DIABETIC RETINOPATHY AND ASSOCIATED FACTORS IN PATIENTS WITH DIABETES MELLITUS AT MUHIMBILI NATIONAL HOSPITAL

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DIABETIC RETINOPATHY AND ASSOCIATED FACTORS IN PATIENTS WITH DIABETES MELLITUS AT MUHIMBILI NATIONAL HOSPITAL

By

Peter Hinju

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: **"*Diabetic retinopathy and associated factors in patients with diabetes mellitus at Muhimbili Natinal hospital*",** in (partial) fulfillment of the requirement for the degree of Master of Medicine (Ophthalmology) of the Muhimbili University of Health and Allied Science.

_____

Dr. Suzan Mosenene

(Supervisor)

Date_____

DECLARATION AND COPYRIGHT

I, **Dr. Peter Hinju**, 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.....

ACKNOWLEDGEMENT

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I would like to acknowledge the sacrifice, patience and support from my family who deserved a lot more than I could give during this demanding period.

Last but not least, I am grateful to Almighty God for giving me health and capability to accomplish this work.

DEDICATION

To my loving wife, Beatrice Francis and our children Agnes , Goodluck, Glory and Brian for their endless love and support. Also to my parents the late Coin .D. Hinju and Mrs Agnes hinjo for the encouragement and prayers.

ABSTRACT

Background;

Diabetes mellitus(DM) is a non communicable disease and chronic metabolic disorder, regarded as an important public health problem . Globally affects 463 million people with DM . Diabetic retinopathy is a sight threatening microvascuar cmplication of diabetes mellitus. Causing visual impairment in 2.6 million and blindness in 2.52 million people, predicted to double by the year 2030. Blindness related to diabetic retinopathy is projected to increase in developing world including Tanzania. However several factors are associated directly or indirectly involved in the development and progression of DR, evidence suggested that good control of the associated factors reduces the risk of DR.

The diabetic clinic at the Muhimbili National Hospital attends an average of 75 patients per clinic day, potentially all are at risk of developing DR. Despite having many patients presenting to the diabetic clinic, the last study done on factors associated with DR at MNH was in 1990. The time since this last study done is long enough for relaying on its report ,hence there was a need of evaluating current information of these factors.

Aim;

The aim of this study was to provide current information on prevalence and associated factors for DR.

Methodology:

A cross section descriptive hospital based study was conducted at Muhimbili national hospital at diabetic clinic,from May to June 2021. Including 370 participants, all were adults 18 years and above DM patients. They were selected through systematic sampling technique .Clinical history, systemic and ocular examination (retinopathy screening) was done. A structured questionnaire was used to collect information on clinical and laboratory findings. Analysis was done using SPSS. Binary logistic regression followed by multiple logistic regression analysis was conducted to identify associated factors.

Result;

There were 39.9% participants with DR. Participants with age <40 had only 2.7% of DR. Peasants were found with less proportion compared to employed (1.7%,51,4%) respectivey. Employed were about three times likely to develop DR than peasants (AoR 2.68(95%CI1.47-4.88), duration (>10years DM) participants were 2.5 times likely to have DR than those with less than 10 years of DM (AoR 2.53 (95%CI 1.5-4.10) and participants in moderate glycaemic control (6-8%) HbA1c were twice likely to develop DR (AoR 2.8(95%CI 1.025.-5.12) than those with the normal range(<6%), level of no formal/pimary education found to have 2.21 Odd (AoR 2.21(95%CI 11.114.39) of developing DR than those with collage level of education. While participants with hypertension had significant association with DR with an odd ratio of nearly twice of the non hypertensive. (AoR 1.86 (95% CI 1.11-3.11).

Conclusion;

More than a quarter of the participants had diabetic retinopathy were office working employed particiants, duration of illness, glycaemic control, low level of education and hypertension were significantly associated with DR.

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ABBREVIATIONS

1DM	Type one diabetes Mellitus
2DM	Type two diabetes MAellitus
CSME	Clinically Significant Macular Edema
DCCT	Diabetic Control and Complication Trial
DM	Diabetic Mellitus
DME	Diabetic Macular Edema
DR	Diabetic Retinopathy
ETDRS	Early Treatment of Diabetic Retinopathy Study
HbA1c	Hemoglobin A1c
IDDM	Insulin-Dependent Diabetic Mellitus
NIDDM	Non-Insulin Dependent Diabetic Mellitus
NPDR	Non-Proliferative Diabetic Retinopathy
OPD	Out-Patient Department
PDR	Proliferative Diabetic Retinopathy
UGDP	University Group Diabetes Program
UKPDS	UK-Prospective Diabetes Study
VA	Visual acuity
VEGF	Vascular Endothelial Growth Factor
VI	Visual Impairment
WESDR	Wisconsin Epidemiologic Study of Diabetic Retinopathy
WHO	World Health Organization

DEFINITION OF TERMS

Diabetic mellitus: Is a chronic metabolic disorder characterized by elevated levels of glucose in the blood (hyperglycemia) due to lack of or resistance to insulin.

Diabetic retinopathy: Refers to retinal changes seen in patients with diabetes mellitus. Presence of micro aneurysm and any of the following, hemorrhage, exudate, cotton wool spots, intraretina micro vascular anormalies (IRMA), vein beading and new vessles.

Diabetic maculopathy: Refers to macular changes as part of diabetic retinopathy and mainly characterized by macular thickening (edema) and exudations.

Proliferative Diabetic Retinopathy; Refers to diabetic retinal changes involving new vessels formation.

Normal systemic blood pressure; Refers to a range of Systolic 120 – 140 mmhg and Diastolic 80 – 90 mmhg

Hypertension; Will be defined as blood pressure reading above 140/90 mmhg

Hyperlipidaemia: Basing on Muhimbili Nationa Hospital is the presence of high levels of lipid in the blood (Total cholesterol > 5.17mmol/l, LDL >3.34mmol/l)

Hyperglycaemia; Is the presence of high level of blood sugar (FBG $\geq$ 11mmol/l, HbA1c $\geq$ 6.5%)

CHAPTER ONE

1 INTRODUCTION

1.1 Background

Diabetes mellitus is a chronic metabolic condition characterized by elevated blood glucose levels (hyperglycemia), due to insulin deficiency or resistance. Diabetes mellitus is considered a significant health concern worldwide since it affects all ages and races (1). Worldwide, there are 463 million people with DM (diabetes mellitus) projected to rise to 700 million by 204 (2,3). Demographically there are 72.0 percent of people aged 20 to 60 with DM, 27.8 percent over the age of 65 and 0.2 percent of children and teenagers. Overall, the prevalence is higher in urban areas (10.8%) than in rural areas (7.2%), although this gap is narrowing on the increase in rural prevalence (2).

Africa as a continent found to have a prevalence of 4.7% in 2019 which is expected to rise to 5.2% in 2045 (9). Countries with highest estimated numbers with a person with diabetes includes South Africa (4.6 Million), Nigeria (2.7 Million) and Democratic Republic of Congo (1.8 Million). Tanzania has approximately 1 million people with DM that makes a prevalence of 3.7% among adult population (2). A number of studies associated this increasing prevalance with changing of lifestyle patterns (e.g. higher calorie intake, increased consumption of processed food, and sedentary lifestyle, which is mostly seen in patients with type 2 DM (3).

Diabetic retinopathy is one of several Diabetes-related complications. It is the leading cause of blindness and visual impairment in the working-age population of the developing world (4). The total population affected by the diabetic retinal disease is estimated to be 382 million and is projected to reach 592 million by 2025. A continuation systematic review and meta-analysis of data from 288 population-based studies among 3,983,541 participants from 98 countries in the year 2015, showed diabetic retinopathy caused visual impairment in 2.6 million and blindness was 2.52 million people, with expectation of 3.2 million people to have visual impairment by the year 2020 (5). A community based study done in Kilimanjaro region in Tanzania in 2010 to 2014 showed a prevalence of 27.9% of diabetic retinopathy

and the unpublished study done at MNH Dar-Es-Saalam in 2016 showed a prevalence of 57% (6) .

Pathophysiology of diabetic retinopathy:

Diabetic retinopathy (DR) has long been recognized as a micro-vascular disease. Hyperglycemia as one of the major risk factors, considered to play an important role in the pathogenesis of retinal micro vascular damage. The presence of persistence high blood glucose trigger pericyte loss which is the hall mark of the early events of diabetic retinopathy. Since pericytes are responsible for providing structural support for capillaries, the loss leads to localized out pouching of capillaries walls forming micro aneurysms an early clinical sign of DR.

These vascular changes together with hematological changes alter normal lamina flow of blood, causing formation of micro thrombus then micro capillaries occlusion hence retinal ischemia. Retinal ischemia/hypoxia leads to up regulation of Vascular Endothelial Growth Factor (VEGF) through activation of hypoxia-inducible factor 1 (HIF-1), which will influence growth of new blood vessels. These new vessels are prone to bleeding, oedema and the accompanying fibrosis leading to traction retinal detachment. This distorts the anatomical structure of the retina and leads to functional alterations of the retinal neurons and glial cells (1,9-11,18).

Early Treatment of Diabetes Retinopathy Study (ETDRS) classify diabetic retinopathy in two major groups which are Non-proliferative diabetic retinopathy (NPDR) and Proliferative diabetic retinopathy (PDR). NPDR is further classified into mild NPDR, moderate NPDR, severe NPDR, and very severe NPDR. PDR is classified into high risk and low risk depending on extent of the disease. High risk proliferative diabetic retinopathy is characterized by presence of new vessels at the disc (NVD), new vessels elsewhere (NVE) with presence of vitreous or pre-retinal hemorrhages. Diabetic maculopathy is the third category under ETDRS (1,12).

Factors associating with diabetic retinopathy:

A number of studies correlated with rising urbanization and evolving lifestyle habits (e.g., higher calorie intake, increased consumption of processed food, and sedentary lifestyle). This has been observed mainly among patients with type 2DM, thus it suggest as the main cause of rise in DM prevalence in Africa (11).

Due to the rapid increase of patients with DM in the country it was necessary to conduct a research on DR and associated factor so as to identify the common factors which predispose patients with DM, in order to improve their management.

The development and progression of retinopathy is related to glycemic control (HbA1c), blood pressure, age at DM diagnosis, DM duration, anemia, hyperlipidemia, smoking and obesity. All the mentioned risk factors are modifiable except age and duration of the the diabetes (7).

1.2 PROBLEM STATEMENT

The overall world population affected by the diabetic retinal disease is estimated to be 382 million and is projected to reach 592 million by 2025 and Africa has the prevalence of 30.2 to 31.6% people with diabetic retinal diseases. Diabetic retinopathy is reported to cause visual impairment in 2.6 million and blindness in 2.52 million people, predicted to double by the year 2030.

Blindness related to diabetic retinopathy is projected to increase in developing world including Tanzania. Visual impairment and blindness resulting from DR are major public health problems causing significant suffering, visual disability, loss of productivity, and diminishing quality of life for millions of people aged 18 years and above.

The life span of patients with DM have increased in most developing countries due to availability and accessibility of treatment hence high chances of developing diabetes complications including DR. However according to estimations, DR will develop in more than 75% persons within 15-20 years of diabetes and evidence suggested that good control of the associated factors reduces the risk of DR..

An increase in the incidence of Diabetic retinopathy has been reported in various countries in the late years and a strong association between the risk factors such as duration of DM , controlled blood glucose, hyperlipidaemia plus hypertension and Diabetic retinopathy has been previously demonstrated. In recent years a lot of focus have been made on the management of NCD like DM in developing countries including Tanzania. However there is no current information on the risk factors and magnitude of Diabetic Retinopathy in our settings.

At MNH the last study done on factor associated with DR was conducted 30 years ago by M. Mafwiri et al, showed 50.5% prevalence of DR. This study aimed at providing a current information on magnitude and associating factors for DR in patients at MNH.

1.3 RATIONALE

The findings of this study has provided basic information on the prevalence of DR and associated factors and result will be used for establishing institutional management protocols for patients with DM in order to prevent complications like diabetic retinopathy.

1.4 CONCEPTUAL FRAMEWORK

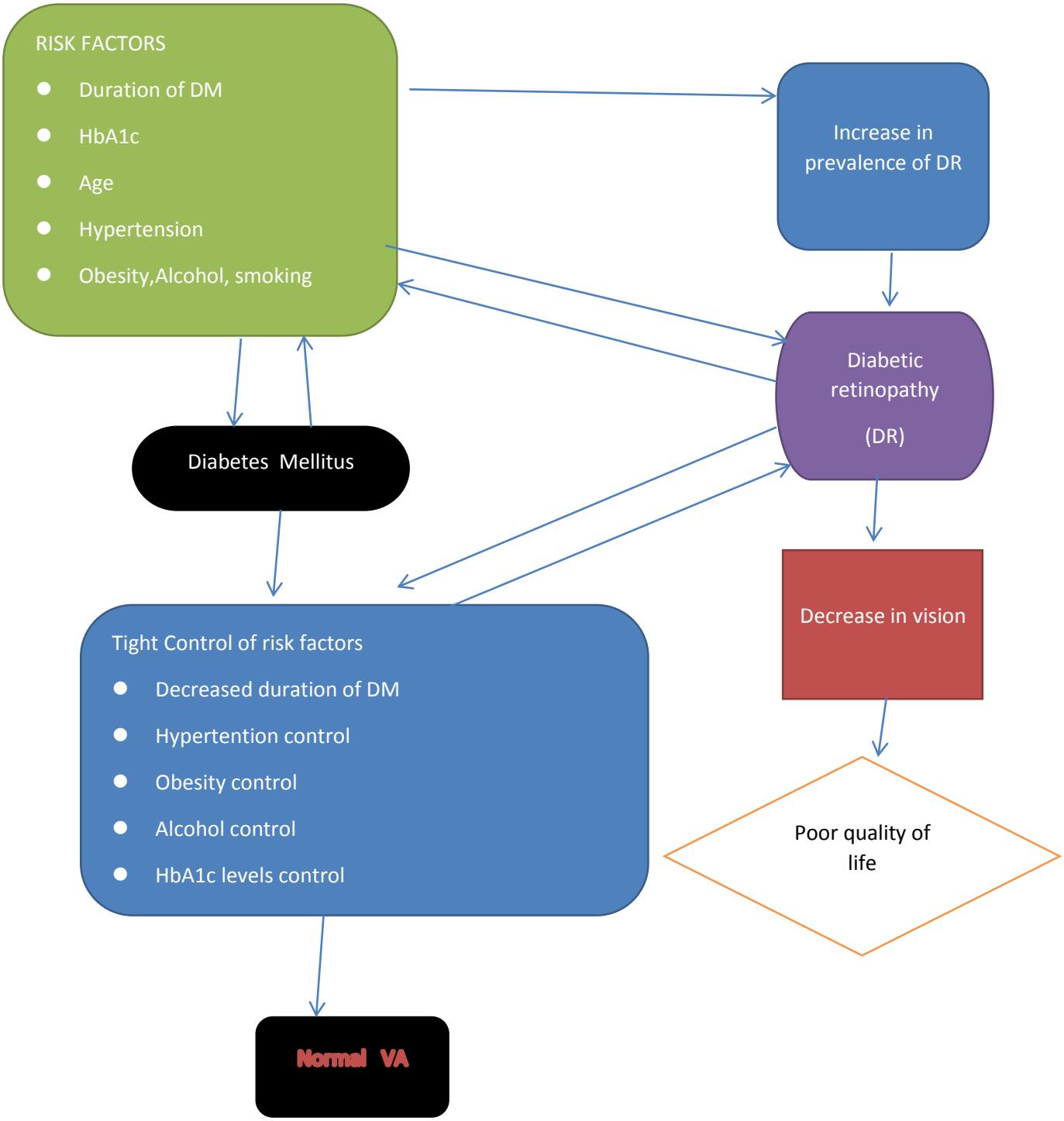

Figure 1: Conceptual flame work.

1.5 RESEARCH QUESTIONS

1 What was the proportion of diabetic retinopathy among patients with diabetes mellitus at MNH.

2 What were the factors associated with diabetic retinopathy among patients with diabetes mellitus at MNH .

1.6 OBJECTIVES:

1.6.1 BROAD OBJECTIVE:

To determine the magnitude of diabetic retinopathy and associating factors among patients with diabetes mellitus at Muhimbili National Hospital.

1.6.2 SPECIFIC OBJECTIVES:

1 To determine the proportion of diabetic retinopathy among adult patients with diabetes mellitus at MNH.

2 To determine factors associated with diabetic retinopathy among patients with diabetes mellitus at MNH

CHAPTER TWO

2 LITERATURE REVIEW

The increase in prevalence of diabetes in many countries and regions was correlated with rapid urbanization and mostly shifts towards sedentary life. It is estimated that the total population affected by the diabetic-related retinal disease will be 382 million and is projected to reach 592 million by 2025 (3).

Diabetic retinopathy takes the highest rank of the cause of blindness and visual imparement among people of working age group with DM in the world (22). The meta analysis study done in 2015 showed 2.6 and 2.32 million people were having impaired vision and blindness respectively. The impairment of vision expected to rise to 3.2 million people by the year 2020 (13).

Risk factors for progression to DR includes, poor glyceamic control, coexisting hypertension, smoking, lipidaemia, obesity which are modifiable factors while the duration of DM, gender and age of the patient, are non-modifiable factors (4).

Glycated hemoglobin (HbA1c) in DR

Glycated hemoglobin (HbA1c) is also called glycosylated, or glycohemoglobin. The HbA1c test assesses the average amount of glucose in the blood over the past 2 to 3 months by calculating the level of hemoglobin glycated (glycosylated). It is important test for people with diabetes as the higher the HbA1c, the greater the risk of developing complications associated with diabetes . The American Diabetic Association recommend the test as the best predictor of the glycemic value of the past 8-12 weeks (14,15). Two large-scale trials, the UK Prospective Diabetes Survey (UKPDS) and the Diabetes Control and Complications Test (DCCT) have shown that decrease of HbA1c by 1% (or 11 mmol / mol) in people with type 1 diabetes or type 2 diabetes decreases the risk of micro-vascular complications by 25% (16-17).

Levels of Blood HbA1c show how well Diabetes is regulated. The standard level range for hemoglobin A1c is less than 6 percent. In UK, it is recommended that a 48mmol / mol HbA1c (6.5 percent) be used as the cut point for DM diagnosis. A value of less than 48mmol

/ mol (6.5 per cent) does not exclude DM, which has been diagnosed using glucose tests (22,24). HbA1c levels reflect blood glucose levels in the past, it assesses the long-term metabolic regulation in patients with DM (9). HbAIc does not indicate normal blood glucose ups and downs. It predicts the hyperglycemia rate for 2 to 3 months (18). The amount of HbA1c in healthy people is less than 6 per cent of total haemoglobin. Research have shown that diabetes problems can be prevented or avoided if the amount of HbA1c can be held below 7 per cent. It is recommended that diabetes care be oriented to maintaining the HbA1c level of a patient as near as possible to normal (< 6 percent) without episodes of hypoglycemia (low blood glucose levels) (8).

HbA1c is usually calculated to assess how well a program for the treatment of type 1 or type 2 diabetes (including medication, exercise, or dietary changes) performs (10,11,12).

The levels of glycated Hemoglobin among patients with diabetic retinopathy.

A cross-sectional analysis with the key outcome variables of HbA1c and risk factors, control and their association with DR and visual acuity(VA) was performed in Rabin Medical Center in Israel for 4 months. The research comprised 178 clinical settings study population and 107 community-based population, studded the two settings groups both with type two DM consecutively in the same period. Those at clinical settings had a mean level of 8.2 % (SD 1.9) while those at community had 7.7% (SD 1.6).The study generally found better diabetic retinopathy in patients with ≤ 7% HbA1c (13).

A hospital-based descriptive retrospective study was performed in India in 2012 to assess the prevalence of DR in combination with HbA1c and also compare the frequency of DR with HbA1c. This research showed that the levels of HbA1c also raised as the frequency of the severity of DR raised. It was therefore mentioned that HbA1c is a useful tool for assessing DM's long-term control and DR progression (9,14).

However all of the reviewed studies in this objective did little attention on other factors that may associate with this gylcaemic control in worsening the DR status among participants in hiarache manner.

The levels of glycated hemoglobin according to the severity of diabetic retinopathy.

A study done at Goma Bai in Neemuch city in India,which included 80 participants confirmed having type two DM ,whom were rondamly selected and examined for retina by retina specialist and HbA1c was determined clinically. The study found significant difference between NPDR and PDR than control.HbA1c of less than 7% observed in 60% of patient with no DR and 10% of NPDR. The HbA1c of 7-8 was observed in 40% of patients with no DR, 57.4% patients with NPDR and 50% in patients with PDR. HbA1c of > 8 was not found among patients with no DR, but was observed in 14.28% in NPDR and 50% of PDR patients.This study signified that the value of glycosylated haemoglobin increases with the increase of severity of DR (15,16,17,18,34).

The studies under this objective have explored associations between glycaemic level (using HbA1c) and extend of severity of DR . However non of findings indicated evidence of ranking glycaemic control with other factors in causing DR .

Apart of correlation of diabetic retinopathy with presence of uncontrolled blood glucose ,it was important to study further the contribution of other factors for diabetic retinopathy. This study was also investigated association in patients with diabetic retinopathy who will attend at MNH diabetic clinic as it was studied in other places and make a comparison with our findings.

Duration of DM

In a number of studies, the length of diabetes has been found to be strong factor in the development of diabetic retinopathy. A research performed by Wisconsin Epidemiological Study of Diabetic Retinopathy (WESDR) among younger onset diabetes patients, the incidence of some retinopathy was 8% at 3 years, 25% at 5 years, 60% at 10 years, and 80% at 15 years. The prevalence of PDR at 3 years was 0 per cent and increased at 15 years to 25 per cent (19).

Lamoureux et-al's global prevalence and major risk factors from the Feb 2010 DR report provided results from 35 studies that included 22,896 patients with DM. DR prevalence increased with the duration of DM where patients with DM less than 10 years after onset had

21.1% of DR versus 76.3% of patients with DM greater or equivalent to 20 year (20,21,22,23,24).

Results of a case-control study conducted in Brazil among DM patients with DR and no DR, who attended the University of South Santa Catarina DM clinic showed that individuals with poor glycemic control were about 4 times likely to have DR with an OR 3.83. The study showed higher risk of disease in 11-15yrs OR 7.52 and > 15 years OR 9.0.This shows diabetic patients after 10 years of disease with poor glycaemic control have high chance of DR (31,38).

Hypertension

Hypertension is an important factor in the control of DR. In a randomized controlled trial done in England, Scotland and Northern Ireland (UKPDS) to determine whether tight control of blood pressure prevents occurrence of diabetic retinopathy among people with DM.The mean follow up time was 8.4 years,patients assigned to tight monitoring reported to have a 34% reduction in risk of developing retinopathy (25).

Results of a study done in Khartoum Sudan, on assessment of the frequency and associating factors of DR among Sudanies with diabetes, who were attending Makka Eye Complex clinic showed overall frequency of DR of 261(82.2%) and PDR of 126 (39.9%) while NPDR were 135(42.7%).Hypertension found to correlate with the severity of DR which triple the risk developing DR (16 ,21).

Milka et al, reported positive association between hypertension and DR . Among 387 patients 18.6% had blood pressures of more than 160/95mmHg or where on treatment for hypertension. The proportion of patients with both retinopathy and hypertension significantly exceeded those with retinopathy but without hypertension (38).

Obesity

Obesity is a disorder involving excessive body fat that increase the risk of health problem, one of disease associated with it is the DM and its complications. In Sweden's Diabetic Incidence Study involving mainly participants with type 1 diabetes, the probability of developing DR was found to increase among obese participants (26).

A meta-analysis review (1993-2016) explored the possible correlation between obesity and DR in 13 studies. Obesity was associated with a substantial increase in the incidence of DR with a rate of 59.6%. When considering only proliferative DR (PDR) no important association was found between obesity and PDR risk. Significant adverse effects were reported in type 2 diabetes mellitus group (27,28).

Hyperlipdaemia

High serum lipid levels have also been proposed as a risk factor for DR.High lipid levels are known to cause endothelial dysfunction due to reduced bio-availability of nitric oxide and this endothelial dysfunction was suggested to pray a role in formation of DR (39) .

However large clinical studies showed discrepancy about the association of serum lipid with severity of DR or DME. ETDRS reported high total cholesterol and low density lipoprotein (LDL) levels were associated with retinal hard exudates. In the study Chennai Urban Rural Epidermiology study, serum lipid were higher in patients with DR than those without (40,42). Though other large studies like Multi Ethnic study of Atherosclerosis ,Australian Diabetic Obesity and life style study and Singapore Malay Eye study reported lipid to be protective of any retinopathy (43,44 ,45).

Cigarette smoking

Cigarette smoking is commonly known to be unhealthy life style, it harms nearly every organ in the body including an eye. A population based cohort study by Scot. E.Moss et-al, on cigarette smoking , aimed to examine the association between cigarette smoking and the incidence and progress of diabetic retinopathy among participants aged >30 years who were categorized into two groups 485 patients who are taking insulin and 502 patients not taking insulin, followed for baseline examination for 4 and 10 years. Neither smoking status (smoked less than 100 cigarettes in their life time and not smoking currently) nor pack-years smoked (clinical significant cigarette smoker e.g 1 pack per day for 1 year) showed significant associations with increased risk of retinopathy. There fore Cigarette smoking was not found to be a risk factor for the long-term incidence of retinopathy (29).

A review of meta-analysis analyzed 73 studies, that associated DR and risk factors, in type 1 diabetes, the risk of diabetic retinopathy increased significantly in smokers compared with non-smokers, and the risk of proliferative diabetic retinopathy also increased significantly in smokers . For type 2 diabetes, the risk of diabetic retinopathy decreased significantly for smokers compared with non-smokers , and the risk of proliferative diabetic retinopathy also decreased significantly in smokers. The study thus showed a substantial rise in the risk of diabetic retinopathy in smokers with type 1 diabetes (27,33,39).

Alcohol

Alcohol being a chemical substance it has an influence in alteration of the body metabolism, hence regular consumption of even moderate amounts can alter diabetic blood sugar control. One serving of alcoholic beverage equals 300mls of beer , 100mls of wine or 30ml of distilled drinks corresponding to 10 -12 gm of pure alcohol (29). Alcohol consumption drinking definition according to the Centers for Disease Control and prevention, is defined as binge drinking in four or more doses for women and five or more doses for men. The low risk consumption can be estimated for 4 doses,or less on a single day and no more than 14 doses per week for men . For women this consumption can not exceed 3 doses in a single day and no more than 7 doses per week (29).

The number of studies are done to find out it's association with diabetic retinopathy.

A meta-analysis of 15 observational studies performed up to May 2016 reported a total of 12,875 DR cases among 37,285 participants when comparing the non-alcohol consumption category with moderate alcohol consumption in relation to DR. Research stratified by research design found that there was no substantial correlation between alcohol intake and DR occurrence in a cluster, case-control or cross-sectional research (31,32,33,38).

Despite these other risk factors showing direct association with the DR , much uncertainty still exists about the relationship in rank between these factors , thus which one among the factors takes highest rank and which one takes list rank in magnitude of worsening DR.

CHAPTER THREE

2 METHODOLOGY:

2.1 STUDY DESIGN:

Hospital based cross sectional study which employed quantitative methods of data collection.

2.2 STUDY PERIOD:

Data collection of this study started from May to June 2021

2.3 STUDY AREA:

The study was conducted at Muhimbili National Hospital . Which is a tertiary referral hospital in Tanzania. Located in the city centre of Dar es salaam in Ilala district. The hospital attends patients from different regions of the country and is used as the main teaching hospital for Muhimbili University of Healthy and Allied Science (MUHAS).

The Diabetic clinic is under the department of internal medicine, it is a specialized clinic attending patients from Dar es Saalam and other regions. In this clinic patients are monitored their DM progress and receives medication. It also have a sub unit clinic that screen patients with diabetes retinopathy which is run by specialist from ophthalmology department. Diabetic clinic is done in 4 days of the week. Monday is for type 1DM and some with type 2DM, approximately attends 50 patients . Tuesday, Wednesday and Thursday is for type 2DM, attendance is approximately 50-100 patients per each clinic day.

2.4 STUDY POPULATION:

All adult diabetic patients from 18 years old and above with diabetc mellitus attending diabetic clinic at MNH from May to June 2021.

2.4.1 INCLUSION CRITERIA:

All patients aged 18 years and diagnosed with DM, attending diabetes clinic at MNH from May to June 2021.

2.4.2 EXCLUSION CRITERIA:

Patients with hazy ocular media that obscured the fundus view for examination for grading diabetic retinopathy.

Patients who had undergone retina laser photo coagulation or treated with ant VEGF that may alter retinal findings for grading retinopathy.

2.5 SAMPLING TECHNIQUE

This study involved two different groups of patients with diabetes mellitus those with type 1DM and 2DM, the groups attends clinic in different days hence the study used stratified random sampling in which two strata will be sampled; type 1DM and type 2DM then followed by systematic random sampling based on proportion of each strata who were finally selected based on simple random sampling technique.

The rate of attendance among type 1DM per week is 12 patients who attends once on Monday expecting to have (12x4=48patients) per month. While type 2DM attends four times per week with a rate of 50 patients per each clinic day that makes a total of 200 patients per week and (200x 4=800 patients) per month. Hence the grand total of patients per month is 848.

The systematic random sampling based in proportion for type 1DM was (48/848 x100=6%), while type 2DM was (800/848 x 100=94%).

Having known the sample size of this study is 370 participants. Type 1DM group/strata involved 6/100 x 370=22 patients) and type 2DM were (94/100 x 370 =348patients). Since the study period had 8 weeks an average of 3 patient expected to be enrolled weekly by systematic sampling technique , which was preceded by a simple random (rotary method) sampling were by a number was randomly picked from a patient register (sample frame) and constant K was calculated K/3 which gave an interval of a sequence for the consecutive participants to obtain the required number of the particular clinic day. The same was done among type 2DM were 11 participants were recruited per each clinic day, the constant K was K/11.

2.6 SAMPLE SIZE

The following formular was used to determine the sample size from the study population.(35)

$$n = \frac{NZ^2P(1-P)}{d^2(N-1) + Z^2P(1-P)}$$

Where;

n= Minimum required sample size

N= Size of the average number of patient attended DM clinic at MNH for 6 months. (N=5,088)

Z2= Statistic for 95% level of confidence equal to 1.96

P = Estimated prevalence of diabetic retinopathy 57% (Prevalence from study done by Aza et al at MNH in 2016.

1-P =Expected proportion of subjects without the disease

d^2 Margin error= 5%

$n = 5{,}088 \times 1.96^2 \times 0.57 (1-0.57) \div 0.05^2 \times (5{,}088-1) + 1.96^2 \times 0.57 (1-0.57)$

n= **333.**

With consideration of non response rate of 10% then the actual sample size will be

n′ = n x Adjusted factor

Adjusted factor = (100% / 100%-f %)

n’ = n x (100%/100%-f%)

n’ = 333 x (100%/100%-10%)

n’=333 x 1/r

n’=333 x 1/0.9

n’ =333 x 1.11= patients.

Therefore the actual sample size required will be **370** patients.

2.7 DATA COLLECTION TOOLS

A structured questionnaire was used to collect information on social demographics and clinical information. The questionnaire was structured with five important areas of extracting informations. The first part included questions of the demographic characteristics .The second part focused on clinical aspects in identifying factors associating with DR , the third

part included examination findings to identify grades of the DR. The last part involved laboratory findings for HbA1c levels and lipid profile (Total cholesterol and low density lipoprotein(LDL). This was aided by other tools, namely, a weighing machine, a tape measure, a sphygnomanometer (BP machine), Snellen chart, illiterate "E" chart for literate and illiterate patients respectively, pen torch, slitlamp, retinal/fundus cameras, tropicamide eye drop, 90D lens for indirect ophthalmoscope and HbA1c kit.

2.8 DATA COLLECTION PROCEDURE

Eligible participants who agreed to participate were recruited in every clinic day from 7.30 to 9.30 am arriving time, from diabetic clinic among DM patients who routinely attended the clinic for check up.Were by a non probability sampling technique was used to select them as narrated in sampling technique above. After sorting exclusion and inclusion criteria among the agreed to participate the eligible participants signed the written informed consent. We used a structured questionnaire prepared in English then translated into Swahili to collect data. The questionnaire was pretested to selected participants.

The research assistant took visual acuity of participants by using Snellen chart for literate patients and E-chart for illiterate patients. Visual acuity (VA) categories was recorded according to World Health Organisation (WHO) standard. A VA of 6/18 and above was considered normal vision, 6/24 to 6/60 as moderate visual impairment, below 6/60 to 3/60 was considered severe visual imparement and below 3/60 –PL was blindness.

History taking was done by the principal investigator followed by anterior segment examination using slit lamp biomicroscope and fundus photo by digital fundus camera .The history focused on duration of the disease, type of DM, type of treatment of DM received, presence of comorbidity illness like hypertension, lifestyle e.g. consumption of alcohol and smoking,body weight and height was measured for calculating body mass index (BMI) in Kg/m^2. A BMI of 18.5 Kg/m^2 or less was regarded as under weight, 18.6 to 24.9 Kg/m^2. as healthy weight, 25-29.9 Kg/m^2 as overweight and above 30 Kg/m^2 as obesity.(36) Blood pressure was measured and recorded, normal systolic was from 120 to 140 , and diastolic from 80 to 90. Any BP above 140/90 was regarded as hypertension (37).

The examination of anterior segment was done by slit lamp bio microscope and fundus examination for diagnosing and grading diabetic retinopathy, using ETDRS. The anterior segment was examined to ascertain the presence of medial clarity, both pupils were dilated with tropicamide 1% eye drops and the fundus was examined using slit lamp with an aid of 90 D lens, in addition digital ocular fundus imaging was taken from every participant for record keeping as well as for specialist to see for verification of findings and grades. Diabetic retinopathy was defined as the presence of micro aneurysms plus any of the following;dot-blot hemorrhages, intra-retinal micro vascular anomalies (IRMA), and new vessels on the disc or elsewhere, cotton-wool spots, exudates, and clinically significant macular edema. Grading of DR followed the Early Treatment Diabetic Retinopathy Study (ETDRS) grading scale. (Mild DR, Moderate DR, Severe DR, Very severe DR, Proliferative DR, and High-risk PDR), as it is shown in the index v. The eye with high grade of DR was defining the patient's class of DR and was taken for analysis. These diabetic retinopathy findings were rechecked by the ophthalmologist for verification, then reported in data-sheets.

For all selected patients, HbA1c was estimated in MNH general Laboratory in biochemistry department by the Laboratorytechnician. A blood sample was taken by the laboratory technician and HbA1c test done by the use of DCA 2000TM KIT (Roche Diagnostics Ltd, CH-6343 Rtkreuz, Switzerland) which require a small few minutes to give the result and a small whole blood sample (1 microliter). Patients were grouped into a very good control group (HbA1c<6), moderate control group (HbA1C between 6 and 8) and poor control group (HbA1c >8).

2.9 STUDY VARIABLES

2.9.1 Dependent Variables:

Diabetic retinopathy was the only dependent variable (outcome) for this study. For statistical computation , the variable was binary with the categories Yes '1' for patients with DR and no '2' for those without DR.

2.9.2 Independent Variables:

The in-dependable variables for this study was age , sex , glycaemia,duration of DM, systemic hypertension, lipid levels obesity cigarette smoking and alcohol.

2.9.3 Comfounding Variables:

Age of patient can confound with diabetic retinopathy as most of the old people do presents with comorbidity conditions like hypertension this do confound some findings of diabetic retinopathy, more over the duration of DM and age of a participant can also confound each other. HIV retinopathy can also cause retinal changes that can be confused as diabetic retinopathy.

2.10 DATA MANAGEMENT AND ANALYSIS

After the collection of data in structured questionnaires, the datas was cross checked by the principal investigator at the end of each interview and all missing or wrong entries was corrected. All information collected was confidential and locked in a secure cabinet, they were stored on secured password protected computer. Then data was entered into statistical Package for social sciences (SPSS) software version 23 for cleaning and analysis.Data analysis began with frequency distribution of each variable through one-way tabulations to assess distributional characteristics of the study population. Then bivariate analysis was conducted to determine the association between the dependent variable (diabetic retinopathy) and each of the independent variables (i.e. duration of DM, hypertention, obesity, cigarrete smoking, alcohol drinking, age and sex). Chi-square was used to test the associations involving catergorical variables, and t-test. Finally, multivariate logistic regression was performed to identify factors associated with DR. Odds ratios and their corresponding 95% confidence intervals and p-values reported. Factors with p-value less than or equal to 5% ($p \leq 0.05$) inferred to be significantly associated with DR. Results was presented in tables, bar charts, histograms and pie charts as appropriate.

2.11 ETHICAL CLEARANCE AND CONSIDERATION

Ethical clearance was sought from Muhimbili University of Health and Allied Sciences, Ethics and Research Committee. Permission to conduct the study was requested from the Excutive Director of MNH through the head of department of Ophthalmology.

Written consent of all the patients was taken after fully explaining the procedure and purpose of the study to the patients. Participants were free to withdraw from the study should they feel to do so at any time. Participants were informed comprehensively about the purposes and benefits of the study. Either the participants were informed about minimal samples of blood had to be taken as the part of study for quantifying the level of blood glucose. The whole technique was explained to the participants before sample drown, thus it had to be done under sterile and safety technique by following the national guideline for infection prevention control. More over they were informed about possibility of minimal tolerable pain that might be felt during sample taking. Participants found to be severly sick were directed to particular clinic for care first, then involve them in the study after recovery. No any risk was associated with participating in the research and participant's information were kept confidential.

FLOW CHART;

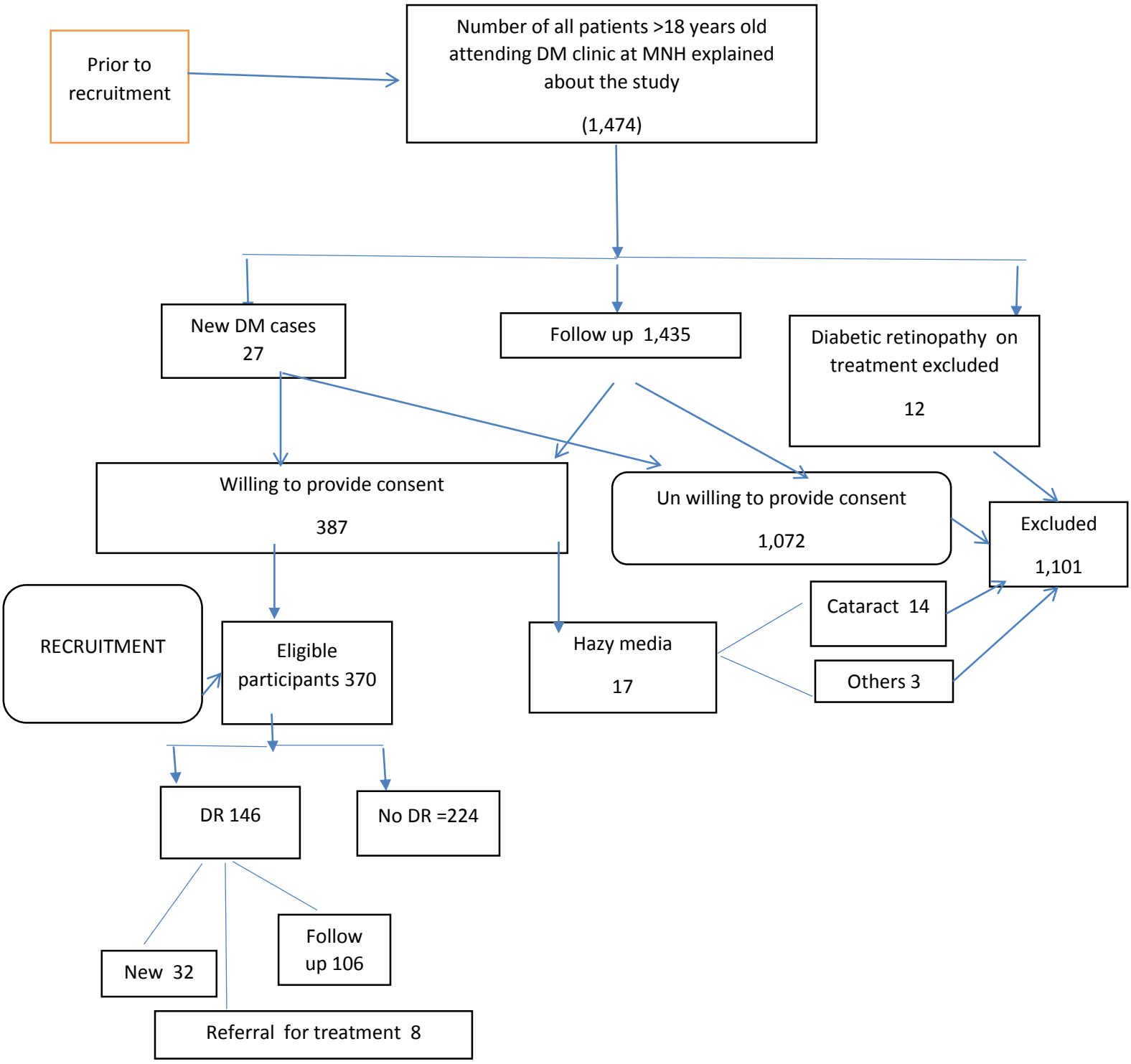

Figure 2:Flow diagram

CHAPTER FOUR

3 RESULTS:

Three hundred seventy patients were enrolled for the study and were all included in the analysis. Most of the patients were aged above 40 years with a mean age of 55.90±14.2, and a range between 18 to 82 years. There were more females (59.5%) than males (40.5%), with a male:female ratio of 2:3. Most of the participants were the residents of Dar-es-Salaam (86.1%). (Table 1)

Table 1:Social demographic characteristics of the study population, N=370 participants

Characteristic	Frequency	Percent
Sex		
Male	150	40.5
Female	220	59.5
Age (Years)		
18-39	48	13.0
40-59	114	38.9
60+	178	48.1
Mean (Sd)	55.9 (14.2)	
Level Of Education		
No Formal Education	16	4.3
Primary Education	169	45.7
Secondary Education	118	31.9
College Education	67	18.1
Marital Status		
Single	48	12.9
Married	241	65.1
Widowed	74	20.0
Divorced	7	1.3
Occupation		
Peasant	80	21.6
Student/Pupil	21	5.7
Self Employed	144	38.9
Employed	67	18.1
Retired	58	15.7
Residence		
Dar Es Salaam	317	86.1
Others*	51	14

**Other regions*: Arusha, Dodoma, Iringa, Kagera, Kigoma, Lindi, Mara, Morogoro,Katavi, Mwanza and Njombe.Kiimanjaro,Pwani,Tanga and Mtwara.

More than a quarter of the participants had diabetic retinopathy(39.9%) N=370 Participants

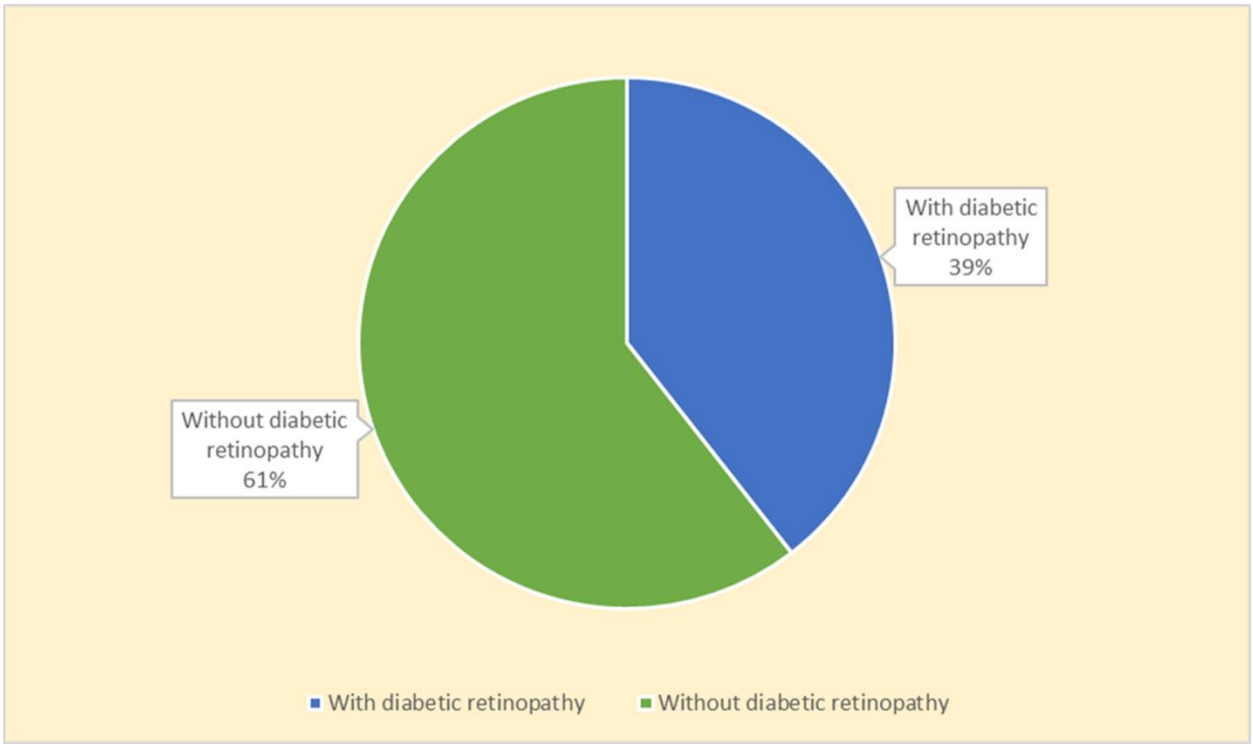

Figure 3: Proportion of diabetic retinopathy among study population

Table 2: Bivariate analysis on the factors associated with diabetes retinopathy, N=146

Factor		Diabetic retinopathy			P-Value
		Yes	No	Total	
		No(%)	No(%)	No(%)	
Sex					
	Male	65(43.33)	85(56.67)	150(100)	0.208
	Female	81(36.82)	139(63.18)	220(100)	
Age (Years)					
	18-39	4 (8.33)	44 (91.67)	48 (100)	<0.001[f]
	40-59	61 (48.36)	83 (57.64)	144 (100)	
	60+	81(45.5)	97 (54.09)	178 (100)	
Level Of Education					
	No formal/ primary Education	85(45.95)	100(54.05)	185(100)	0.037
	Secondary education	38(32.20)	80(67.80)	118(100)	
	College	23(34.33)	44(65.67)	67(100)	
Occupation					
	Peasant/students	26(25.74)	75(74.26)	101(100)	0.002
	Employed/self Employed	98(46.45)	113(53.55)	211(100)	
	Retired	22(37.93)	36(62.07)	58(100)	
Alcoholic					
	Yes	69(46.31)	80(53.69)	149 (100)	0.027
	No	77(34.84)	144(65.16)	221 (100)	
Smoking					
	Yes	23(58.97)	16(41.03)	39 (100)	0.008
	No	123(37.16)	207(62.84)	331 (100)	
Bmi					
	Underweight/normal	51(42.50)	69(57.50)	120(100)	0.725
	Over weight	49(37.98)	80(62.82)	129(100)	
	Obese	46(38.33)	74(61.67)	120(100)	
Hypertensive					
	Yes	109(47.81)	119(52.19)	228(100)	<0.001
	No	37(26.06)	105(73.94)	142(100)	
Duration Of Dm					
	10 years and below	57(29.23)	138(70.77)	195(100)	<0.001
	more than 10 years	89(50.86)	86(49.14)	175(100)	
Hba1c					
	<6%	11(21.57)	39(78.43)	50(100)	0.014
	6-8 %	68(39.77)	103(60.23)	171(100)	
	>8%	67(45.27)	81(54.73)	148(100)	
Total Cholesterol					
	Normal	102 (36.04)	181 (63.96)	283 (100)	0.016
	Raised	43 (39.40)	42 (60.60)	85 (100)	
LDL					
	Normal	95 (36.40)	166 (63.60)	261 (100)	0.066
	Raised	50 (46.73)	57 (53.27)	107 (100)	

Duration of diabetes (>10yrsDM) , age, hypertension, occupation, HbA1c, Total cholesterol, alcohol, smoking and level of education were associated with diabetic retinopathy ($p<0.05$).

Table 3:: Multivariate analysis of factors for diabetic retinopathy, N=146

Factor	Patients With Diabetic Retinopathy	Cor (95% Ci)	P-Value	Aor (95% Ci)	Total	P-Value
Age (Years)						
18-39	**4(2.7)**	Ref			48(13.0)	
40-59	61(41.8)	8.08(2.76-23.70)	0.000	5.13(1.60-16.36)	144(38.9)	0.006
60+	**81(55.5)**	9.19(3.17-26.65)	0.000	5.19(1.6-17.07)	178(48.1)	0.007
Level Of Education						
No Formal/ Primary Education	85(46.0)	1.79 (1.10-2.90)	0.018	2.21 (1.11 – 4.39)	185(50.0)	0.024
Secondary Education	38(32.2)	1.10 (0.58-2.08)	0.768	1.14 (0.55-2.34)	118(31.9)	0.724
College Education	23(34.3)	Ref		Ref	67(18.1)	
Occupation						
Peasant/Students	26(25.7)	Ref		Ref	101(27.3)	
Employed/Self Employed	98(46.5)	2.50 (1.48-4.22)	0.001	2.68 (1.47 -4.88)	211(57.0)	0.001
Retired	22(37.9)	1.76 (0.88-3.53)	0.109	1.81 (0.80-4.09)	58(15.7)	0.155
Alcoholic						
Yes	69(46.3)	1.61 (10.5-2.47)	0.027	1.13 (0.68 – 1.87)	149 (40.3)	0.643
No	77(34.8)	Ref		Ref	221 (59.7)	
Smoking						
Yes	23(57.0)	2.43 (1.24 -4.78)	0.01	1.87 (0.86-4.06)	39 (10.5)	0.113
No	123(37.1)	Ref		Ref	331 (89.5)	
Hypertensive						
Yes	109(47.8)	2.60 (1.65-4.10)	<0.001	1.86 (1.11-3.14)	228(61.6)	0.019
No	37(26.1)	Ref		Ref	142(38.4)	
Duration Of Dm						
10 Years And Below	57(29.2)	Ref		Ref	195(52.7)	
More Than 10 Years	89(50.9)	2.51 (1.63 -3.84)	<0.001	2.53 (1.5 -4.10)	175(47.3)	<0.001
Hba1c						
<6%	11(22.0)	Ref		Ref	50(13.6)	
6-8 %	68(39.8)	2.34 (1.12-4.89)	0.024	2.28 (1.02 – 5.12)	171(46.3)	0.045
>8%	67(45.3)	2.93 (1.39 -6.17)	0.005	2.22 (0.96-5.13)	148(40.1)	0.061
Total Cholesterol						
Normal	102 (36.0)	Ref		Ref	283 (76.9)	
Raised	43 (50.6)	1.82 (1.11-2.96)	0.017	1.98 (0.92-4.28)	85 (23.1)	0.082
LDL						
Normal	95 (36.4)	1.53 (0.97 – 2.42)	0.066	1.29 (0.62-2.69)	261 (70.9)	0.492
Raised	50 (46.7)	Ref		Ref	107 (29.1)	

In multivariate analysis, factors associated with diabetic retinopathy were: older age, having no formal education, being employed, being hypertensive, a higher glycated Heamoglobin and a longer duration of diabetes mellitus.

The grade of diabetic retinopathy increased with the increasing levels of glycated heamoglobin.

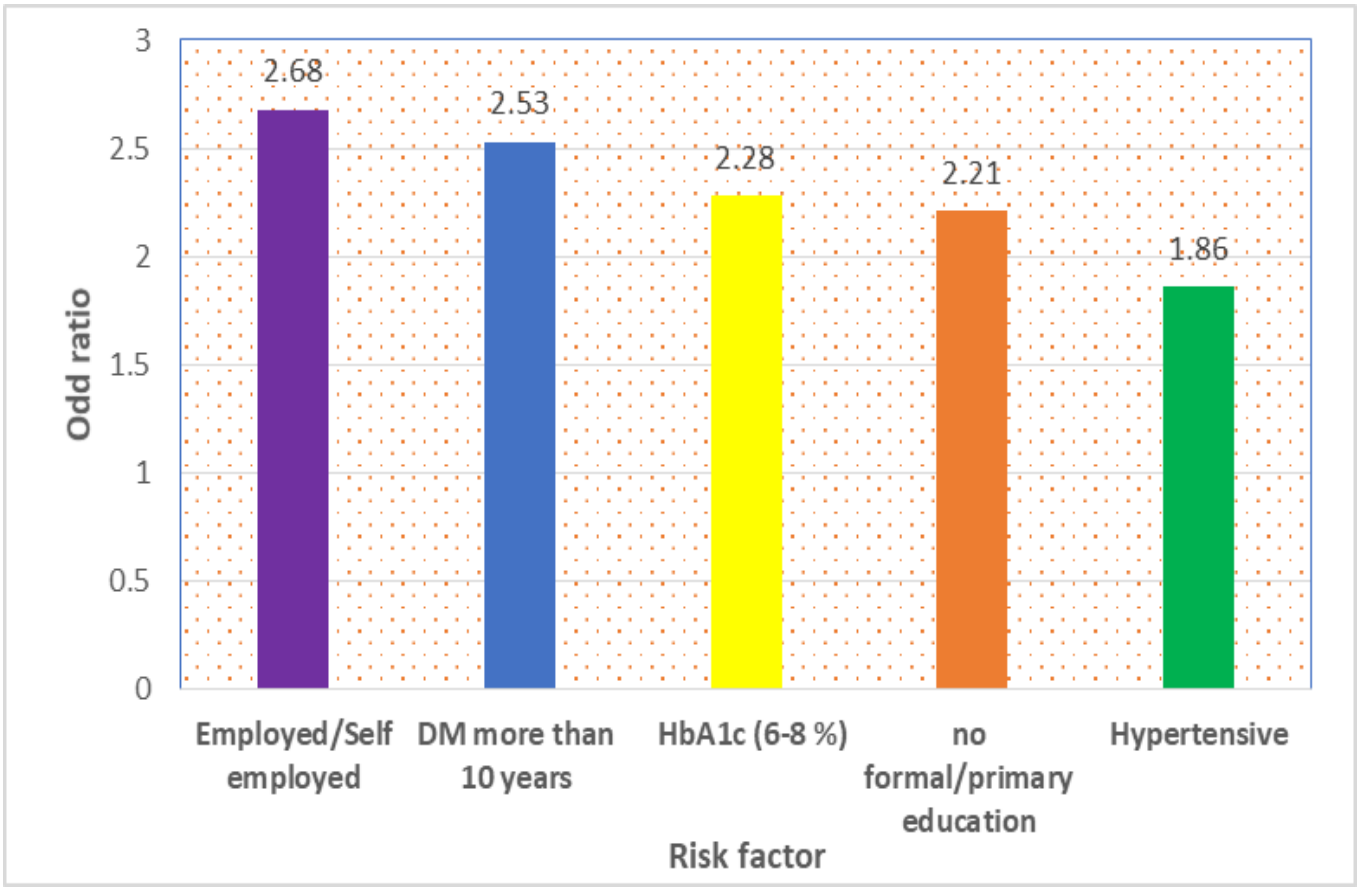

Figure 4: Risk factors for diabetic retinopathy.

CHAPTER FIVE

4 DISCUSSION

4.1 Discussion

This study had a high ratio of female as compared to male ,this could be related to attitude of females being more precocious of their health than men. These demographic characteristics were also observed in Nigeria, Iran and South Sudan. (22, 57, 49)

Diabetic retinopathy is one of the complication of diabetes Mellitus and commonly appear after 10 years of duration of DM. The results of this study showed more than a quarter (39.9%) of the studied patients had diabetic retinopathy. This is consistence with a study in Ethiopia which showed 41.4% (46). However, this proportion of diabetic retinopathy is higher than the studies done in Kilimanjaro-Tanzania (27%), Zimbabwe (28.4%), and South-Sudan 13% (7,50,49). Moreover, this proportion is less than what was found in Lusaka Zambia (47.4%), Khartoum Sudan (82%) and India (64%). It is also less than previous studies done at MNH-Tanzania by M.Mafwiri et al (50.5%) and an unpublished study by Aza et al (57%) in 2016. (34,16,10,38). This variations in proportion may be explained by different study settings, diagnostic methods, quality of health care services at particular area and health seeking behavior among different study population.

Younger patients had a smaller proportion (2.7%) of diabetic retinopathy compared to those above 60 (55.5%) years. The reason for this differences it could be due to short duration of diabetes and absence of co-morbidities among young patients.

In our study, patients who were single, were less likely to develop diabetic retinopathy compared to their married counterparts (6.2% vs 72%). This might be confounded by patient's age and duration of diabetes, since most of the single patients are young with a shorter duration of having diabetes.

The proportion of diabetic retinopathy among employed was higher as compared to peasants (51.4% vs 1.7%) . This study revealed a significant association of developing diabetes retinopathy among formal/self-employed in reference to peasants . The bi-variate showed

67.1% employed with DR while 17.8% peasants with DR. Multivariate analysis showed the odd of developing DR among employed participants was 2times those of the peasants. This is probably a reflection of being busy and do not have time to attend properly their clinic ,lack of physical activities and affluent diet among employed people, which is commonly associated with poor glycaemic control of diabetes and predisposes patients to the development of diabetic retinopathy (54) .

Duration of diabetes remained significantly associated with diabetic retinopathy in both bivariate and multivariate analysis . The finding is similar to reports from North Central Nigeria by Rita. O. Ewuga et al who reported DM patient of 10 years duration had high rate of DR than those of less than 10years (22). Mathenge et al in a study done in Nakuru Kenya reported 55% of DM patient and 23% patients who had DM for more than 10 years and less than 5 years respectively had DR (23). The study in North West Ethiopia reported similar results , the odd of developing DR in >10DM years was nearly quadruple those of below 10 years (46). This observation explain the longer period the patient lives with uncontrolled blood glucose predispose retina to DR.

This study observed a number of factors associated with diabetic retinopathy, among them is the persistant increased level of blood glucose, which is presented as glycated hemoglobin (HbA1c). HbA1c is a blood test that determine the levels of blood glucose over the past 8-12 weeks. Almost half (45.9%) of patients with HbA1c level of 6-8% had diabetic retinopathy as compared to those with HbA1c of <6 (7.5%). This findings were consistent with the results reported in a cross sectional study on risk factors for DR in Nigeria whereby out of 44 patients with diabetic retinopathy, 17 (38.6%) had HbA1c $\leq$ 7.0% while 27 (61.4%) had HbA1c above 7% (14). Similary, the meta analysis study on global prevalence of DR by Joanne et al, reported rise on the levels of HbA1c goes in hand with the odd of developing DR (20). Other studies of similar findings were from Israel (13), India (10) and Ilorin Nigeria (14). Persistent hypeglycaemia leads to excess by- products from metabolism of sugar (sorbitol) a chemical that damage the microvasculature causing diabetic retinopathy.

The multivariate analysis revealed an OR of developing DR in patients with HbA1c (6-8%) was 2.22 while the OR of developing DR with HbA1c (>8) was 2.18 . This observation is similarly reported by Sohaib. A.Virk et al and Melkamu Tilahun et al (51,46).

Observation from this study showed the levels of HbA1c increased with the increasing of ETDRS DR grade. This findings was similarly reported in a study done in Neemuch City India where by HbA1c of less than 7% was observed in 60% of patients with no DR and 10% of NPDR, 50% of patients with PDR and 57.4% of patients with NPDR had HbA1c of >8% (16).Similar finding were reported in Khartoum Sudan, India –by Pragati Garg et al, Saudi Arabia and Lusaka Zambia (16,17,18,34). This findings confirm that the high the glucose level predispose the patients to more chances of developing DR.

The level of education of the participants studied, found to have significant association with DR. This study observed participants with no formal/primary education had a high chance of developing severe form of DR than the participants who had collage level of education. (59.6%,12.5%-NPDR and 50% ,29%-PDR) respectively. This can be explained based on lack of awareness and knowledge on adhering to preventive measures among participants with low levels of education while those with collage education can easily understand the instruction or even look for information about their disease.

This study found more than half (61.6%) of the study population had hypertension. Additionally, 47.8% of the patients with hypertension had diabetic retinopathy. According to this study, patients with hypertension were twice more likely to develop diabetic retinopathy compared to those who had normal blood pressure. This results are in agreement to those of a hospital based cross sectional study in Ethiopia by Tinahum at el that reported odd of developing DR among hypertensive patient with DM were three times than those of non-hypertensive (46). A randomized controlled trial study done in England, Scotland and Northern Ireland (UKPDS) reported similar proportion (40% to 60%) of hypertension and 34% reduction in risk of developing retinopathy among hypertensive patients assigned to tight monitoring of hypertension (25). These results were similarly found in studies done in Khartoum Sudan, Kenyatta National Hospital and Uganda(16,47,55). Finding a high

proportion of our patients having hypertension imprising a need of focusing on proper control of hypertension in order to improve outcomes of treatment of diabetic retinopathy.

Patient age is another factor that was found to be associated with diabetic retinopathy among patients with DM. This study showed the Odd of developing DR among patients with age above 40-59 is about 5times, than those with age 18-39. Luis Forga et al reported similar observation in the study on age influence in DR done in Complejo hospital that the odd of developing DR among DM patient above 45years was about 4 times those of less of 45 years (56). Wisconsin Epidemiological study of Diabetic retinopathy (WESDR) showed the prevalence of DR at 3 years of age was 0% and increased at 15 years to 25%. (19) This variation of age and prevalence of DR can be explained by factors relating to body physiology, as insulin resistances manifesting mostly after puberty age (52) and elderly people to have DR can be confounded by duration of DM.

Moreover this study observed a number of other factors which were statisticaly non significant, these are obesity, lipidaemia, smoking cigarette and alcohol drinking. Findings in other studies are mostly coinciding with this current study but few do not (28,51,54,55). This differences can be explained by difference life style, culture/behavior among different population.

CHAPTER SIX

5 CONCLUSION, STUDY LIMITATION AND RECOMMENDATION

5.1 Conclusion

More than a quarter of the adult patients with DM had DR, and patients who were 40 years and above were found to have more risk of developing DR than younger age, employed participants, long duration of DM >10years, high levels of blood glucose, low level of education and hypertension were factors associated with DR. Alcohol, smoking, obesity and hyperlipidaemia were not associated with DR. The higher levels of glycated hemoglobin was associated to DR, while moderate rised levels of glycated hemoglobin (6-8%) was observed in participants with high grades of DR.

5.2 Study Limitation

This study was prone to information bias as it relied on the direct responses given by the respondent during the patient interviews on some of the associating factor variables which were used in the study like chronic non-communicable diseases, years of having diabetes, smoking and alcohol drinking were based on self-report of the patients

5.2.1 Study Mitigation

This was reduced by adequately training the research assistants on how to properly conduct patients interview .

5.3 Reccomendation

- Regular ophthalmic screening for DR changes have to be emphasized in the diabetic clinic at MNH in order to diagnose early DR changes in its early stages.
- Awareness and sensitization on diabetic retinopathy among patients with DM through health education should be re-enforced in the diabetic clinic at MNH in order to improve patients eye health care
- Emphasize on a culture of doing physical exercises among employed patients with DM and entire society**.**

- Screening for DR should be part of the management protocol for patients with DM.
- An on going custum of frequency check up of blood glucose by gycated heoglobin and properly control it to the optimal levels(≤6% HbA1c), has to enhanced among patients attends diabetic cinic at MNH in order to avoiding occurance of DR.
- We recommend further study to be done on:

Understanding and reducing the barriers to ophthalmic screening for Diabetic Retinopathy among Diabetic Patients in Tanzania.

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APPENDIX

Appendix i: - Questionnaire in English Version

QUESTIONNAIRE

ASSESSMENT OF LEVELS OF GLYCATED HEMOGLOBIN (HbA1c) AND OTHER FACTORS RELATED TO DIABETIC RETINOPATHY AMONG ADULT PATIENTS ATTENDING EYE CLINIC AT MUHIMBILI NATIONAL HOSPITAL

1-Patient identification No……..

2-Date of an interview……

3-Hospital Reg No……..

4-Phone No……..

SECTION A; DEMOGRAPHIC INFORMATION

SN	QUESTION AND ANSWER	CODE	RESPONSE
1	Registration No		
2	District		
3	Region		
4	Age(years)		
5	Sex	1-male 2-female	
6	Education level	1-Non 2-Primary 3-Secondary 4-Tertiary	
7	Marital Status;	1-Single 2-Married 3-Widow 4-Divorced 5-Cohabit 6-Separated	
8	Occupation;	1-Peasant 2-Student/Pupil 3-Self employment 4-Employed 5-Ritired	

PART B

CLINICAL HISTORY

SN	QUESTION	CODING CATEGORIES	RESPONSE
11	For how long have you been diagnosed to have DM(YRS)	1-Below 10yrs 2-Above 10yrs	
12	Do/did you drink alcohol? (consistently for at list 2yrs prior or after DM illness)	1-Yes 2-No	
13	Do/did you smoke(consistently for at list 2yrs prior or after DM illness)	1-Yes 2-No	
14	Are you hypertensive?	1-Yes 2-No	
15	If no from 14 above	Measure BP	
16	Are you in the treatment of DM?	1-Yes 2-No	
17	If yes in question 15 what type of treatment you use? Injection(insulin) or Drugs(OHGD)	1-Inje 2-OHGD 3-Mixed 4-Diety	
18	What type of diabetes mellitus does the patient suffer from?	1.IDDM 2.NIDDM	

PART C

EXAMINATION FINDINGS

SN	QUESTIONS	CODING CATEGORIES	RESPONSE
19	Is there a high BMI? (≥ 25) The BMI normal-(18.6-24.9) The BMI for Obesy (≥30)	1-Under weight(<18.6) 2- (18.6-24.9) Normal 3-(25-29.9) High 4-(≥30)	
20	Visual acuity	1-Normal >6/18 2-Impared <6/18 -6/60 3-Severe imparement <6/60-3/60 4-Blindness <3/60-PL	RE--- LE----
21	Retinal findings for DR	1-Yes 2-No	
22	If yes in 21 above are there any DR changes in any of the eyes?	1.Mild NPDR 2.Moderate NPDR 3.Severe NPDR 4.Very severe NPDR 5.PDR without High-risk changes 6.PDR with High-risk changes.	RE---- LE----
23	Are there any Diabetic Maculopathy changes in any eye?	1-Yes 2-No	RE----- LE------
24	If 'yes' in Q23, what is the stage of Maculopathy?	1.Clinically Significant macula edema 2.Non-clinically significant macula edema	RE------ LE-------
25	Are there feature of dvanced diabetic end stage disease	1-Yes 2-No	RE…… LE……..

PART D: LABORATORY FINDINGS

SN		CODING	RESPONSE
26	HbA1c (%)	(1) <6% (2) 6-8% (3) >8%	
27	Total Cholesterol	(1) 0-5.17mmol/l(Normal) (2) >5.17mmol/l(Raised)	
28	LDL	(1)0-3.34mmol/l(Normal) (2)>3.34mmol/l(Raised)	

Appendix ii : Questionnaire (Swahili Version)

Utangulizi:

DODOSO (Lijazwe na mtafiti)

TAFITI YA KIWANGO CHA SUKARI MWILINI NA SABABU ZINGINE ZINAZOCHANGIA KUWEPO KWA KIWANGO CHA JUU CHA SUKARI MWLINI KWA WAGONJWA WA KISUKARI WATU WAZIMA, AMBAO WANASHIDA KATIKA PAZIA LA KUONEA WANAO PATA HUDUMA KATIKA KITENGO CHA MACHO HOSPITALI YA TAIFA YA MUHIMBILI..

1-Namba ya usajili……..

2-Namba ya orodha……..

3-Tarehe ya majadiliano……

SEHEMU A;

KUMBUKUMBU ZA MGONJWA

Namba ya swali	Swali	Migawanyo ya kung'amua	Jibu
4	Wilaya		
5	Mkoa		
6	Umri(miaka)		
7	Jinsia kiume Kike	1-Kiume 2-Kike	
8	Kiwango cha elimu		
	-Hakuna	1-Hakuna	
	-Msingi	2-Msingi	
	-Sekondari	3-Sekondali	
	-Ya juu	4-Daraja la tatu na kuendelea	
9	Ameoa/Kaolewa		
	Anaishi pekeyake		
	Mjane/Mgane		

	Kangana		
	Anaishi na awala		
10	Mkulima		
	Mwanafunzi		
	Mjasiliamali		
	Muajiliwa		

SEHEMU B

No	Swali	Migawanyo ya kung'amua	Matokeo
11	Kwa muda gani umekuwa na kisukari(miaka)	1-Chini ya miaka 10 2-Zaidi ya miaka 10	
12	Uliwahi/Unakunywa pombe(kwa muda wa miaka 2 kabla ya kisukari)	1-Ndiyo 2-Hapana	
13	Uliwahi/Unavuta sigara(mfululizo kiasi cha muda wa miaka 2 kabla au baada ya kisukari)	1-Ndiyo 2-Hapana	
14	Je Ni mgonjwa wa shinikizo la damu ?	1-Ndiyo 2-Hapana	
15	Je Unatumia matibabu ya kisukari ?	1-Ndiyo 2-Hapana	
16	Kama ni ndiyo kwenye swali numba 15. Ni matibabu gani unatumia,kuchoma sindano au kunywa dawa?	1-Sindano 2- Kunywa dawa	

17	Ni aina gani ya kisukari ambayo mgonjwa anayo ?	1-Tegemezi kwa sindano 2-Isiyotegemezi kwa sindano	

SEHEMU YA C

MATOKEO YA UCHUNGUZI (EXAMINATION)

Numba	Kipimo	Migawanyo ya kung'amua	Matokeo
18	Kuna uzito wa juu au wa chini ?	1-Ndiyo 2-Hapana	
19	Kuna shinikizo la damu ?	1-Hapana 2-Ndiyo	
20	Kiwango cha uono	Kulia…… Kushoto…….	
21	Kuna dalili za uhalibifu wa pazia la kuone kutokana kisukari	1-Ndiyo 2-Hapana	
21	Kamajibu ni'ndio' kwenye SW20, ni kwa kiasi gani?	1-Kidogo 2-Wastani 3-Sana 4-Sana Kuzidi 5-Madhara endelevu bila halihatarishi. 6-Madhara endelevu na hali hatarishi	
22	Kuna dalili za kisukari zinazohusisha	1-Ndiyo 2-Hapana	

	macula ya jicho lolote?		
23	Kama ni ndiyo swali numba 21 ni za kiwango gani.	1-Kiasi cha maana 2-kiasi kisicho cha maana	

SEHEMU D

Numba	Kipimo	Migawanyo ya kung'amua	Matokeo
26	HbA1c	(1) <6%	
		(2) 6-8%	
		(3)>8%	
27	Total Cholesterol	(1) 0-5.17mmol/l(Normal) (2) >5.17mmol/l(Raised)	
28	LDL	(1)0-3.34mmol/l(Normal) (2)>3.34mmol/l(Raised)	

Appendix iii: Consent Form (English Version)

Reg No. …….. Date……

Consent to participate in a research study

Greetings. I am Dr. Charles . P. Hinju, a postgraduate student, doing a master's of medicine in ophthalmology at the Muhimbili University of Health and Allied Sciences. I am researching intending to determine the levels of HbA1c and other factors related to diabetic retinopathy among adult patients attending diabetic clinics at Muhimbili national hospital.

Purpose of the study

To determine the levels of HbA1c and other factors related to diabetic retinopathy among adult patients attending diabetic clinic at Muhimbili national hospital.

Participants of the study

All adult diabetic patients diagnosed to have diabetic retinopathy attending Muhimbili national hospital diabetic clinic will participate in this study. The participants will undergo ocular examinations and noninvasive ocular investigations.

Confidentiality

All the participants who will join the study their names will not be required but will be identified by the use of numbers. The information obtained during data collection will be kept under a strict locked environment where it is only the researcher 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 the study.

Benefits

Results of this study will provide the baseline level of HbA1c and related factors in diabetic retinopathy and hence provide the basis on the prevention of all diabetic patients even before they develop visual impairment and blindness

Right to withdrawal

Joining in this study is completely your choice. You can withdraw at any particular moment even after signing the consent form. Withdrawal will not involve penalty or any benefits to which you are entitled.

Whom to Contact

In case of any concern or question about the study you can contact the researchers, Dr. Charles .P.Hinju (mob. 0713892273), and Dr. John Kisimbi(mob.0689093844) at Muhimbili University, P.O. BOX 65001, Dar es Salaam. You can also contact the Director for, research and Publications Dr Bruno Sunguya P.O.BOX 65001, Dar es Salaam, for any matters concerning this study.

I ……..have 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…….

Appendix iv : 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 Dr Charles . P. Hinju, mwanafunzi wa shahada ya pili ya udaktari, idara ya macho, chuo kikuu cha afya Muhimbili.Nafanya utafiti kuangalia kiwango cha uwingi wa sukari kwenye damu na mahusiano mengine yanayoleta uharibifu wa 'retina' ya macho miongoni mwa wagonjwa wa kisukari watuwazima(rika kubwa) wenye uharibifu wa retina ya macho katika hospitali ya taifa 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 kiwango cha uwingi wa sukari kwenye damu na mahusiano mengine yanayoleta uharibifu wa 'retina' ya macho miongoni mwa wagonjwa wa kisukari watuwazima(rika kubwa) wenye uharibifu wa retina ya macho katika hospitali ya taifa Muhimbili.

Washiriki wa utafiti

Washiriki kwenye utafiti huu ni wagonjwa wa kisukari ambao ni watu wazima waliogundulika kuathirika kwa pazia la kuonea kutokana na kisukari , wanaodhuria kliniki ya kisukari katika hospital ya taifa Muhimbili.Washiriki watafanyiwa uchunguzi wa macho wa kawaida na kwa kutumia vifaa ambavyo havihatarishi hali ya macho.

Madhara

Hakuna madhara yanayotarajiwa kwa washiriki wa utafiti.

Faida

Matokeo ya utafiti huu yataonyesha kiwango cha sukari kwenye damu na kuoanisha madhara ya kisukari kwenye 'retina' za macho miongoni mwa wagonjwa wa kisukari ambao wamegundulika kuathirika retina /pazia , kwa wagonjwa wote wa kisukari watu wazima wanaopata huduma katka hospitali ya Muhimbili.

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 Dr Charles.P.Hinju (mob. 0713892273),) and Dr John Kisimbi(mob.0689093844), 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 Dk. Bruno Sunguya , S.L.P 65001, Dar es salaam.

Sahihi ya mshiriki…….

Sahihi ya mtafiti/mtafiti msaidizi……..

Appendix v: (Description of stages of diabetic retinopathy)

SN	CATEGORY	DESCRIPTION
1	NPDR	
1.1	Mild-NPDR	• At list one micro aneurism or intra retinal hemorrhage. • Hard/soft exudates may or may not be present.
1.2	Moderate-NPDR	• Mild NPDR plus ; • Cotton wool spots • Venous changes • IRMA
1.3	Severe-NPDR 4:2:1 rule	• Moderate –NPDR plus one of ; • Micro aneurism • Retinal hemorrhage in all four quadrants • Venous changes(beading) in 2/more quadrants • IRMA at least in 1 quadrant
1.4	Very severe -NPDR	• Two or more of the above features on severe NPDR
2	PDR	
2.1	Mild/Non high-Risk PDR	• New vessels on the disc (NVD) or new vessels elsewhere(NVE), but extent insufficient to meet the high risk criteria.

2.2	High –Risk PDR	➢ New vessel on disc: -More than 1/3rd of Optic disc diameter with /without hge -Less than 1/3rd of optic disc diameter with hge (preretinal and vitreous hge) ➢ New vessel elsewhere in fundus: -More than ½ of Optic disc diameter with /without he -Less than ½ of Optic disc diameter with hge.(preretinal & vitreous hge)
3	DIABETIC MACULOPATHY	T Termed as clinical significant macular oedema (CSME) if one of the following three criteria are present on slit lamp examination with 90D lens: -Retinal oedema within 500 micron of central fovea. -Hard exudate within 500 micron of fovea centralis associated with adjacent retinal thickening. -Retinal edema that is 1 disc diameter or larger , any part of which is within 1 disc diameter of the fovea centralis.
4	ADVANCED DIABETIC EYE DISEASE	One of the following: 1.Preretinal(retrohyaloid) and/ or intragel hemorrhage 2.Tractional retinal detarchment 3.Tractional retinoschisis 4.Rubeosis iridis (iris neovascularization).

Appendix vi: Ethical clearance

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

OFFICE OF THE DIRECTOR OF RESEARCH AND PUBLICATIONS

P.O. Box 65001
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Ref. No.DA.282/298/01.C/

Date: 11/08/2020

MUHAS-REC-08-2020-341
Charles Peter Hinju
MMed Ophthalmology, School of Medicine
MUHAS

RE: APPROVAL FOR ETHICAL CLEARANCE FOR A STUDY TITLED: LEVELS OF GLYCATED HAEMOGLOBIN(HbA1c) AND OTHER FACTORS RELATED TO DIABETIC RETINOPATHY 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: 11/08/2020
EXPIRATION DATE OF APPROVAL: 11/08/2021

STUDY DESCRIPTION:
Purpose:
The purpose of this cross sectional observational study is to determine the levels of glycated hemoglobin and other related factors among patients with diabetic retinopathy attending eye 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-%2016.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 data transfer agreement (DTA) from NIMR if data will be transferred to a foreign country.
8. Apply for and obtain material transfer agreement (MTA) from NIMR, if research materials (samples) will be shipped to a foreign country,
9. 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)
10. The PI is required to ensure that the findings of the study are disseminated to relevant stake holders.
11. 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/.

Muhimbili University of Health and Allied Sciences
DIRECTOR
Research & Publications
Box 65001

Dr. Bruno Sunguya
Chairman, MUHAS Research and Ethics Committee

Appendix viii: Permission letter

THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH, COMMUNITY DEVELOPMENT, GENDER, ELDERLY AND CHILDREN

MUHIMBILI NATIONAL HOSPITAL

In reply please quote;

Ref. No.:MNH/TRCU/Permission/2020/055 **Date: 17th** August, 2020

Head of Department,
Ophthalmology
Muhimbili National Hospital

RE: PERMISSION TO COLLECT DATA AT MNH.

Name of Student	Charles Peter Hinju
Title	**"Levels of Glycated Haemoglobin (Hbalc) and other Factors Related to Diabetic Retinopathy at Muhimbili National Hospital".**
Institution	Muhimbili University of Health and Allied Sciences
Supervisor	Dr. John Kisimbi
Co – supervisor	Dr. Suzan Mosenene
Period	17h August, 2020, to 28th February, 2021

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,

H.O.D. TEACHING, RESEARCH & CONSULTANCY UNIT P.O.Box 65000 DAR ES SALAAM MUHIMBILI NATIONAL HOSPITAL

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

c.c DSS
c. c Charles Peter Hinju

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