria and the Ahmedabad study of Gujarat India, where they also reported macular edema as the major ocular complication in all types of RVO (4)(6)(17)(28).

CHAPTER FIVE

5.0 CONCLUSION AND RECOMMENDATIONS

5.1 Conclusion

Our study shows that the proportion of RVO in our hospital is relatively high and affects males more than females. Central retinal vein occlusion is the commonest type of retinal vein occlusion followed by branch vein occlusion. RVO is a significant cause of visual impairment and blindness. Increasing age, hypertension, and hyperlipidemia were associated with RVO. The commonest ocular complication of RVO was macular edema.

5.2 Recommendations

- To strengthen primary prevention of the modifiable risk factors and unhealthy lifestyles to reduce the incidence of RVO and complications in general population.
- To improve our facilities for investigation and effective treatment of the disease, is of paramount importance and could help reduce visual impairment due to RVO.
- Further studies should be done involving the use of fluorescein fundus Angiography and electroretinogram to better quantify the degree of retinal ischemia.
- Further prospective studies should be done in a longer time and population based in order to get true magnitude of RVO in our environment.

5.3 Study limitations and mitigations

- The quantification of the degree of retinal ischemia was limited by absence of fluorescence angiography machine at our facility. However the classification of RVO into ischemic and non-ischemic was made based on clinical findings and OCT thereby getting a true reflection of ischemic and no-ischemic disease.
- The duration of the study was short to give a true representation of magnitude. Therefore the study should be prolonged for a better assessment.
- This study, describes only a snapshot on the pattern and associated factors for RVO among patients attending MNH Hospital hence results cannot be generalized for the whole community. However, it is a tertiary hospital which receives patients referred from different parts of the country; this will increase the generalization of our findings.

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Appendices

Appendix I: Questionnaire (English Version)

Serial number.....

Registration number.....

Recruitment Date:

Phone contact number.....

PART I: BASELINE INFORMATION

Demographic data

SN	QUESTION	CODING CATEGORIES	RESULTS `
1.	Age	1. 18-40 years 2. 41-60 years 3. 61+	
2.	Sex	1. Male 2. Female	
3.	Race	1. African 2. Asian 3. Caucasian	
4.	Residence (Fill district and region)	1. Region..... 2. District.....	
	Level of education	1. No formal education 2. Primary 3. Secondary 4. College	
5.	Occupation	1. Public servants 2. Trading	

		3. Peasant 4. Technicians 5. Unemployed 6. Others specify	
6.	Do/did you smoke cigarette prior or during illness?	1. Yes 2. No	
7.	Do/did you drink alcohol prior or during?	1. Yes 2. No	
8.	Are you hypertensive?	1. Yes 2. No	
9.	If yes in Q8, are you on any treatment?	1. Yes 2. No	
10.	If No in Q9, proceed to blood pressure measurement		
11.	Are you diabetic?	1. Yes 2. No	
12.	If yes in Q11, are you on any treatment?	1. Yes 2. No	
13.	If No in Q12, proceed to blood glucose measurement's		
14.	Do you have glaucoma?	1. Yes 2. No	

15.	If yes in Q14, are you on any treatment	1. Yes 2. No	
16.	If No in Q15, proceed for glaucoma assessment		
PART II: 'OCULAR HISTORY'			
17.	Chief complaints	
18.	Any history of eye problems	1. Yes 2. No	
19.	Do you have vision problem?	1. Yes 2. No	
20.	If yes in Q19, Does vision problem affect your activity?	1. Yes 2. No	
21.	Does vision problem affect your activities	a) Yes b) No	
PART III: PATIENTS EXAMINATION FINDINGS			
Ocular Examination			
22.	Affected eye (RVO)	1. RE 2. LE 3. BE	
23.	Visual acuity	1. RE 2. LE	
24.	VA category	1. Normal vision (Better than 6/9) 2. Mild visual impairment	

		(6/12-6/18) 3. Moderate impairment (6/18-6/60) 4. Severe impairment 6/60-3/60 5. Blindness (worse than 3/60)	
25.	IOP (mmHg)	RE..... LE..... 1. <21 mmHg 2. >21 mmHg	
26.	Pupillary light response	RE..... LE..... 1. RAPD 2. b) NO RAPD	
27.	Anterior segment examination	RE..... LE..... 1. NVI 2. No NVI	
28.	Posterior segment examination	RE..... LE.....	
	a) Vitreous hemorrhage	RE..... LE..... 1. Yes 2. No	
	b) Optic disc changes optic disc edema, disc neovascularization (NVD),	RE..... LE..... 1. Optic disc changes 2. Optic disc edema	

	cup to disc ratio(CDR)	3. NVD 4. CDR <0.3 5. CDR > 0.3	
	c) macular edema,	RE..... LE..... 1. Present 2. Absent	
	d) dilated tortuous retinal vasculature,	RE..... LE..... 1. Present/Severe 2. Mild/Absent 3. Limited to a branch 4. Limited to hemifield	
	e)Retinal hemorrhage (deep/blot and flame-shaped hemorrhage)	RE..... LE..... 1. Present/extensive 2. Mild/Absent 3. Limited to a branch 4. Limited to hemifield	
	f) cotton-wool spots ("blood and thunder appearance")	RE..... LE..... 1. Present/Multiple 2. Mild 3. Absent	
29.	OCT findings	RE LE..... 1. Macular edema 2. Epiretinal membranes 3. subretinal fluid 4. central macular thickness	
Laboratory investigations			
30.	Complete blood count	
31.	Erythrocyte sedimentation		

	Rate	
32.	Hemoglobin A1c (HbA1c)	1. < 6.5% 2. >6.5%	
33.	Serum total cholesterol	
34.	High-density lipoprotein	
35.	Low-density lipoprotein	
36.	Serum triglycerides	



MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

SCHOOL OF MEDICINE

DEPARTMENT OF OPHTHALMOLOGY



Appendix II: Consent Form (English Version)

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

DIRECTORATE OF RESEARCH AND PUBLICATIONS, MUHAS

Reg No.

Date.....

Consent to participate in a research study

Greetings. I am Dr. Peter Mlundwa a postgraduate student, pursuing a master's degree in medicine in ophthalmology at Muhimbili University of Health and Allied Sciences. I am researching to determine the pattern and associated factor for retinal vein occlusion among patients attending the retina clinic at Muhimbili national hospital.

Purpose of the study

To assess the pattern and associated factors for retinal vein occlusion among patients attending the retina clinic at Muhimbili National Hospital.

Participants of the study

All Adult patients diagnosed with RVO at the retina clinic Muhimbili National hospital during the study period.

The participants will undergo a thorough history, ocular examinations, and non-invasive ocular investigations. This includes measurement of visual acuity, pupillary light response, measurement of intraocular pressure and examination of the anterior and posterior segment of the eyes. History and physical examination will both be performed by me, the principal investigator or volunteer assistant and supervised by a specialist. For laboratory purpose blood investigation will be taken and it will include drawing blood from your body. This will be performed by the investigator and every possible care and standard will be observed. If you decide not to participate in this study, your eye care services will not be affected in any way possible.

Confidentiality

All the participants who will join the study will be identified by their number and thus their names will not appear. The information obtained during data collection will be kept under a strict locked environment where it is only the researcher who will have access and will be destroyed after the dissertation has been submitted and accepted for the award of a postgraduate degree.

Risk

No harm is expected to occur because of joining in the study.

Benefits

If you agree to participate in this study, you will benefit from understanding your condition, plan on treatment and prevention of future complications. The results of the study will also help bridge the gap of knowledge and bring awareness to eye care workers and policymaker authorities that RVO is also a leading cause of blindness, and plan for preventive measures.

Right to withdrawal

Joining in this study is completely your choice. You can withdraw at any particular moment even after signing the consent form. You can even refuse to respond to any question in the questionnaire.

Whom to Contact

In case of any concern or question about the study you can contact the researchers, Dr Peter Mlundwa (mob. 0718444264), Prof Milka Mafwiri (mob. 0784325250) and Dr. Celina Mhina (mob.0719326498) at Muhimbili University, P.O. BOX 65001 Dar es Salaam. You can also contact the Chairperson of the Senate, Research and Publications Committee, Dr. Bruno Sunguya P.O.BOX 65001, Dar es Salaam, for any matters concerning ethical violation of the study.

Ihave read the contents in this form. My questions have been answered and I agree to participate in this study.

Signature of participant.....

Signature of researcher/research assistant.....



MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

SCHOOL OF MEDICINE

DEPARTMENT OF OPHTHALMOLOGY



Appendix III: Informed Consent (Swahili Version)

**CHUO KIKUU CHA AFYA NA SAYANSI SHIRIKISHI MUHIMBILI,
KURUGENZI YA TAFITI NA UCHAPISHAJI**

IDHINI YA KUSHIRIKI KWENYE UTAFITI

Namba ya usajili.....

Tarehe.....

Habari,

Mimi ni Dkt. Peter Mlundwa, mwanafunzi wa shahada ya Uzamili ya udaktari bingwa wa macho, katika chuo kikuu cha Afya na sayansi shirikishi Muhimbili. Nafanya utafiti kuangalia muundo na sababu zinazohusika kusababisha kuganda kwa damu katika mishipa ya damu kwenye pazia la nyuma ya macho, kwa wagonjwa wanao hudhuria kliniki ya ‘retina’ hospitali ya taifa ya Muhimbili.

Usiri

Washiriki wote wa utafiti huu hawatatambuliwa kwa majina yao ila kwa namba. Habari zote za washiriki zitahifadhiwa/zitafungiwa mahali salama ambapo mtafiti mkuu tu ndiye atakayekuwa na funguo na makabrasha yote yatateketezwa mara baada ya utafiti kuisha na mtafiti kutunukiwa shahada ya pili ya udaktari.

Lengo la utafiti

Kuangalia muundo na sababu zinazohusika kusababisha kuganda kwa damu katika mishipa ya damu kwenye pazia la nyuma ya macho, kwa wagonjwa wanao hudhuria kliniki ya ‘retina’ hospitali ya taifa ya Muhimbili.

Washiriki wa utafiti

Washiriki kwenye utafiti huu ni wagonjwa watu wazima wenye ugonjwa wa kuganda kwa damu katika mishipa ya pazia la nyuma ya jicho, ambao wana hudhuria kliniki ya ‘retina’ katika hospitali ya taifa Muhimbili. Washiriki watafanyiwa uchunguzi wa macho wa kawaida na kwa kutumia vifaa ambavyo havihatarishi hali ya macho. Pia watachukuliwa vipimo vya damu katika umakini na viwango vinavyotambulika, haya yatafanywa na mtafiti mkuu chini ya usimamizi wa daktari bingwa.

Madhara

Hakuna madhara yanayotarajiwa kwa washiriki wa utafiti.

Faida

Ushiriki katika tafiti hii utakusaidia kutambua ugonjwa wako, matibabu, athari na pia njia mbali mbali ya kuzuia athari Zaidi. Matokeo ya utafiti huu yatasaidia kuongeza ufahamu kwa wahudumu wa afya na watunga sera kwamba ugonjwa wa kuganda damu katika mishipa ya damu kwenye pazia la nyuma ya macho husababisha upofu, hivyo kuelekeza nguvu katika mbinu kinga.

Haki ya kujitoa

Ushiriki katika utafiti ni wa hiyari, na mshiriki yoyote ana haki ya kuamua kujitoa katika utafiti wakati wowote kujitoa hakutaathiri kiwango cha huduma kwa mgonjwa.

Mawasiliano

Ikiwa kuna swali lolote kuhusu utafiti huu, tafadhali wasiliana na Dkt Peter Mlundwa (sim. 0718444264), Prof Milka Mafwiri (sim. 0784325250) na Dkt. Celina Mhina (mob.0719326498) Chuo kikuu Cha Afya na Sayansi Shirikishi S.L.P 65001 Dar es Salaam. Hata hivyo, ikiwa kuna suala lolote linalohusu mwenendo wa kimaadili ya utafiti wa kimatibabu, wasiliana na mwenyekiti wa kamati ya tafiti na machapisho wa chuo kikuu cha afya na sayansi shirikishi Muhimbili Dkt. Bruno Sunguya, S.L.P 65001, Dar es salaam.

Sahihi ya mshiriki.....

Sahihi ya mtafiti/mtafiti msaidizi.....

Appendix IV: Ethical clearance letter –MUHAS

**MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES
OFFICE OF THE DIRECTOR OF RESEARCH AND PUBLICATIONS**

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Ref. No.DA.282/298/01.C/

Date 22nd June, 2020

MUHAS-REC-6-2020-284

Peter Mlundwa,
Department of Ophthalmology,
School of Medicine,
MUHAS

**RE: APPROVAL FOR ETHICAL CLEARANCE FOR A STUDY TITLED
“PATTERN AND ASSOCIATED FACTORS FOR RETINAL VEIN
OCCLUSION AT MUHIMBILI NATIONAL HOSPITAL”**

Reference is made to the above heading.

I am pleased to inform you that the Chairman has on behalf of the University Senate, approved ethical clearance of the above-mentioned study, on recommendations of the Senate Research and Publications Committee meeting accordance with MUHAS research policy and Tanzania regulations governing human and animal subjects research.

APPROVAL DATE: 2020-06-18

EXPIRATION DATE OF APPROVAL: 2021-06-17

STUDY DESCRIPTION:

Purpose:


The Purpose of this hospital based descriptive cross-sectional study is to assess the pattern and associated factors for retinal vein occlusion among patients attending the retina clinic at Muhimbili National Hospital.

The approved protocol and procedures for this study is attached and stamped with this letter, and can be found in the link provided: <https://irb.muhas.ac.tz/storage/Certificates/Certificate%20-%205.pdf> and in the MUHAS archives.

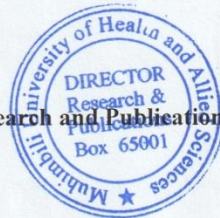
The PI is required to:

1. Submit bi-annual progress reports and final report upon completion of the study.
2. Report to the IRB any unanticipated problem involving risks to subjects or others including adverse events where applicable.
3. Apply for renewal of approval of ethical clearance one (1) month prior its expiration if the study is not completed at the end of this ethical approval. You may not continue with any research activity beyond the expiration date without the approval of the IRB. Failure to receive approval for continuation before the expiration date will result in automatic termination of the approval for this study on the expiration date.
4. Obtain IRB amendment (s) approval for any changes to any aspect of this study before they can be implemented.
5. Data security is ultimately the responsibility of the investigator.
6. Apply for and obtain data transfer agreement (DTA) from NIMR if data will be transferred to a foreign country.
7. Apply for and obtain material transfer agreement (MTA) from NIMR, if research materials (samples) will be shipped to a foreign country,
8. Any researcher, who contravenes or fail to comply with these conditions, shall be guilty of an offence and shall be liable on conviction to a fine as per NIMR Act No. 23 of 1979, PART III section 10 (2)
9. The PI is required to ensure that the findings of the study are disseminated to relevant stake holders.

PI is required to be versed with necessary laws and regulatory policies that govern research in Tanzania. Some guidance is available on our website <https://drp.muhas.ac.tz/>.


Dr. Bruno Sunguya

Chairperson, Senate Research and Publications Committee



Appendix V: Introduction letter-MUHAS

**MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES
OFFICE OF THE DIRECTOR OF POSTGRADUATE STUDIES**

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Ref. No. HD/MUH/T.189/2018

24th June, 2020

Executive Director,
Muhimbili National Hospital
P.O. Box 6500,
DSM.

Re: INTRODUCTION LETTER


The bearer of this letter is Peter Mlundwa (HD/MUH/T.189/2018), a student at Muhimbili University of Health and Allied Sciences (MUHAS) pursuing MMed Ophthalmology.

As part of his studies he intends to do a study titled: **"PATTERN AND ASSOCIATED FACTORS FOR RETINAL VEIN OCCLUSION AT MUHIMBILI NATIONAL HOSPITAL"**.

The research has been approved by the Chairman of University Senate.

Kindly provide him the necessary assistance to facilitate the conduct of his research.

We thank you for your cooperation.


Ms. Victoria Mwanilwa

For: DIRECTOR, POSTGRADUATE STUDIES

cc: ~~Dean, School of Medicine, MUHAS~~
Peter Mlundwa

Appendix V: Permission letter - MNH**MUHIMBILI NATIONAL HOSPITAL**

Cables: "MUHIMBILI"
 Telephones: +255-22-2151367-9
 FAX: +255-22-2150534
 Web: www.mnh.or.tz



Postal Address:
 P.O. Box 65000
DAR ES SALAAM
 Tanzania

In reply please quote:

MNH/TRCU/Permission/ 2020/123

01st July 2020

Head of Department
 Ophthalmology
Muhimbili National Hospital

RE: PERMISSION TO COLLECT DATA AT MNH.

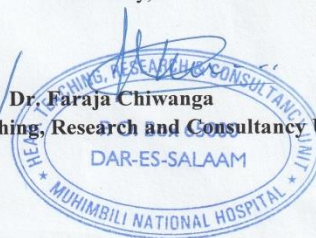
Name of Student	Peter Mlundwa
Title	"PATTERN AND ASSOCIATED FACTORS FOR RETINAL VEIN OCCLUSION AT MUHIMBILI NATIONAL HOSPITAL".
Institution	Muhimbili University of Health and Allied Sciences
Supervisor	Milka Mafwiri
Co – Supervisor	Dr. Celina Mhina
Period	01 st July 2020, to 31 st December, 2020

Approval has been granted to the above mentioned student to collect data at MNH.

Kindly ensure that the student abide to the ethical principles and other conditions of the research approval.

Sincerely,

Dr. Faraja Chiwanga
 Head of Teaching, Research and Consultancy Unit



c. c DSS
 c. c **Peter Mlundwa**

All Correspondence to Addressed to the Executive Director