ACCURACY OF SCREENING FOR DIABETIC RETINOPATHY AND MACULA EDEMA AT KENYATTA NATIONAL HOSPITAL

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DECLARATION

I declare that this research is my original work and has never been published or presented for a degree in any other University.

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LIST OF ABBREVIATIONS

DM	Diabetes Mellitus
DR	Diabetic Retinopathy
VTDR	Visually Threatening Diabetic Retinopathy
PDR	Proliferative Diabetic Retinopathy.
DME	Diabetic Macula Edema
CSME	Clinically Significant Macula Edema
ME	Macula Edema
CI	Confidence interval
VEGF	Vascular Endothelial Growth Factor
ETDRS	Early Treatment Diabetic Retinopathy Study
WHO	World Health Organization
MOPC	Medical outpatient Clinic
KNH	Kenyatta National Hospital
UK	United Kingdom
NVD	Neovascularization at the disc
NVE	Neovascularization elsewhere
DRS	Diabetic Retinopathy Study
SLB	Slit Lamp Examination

ACE	Angiotensin converting enzymes
bFGF	basic Fibroblast Growth Factor
IGF-1	Insulin Growth Factor 1
PDGF	Platelet Derived Growth Factor
EGF	Epidermal Growth Factor
TGF-β_2	Transforming Growth Factor beta 2
MESA	Multi Ethnic Study of Atherosclerosis
DRSP	Diabetic Retinopathy Screening Programs
OCT	Optical Coherence Tomography

ABSTRACT

Background: Low income countries in Asia and Africa have both the highest prevalence of diabetes mellitus (DM) and expected rise in disease burden. Many patients with diabetes are unaware of their diagnosis and may not receive treatment in a timely fashion. These diabetic retinopathy screening programs (DRSP) where regular eye examinations are done,can minimize the risk of visual loss.

In Kenya, most of the patients with diabetes are screened for diabetic retinopathy (DR) with indirect fundoscopy and only few facilities are using the fundus camera. While dilated fundoscopy has been found to be an effective method of screening, it requires to be performed by an experienced person. Fundus camera has been preferred because it does not need a highly experienced person and more people can also be screened per day compared to dilated fundoscopy. Current fundus cameras used for screening are non-mydriatic. However its accuracy has not been validated in our setup.

Objective: The general objective was to assess the accuracy of screening for diabetic retinopathy in diabetic patients attending the medical outpatient clinic at Kenyatta National Hospital (KNH). The specific objectives were: to compare grading of DR using fundus photographs by the technician (screener) and Early Treatment Diabetic Retinopathy Study (ETDRS) clinical grading by the ophthalmologist and to compare diagnosis of macula edema using fundus photographs and optical coherence tomography (OCT).

Materials and methods: This was a cross sectional hospital based study. Patients were recruited in the MOPC.56 patients attending medical outpatient clinic (MOPC) were randomly selected then screened. First consent was taken then a questionnaire administered then fundus photographs were captured in all the patients. After retinal photography, patients were dilated and fundoscopy was done on all patients regardless of their DR status. A questionnaire was administered to all patients with DR who gave consent. The eyes of all patients screened for DR were scanned using OCT. The primary outcome was presence or absence of DR or macula edema.

Results: This study revealed that the mean duration of diabetes was 10.8 years. The sensitivity of the fundus camera in the diagnosis of no DR is 94.8% and a specificity of 86.2%. The positive and negative predictive value for identification of no DR was 87.6% and 94.1% respectively. Sensitivity for identifying mild DR was 60.6%. The Sensitivity for identifying moderate and severe DR was 74.0% and a specificity of 99.3%. Diagnosis of proliferative diabetic retinopathy (PDR) had a sensitivity and specificity of 90.9% and 99.4% respectively. Sensitivity of all grades of DR was 86.2% and specificity of 94.9%.Sensitivity of diagnosis for macula edema was 57.1% and a specificity of 89.8%.

Conclusion: The fundus camera is accurate and can therefore be effectively used to screen for diabetic retinopathy but not for diabetic macula edema. Its accuracy is higher for more advanced stages of DR.

Recommendation: Since the fundus camera is an effective tool for screening of diabetic retinopathy its use be increased nationally due its high accuracy and specificity. KNH needs an OCT as it has been seen that fundus photography tends to over-estimate diabetic macula edema (DME).

1. INTRODUCTION

Diabetic retinopathy (DR) is defined as damage to the micro-vascular system of the retina accompanied by structural change to the retina due to prolonged hyperglycaemia. It occurs in both type 1 and type 2 diabetes mellitus (DM) [26].

Diabetic patients are 25 times more likely to become blind than the general population. If DR is detected and treated early enough, the risk of vision loss and blindness, as well as the complexity and cost of treatment, can be reduced significantly, utilizing well-established and widely available treatments[35].

Effective screening and treatment programs can greatly reduce the burden of blindness. The current standard or screening for DR is either a dilated eye examination performed by an ophthalmologist or dilated ETDRS (Early Treatment Diabetic Retinopathy Study) 7-standard field stereoscopic 30° fundus photography[35].

Fundus camera was introduced in KNH three years ago. Before the introduction of the camera diabetic retinopathy screening was done using dilated fundoscopy. Our study aimed to compare the sensitivity and specificity of fundus camera in screening for diabetic retinopathy and sensitivity of OCT machine in screening for macula edema.

2. LITERATURE REVIEW

2.1 Pathogenesis

The exact mechanisms by which elevated glucose initiates the vascular disruption in retinopathy remain unclear. The vascular disruptions of DR and diabetic macula edema (DME) are characterized by abnormal vascular flow, changes in permeability, and non-perfusion of capillaries.

A hallmark of early DR is the change in the structure and cellular composition of the microvasculature. Endothelial cells are responsible for maintaining the blood-retinal barrier, and damage to them results in increased vascular permeability. In early stages of DME, breakdown of the inner blood-retinal barrier may occur, resulting in accumulation of extracellular fluid in the macula [2].

Pericytes are essential cellular components in the regulation of retinal capillary perfusion, and damage to these cells in diabetes leads to altered retinal hemodynamics, including abnormal autoregulation of retinal blood flow. Because pericytes help regulate retinal capillary perfusion, damage to these cells immediately disrupts retinal haemodynamics[8]. Loss of retinal pericytes represents another early feature of DR and correlates with micro-aneurysm formation. Another common feature of DR is the thickening of the capillary basement membrane and increased deposition of extracellular matrix components[26]. This feature may contribute to the development of abnormal retinal hemodynamics, including abnormal autoregulation of retinal blood flow.

There is evidence that retinal leukostasis may also play an important role in the pathogenesis of DR. Leukocytes possess large cell volume, high cytoplasm rigidity, a natural tendency to adhere to the vascular endothelium, and a capacity to generate toxic superoxide radicals and proteolytic enzymes. In diabetes, there is increased retinal leukostasis, which affects retinal endothelial function, retinal perfusion, angiogenesis, and vascular permeability. In particular, leukocytes in diabetes are less deformable, higher proportions are activated, and they may be involved in capillary nonperfusion, endothelial cell damage, and vascular leakage in the retinal microcirculation[20].

As a result of occluded capillaries, retinal ischemia stimulates a pathologic neovascularization mediated by angiogenic factors, such as vascular endothelial growth factor (VEGF), basic fibroblast growth factor (bFGF) , insulin-like growth factor-1 (IGF-1) , angiopoietin-1 and -2 , stromal-derived factor-1, epidermal growth factor (EGF) , transforming growth factor-beta 2 (TGF-β2) , platelet-derived growth factors (PDGFs) , and erythropoietin [19]. VEGF promotes angiogenesis; causes breakdown of the blood-retinal barrier, stimulation of endothelial cell growth, and neovascularisation; and increases vascular permeability in the ischemic retina[5].

2.1.1 Biochemical processes

In non-enzymatic glycation hyperglycemia leads to formation and accumulation of advanced glycation end products that accumulate in the retina affecting the functioning of retinal vascular endothelial cells. In the polyol pathway mechanism, the enzyme aldose reductase causes increased conversion of glucose to sorbitol. In addition, it also reduces galactose conversion to galactitol. Accumulation of sorbitol and galactitol results in inhibition of biosynthetic and degenerative enzymes resulting in basement membrane thickening. In early stages of the disease, protein kinase C induces various cytokines and angiogenic factors including vascular endothelial growth factor (VEGF). In the later stages, the VEGF is dependent on protein kinase C for both angiogenic and permeability effects. Increase in oxygen-free radicals may impair endothelium dependent vasodilatation and increase the apoptosis of retinal capillary cells [27].

2.1.2 Hemodynamic alterations

The variety of hematologic abnormalities seen in diabetes, such as increased erythrocyte aggregation, decreased red blood cell deformability, increased platelet aggregation and adhesion, predispose the patient to sluggish circulation, endothelial damage, and focal capillary occlusion. This leads to retinal ischemia, which, in turn, contributes to the development of diabetic retinopathy[27].

2.1.3 Paracrine factors

A variety of growth factors have been implicated in the pathogenesis of diabetic retinopathy. Endoplasmic reticulum stress response to nutritional deprivation in diabetes regulates the expression of VEGF and platelet derived growth factor at the level of mRNA translation[27].

2.2 Macula edema

Diabetic macular edema (DME) is the leading cause of vision loss in patients living with diabetes. The common pathway that leads to macular edema is breakdown of the blood–retinal barrier (BRB). The BRB consists of the inner and the outer BRB. The inner BRB is formed by tight junctions between retinal capillary endothelial cells, the surrounding basal lamina, perycytes, astrocytes and microglia. The outer BRB is formed by the tight junctions between retinal pigment epithelium (RPE) cells. Impaired integrity of the BRB leads to leakage of plasma solutes into the interstitial spaces, causing edema through increased osmotic pressure. Fluid subsequently accumulates in different spaces within and underneath the retina[4].

VEGF is a glycoprotein secreted by retinal pigment epithelium cells, Muller cells, ganglion cells and capillary endothelial cells. VEGF increases vascular permeability via multiple mechanisms, including: Leukocyte mediated extracellular injury, formation of fenestration and the dissolution of tight junctions resulting in transcellular bulk flow[27].

2.3 Screening for diabetic retinopathy

Screening is defined as, "*The process of examining a group of people for the presence of a disease*" with its prerequisites being:

- The disease must appear in a defined population
- The population must be identifiable
- The disease must present a health problem
- There must be effective treatment for the disease
- Screening must be cost effective and improve quality of life.

Screening for DR helps to detect early sight-threatening retinopathy, allowing treatment it in a timely fashion and in this way help to avoid expensive, advanced treatment or even prevent the development of blindness. Principles for screening in medicine (Appendix I) were established by Wilson and Jungner in 1968 and accepted by the World Health Organization (WHO)[39] the same year.

2.3.1 Rationale for screening

Screening for DR is important because patients are diagnosed early and those not affected are advised on how to prevent DR. As a result, patients with DR are treated promptly and vision loss from DR is avoided.

2.3.2 Methods of screening

There are several methods currently available for visualizing the retina, including direct and indirect fundoscopy, fundus photography and slit lamp biomicroscopy. Fluorescein angiography is held as the gold standard for detecting DR however, there are side effects to fluorescein making it less desirable for screening.[9]

For the initial screening examination, it is preferred that evaluation be done by an ophthalmologist or optometrist who is experienced in diagnosing and treating DR. Fundoscopy is a reasonable screening method when performed by well-trained personnel on a dilated pupil. The accuracy of fundoscopy is substantially lower when performed by primary care physicians [13].

In one study of 1949 patients participating in the Wisconsin Epidemiology Study of Diabetic Retinopathy (WESDR), there was 86% agreement between ophthalmoscopy and the results of fundus photography, with no significant inter-observer differences[22].

2.3.3. Screening modalities

For any DR screening programme to function effectively it must fulfill certain basic criteria. Firstly, the screening test must have sufficiently high sensitivity (true positive rate) to ensure that substantial numbers of patients with sight-threatening retinopathy are not missed. Secondly, it must have sufficiently high specificity (true negative rate) to ensure that ophthalmic departments

are not overwhelmed with unnecessary referrals[30]. The British Diabetic Association proposed that any screening programme for diabetic retinopathy should have at least 80% sensitivity and specificity, and it is against these figures that any screening modality for diabetic retinopathy is judged[33].

2.3.3.1 Direct ophthalmoscope

Direct fundoscopy alone has no role in a screening programme since the method consistently fails to meet the 80% sensitivity and specificity targets**.** Direct fundoscopy with mydriasis was shown to have a sensitivity of 65% when used by ophthalmologists, 33-66% with general practitioners and 48-83% with optometrists.[11, 25, and 41]

2.3.3.2 Retinal photography

Retinal photography, without mydriasis, utilizing 45° Polaroid colour prints was the first retinal photographic technique to be applied to DR screening. Whilst Polaroid photography offered an instant hard-copy image of the retina, concerns were soon raised about the adequacy of the technique to detect sight-threatening retinopathy in the peripheral retina, particularly when the pupils were small.[33]In contrast, retinal photography through dilated pupils using 35 mm transparencies has proved highly effective, achieving sensitivities and specificities of 89% and 86%, respectively.[3]

Non-mydriatic photography has been shown to be less sensitive mainly due to the pupillary constriction of the second eye following flash photography in the first.[39] Therefore, retinal photography with non-mydriatic cameras following dilation was the recommended method for screening in the UK by the National Screening committee 2000.[33]

In a study done in Brazil there was a high significant agreement (kappa = 0.97, P =.0001) between the degree of retinopathy detected by a single non-mydriatic monochromatic digital photograph and that seen in seven standard 35-mm color stereoscopic mydriatic fields. Sensitivity of direct fundoscopy compared with color photography was 34%, with a specificity of 100%[14].

Fundus photography in a dilated eye has been shown to increase sensitivity upto 87%.This has been made possible when done using high resolution cameras and seven field fundus photographs[15].Thirty degree seven field-ETDRS photography has been used as the gold standard

for screening of diabetic retinopathy. Three color 45-degree non-mydriatic fundus fields have been found to be more superior when compared to one field non-mydriatic photography[32].

2.3.3.3 Slit Lamp Biomicroscopy

The results with the slit lamp biomicroscope have been much more impressive, yielding sensitivities and specificities as high as 80% and 95%, respectively[30]. The widespread availability was an advantage for this method of detection. However, slit lamp biomicroscopy requires considerable skill and the procedure could be time consuming.

2.3.3.4 Optical Coherence Tomography (OCT)

Optical Coherence Tomography is a new diagnostic tool that can perform tomograph/cross-sectional imaging of biological tissues with less or equal to 10μm axial resolution using light waves. It is a non-contact, non- invasive device whereby a broad bandwidth near infrared light beam (820 nm) is projected onto the retina. The light gets reflected from the boundaries between the microstructures and also gets scattered differently from the tissues with different optical properties. It then compares the time delay of the light reflecting from various layers of the retina with the time delay of the light reflected from the mirror at a known distance.

The device has an interferometer that combines the reflected pulses from the retina as well as those from the reflecting mirror, resulting in a phenomenon known as interference. This interference is then measured by a photodetector, which determines the distance traveled by various beams of light varying the distance to the reflector mirror. This finally produces a range of time delays for comparison. The interferometer integrates several data points over 2mm of depth to construct a tomogram of retinal structures. It is a real time tomogram using a color scale. Different colors represent the degree of light back scattering from different depths of the retina.A systemic review of 6 journals from 1998 to 2006 showed a sensitivity of 79% and a specificity of 88%of detecting macula edema[10].

Patients with diabetes, mild to moderate non-proliferative DR and evidence of diabetic maculopathy on non-stereoscopic retinal photographs have a 42.1% chance of having no macular edema on SDOCT imaging as defined by standard OCT definitions of DME when graded by a retinal specialist[28].

Data has shown that many eyes diagnosed as having DME or CSME on monocular fundus photographs have no DME based on OCT CST, while many eyes diagnosed as not having DME or CSME on monocular fundus photographs have DME on OCT. Compared with the DME prevalence based on OCT CST, monocular fundus photographs overestimated the prevalence of macular edema by 40.2% (95% CI, 32.8%-47.7%; $P < .001$) and 27.2% (95% CI, 19.2%-35.3%; $P < .001$) when using Multi Ethnic Study of atherosclerosis(MESA) definitions of DME and CSME, respectively[42].

2.3.3.5 Fluorescein angiography (FA).

FA is generally used for treatment planning. It is a method in which sodium fluorescein is intravenously administered followed by a rapid sequence of photo of the retina to evaluate its circulation through the retinal vasculature. A method using orally administered fluorescein has also been developed. Normally, fluorescein cannot pass through the tight junctions of retinal capillaries; however, in some disease states, such as DR and DME, dye leakage occurs. The method is useful in detecting early alterations of the blood-retinal barrier, capillary closure, and micro-aneurysm formation. The major advantage of FA over fundus photography is its ability to detect macular ischemia denoted by non-perfusion of the retinal capillaries and to detect subtle DME as evidenced by fluorescein leakage from the capillaries. An automated method of quantifying micro-aneurysms from digitized fluorescein angiograms was shown to reliably detect micro-aneurysms with a sensitivity of 82%.

FA and fundus photography are comparable for the detection of no DR or mild and moderate DR. Similar results were reported for comparing digital color photography and oral FA (sensitivity for DR, 87% for both methods), although FA was more sensitive for detecting DME (sensitivity 48% for photography and 87% for FA; $P< 0.01$).Drawbacks to using FA as a screening procedure are its invasiveness, time constraints, expensive equipment, and adverse reactions. Allergic-type reactions to sodium fluorescein have been reported in patients undergoing FA, although the incidences of serious complications are rare[34].

2.3.3.6 Combined modalities

The remaining option for diabetic retinopathy screening is to combine screening modalities and site camera systems within optometrist practices. Combination of screening modalities is not a new idea. Previous studies have shown that sensitivities of around 90% can be achieved by optometrists using fundoscopy and dilated fundus photography, and these figures are all the more impressive when one considers that they were achieved with the direct ophthalmoscope[24]. One disadvantage of a combined modality program is the capital set-up costs.

2.3.4 Screening intervals for diabetic retinopathy

The goal of screening is to identify eyes with sight-threatening DR before symptoms occur, so that photocoagulation or other treatments can be applied in a timely and appropriate manner. A study done by Massino et al, suggested that screening can be repeated safely at 2-year intervals in any patient with type 1 or 2 diabetes and no retinopathy, giving a 95% probability of remaining free of referable lesions according to the same standard adopted by previous reports . It also shows that DR progresses more rapidly to referable severity in patients with type 2 diabetes on insulin treatment and ≥10 years known disease duration. On the other hand, patients with a shorter duration of diabetes can potentially be seen even less frequently (e.g. at 3-year intervals), though prudence is always of the essence, considering that information on the duration of type 2 diabetes is often imprecise[16].

2.4 Natural history

In general, the progression of retinopathy is orderly, advancing from mild non-proliferative abnormalities, characterized by increased vascular permeability, to moderate and severe non-proliferative diabetic retinopathy (NPDR), characterized by vascular closure, to proliferative diabetic retinopathy (PDR), characterized by the growth of new blood vessels on the retina and posterior surface of the vitreous. Pregnancy, puberty, and cataract surgery can accelerate these changes[29].

Vision loss due to DR results from several mechanisms. First, central vision may be impaired by macular edema or ischemia. Second, the new blood vessels of PDR and contraction of the

accompanying fibrous tissue can distort the retina and lead to tractional retinal detachment, producing severe and often irreversible vision loss. Third, the new blood vessels may bleed, adding the further complication of subhyaloid or vitreous hemorrhage[29].

2.5 Classification of diabetic retinopathy and macula edema

DR is a potentially blinding disease in which the threat to sight is through two main mechanisms: growth of new vessels leading to intraocular hemorrhage and possible retinal detachment with profound sight loss, and localized damage to the macula with loss of central visual acuity.

It can be classified as non-proliferative diabetic retinopathy (NPDR) which refers to presence of intra-retinal vascular changes prior to the development of extra-retinal fibrovascular tissue. It is staged using ETDRS grading system as no DR, mild, moderate, and severe NPDR as shown in appendix II. Proliferative diabetic retinopathy (PDR) is the presence of neovascularization due to diabetes induced ischemia and its associated complications. It is staged as early, high risk or advanced eye disease[5] as shown in appendix II.

Clinically significant macula edema (CSME) is defined as macula edema that meets the minimal criteria for size and location as shown in appendix III.

2.6 Prevalence of diabetic retinopathy and macula edema

There are approximately 93 million people with DR, 17 million with proliferative DR, 21 million with diabetic macular edema, and 28 million with visually threatening diabetic retinopathy (VTDR) worldwide. VTDR was defined as proliferative diabetic retinopathy (PDR) and /or diabetic macula edema (DME). Analyses of 35 studies done between 1980-2008 showed that the overall age-standardized prevalence of any DRin diabetic patients was 34.6% (95% CI 34.5–34.8), PDR was 6.96% (6.87–7.04), DME was 6.81% (6.74–6.89), and VTDR was 10.2% .Analyses confined to studies with similar methodologies and rigorous outcome definitions showed that the age-standardized prevalence was 35.4% (35.2–35.6) for any DR, 7.24% (7.15–7.33) for PDR, 7.48% (7.39–7.57) for DME, and 11.7% (11.6–11.8) for VTDR [40](PDR and /or DME).

According to Wisconsin Epidemiological Study of Diabetic Retinopathy (WESDR) non proliferative DR affects 99% of type 1 diabetic patients after 20 years and 60% of type 2 diabetic patients over the same period. Proliferative DR occurs in 50% of type 1 diabetic patients in 20years and 25% of type 2 diabetic patients in 25years. Central vision loss may be due to macula oedema or ischaemia. It may also be caused by tractional retinal detachment, vitreous haemorrhage and neovascular glaucoma[13].

In a systematic review, 62 studies from 21 African countries were included: three population-based surveys; two cohort studies; five case–control studies; 32 diabetes clinic-based studies, nine eye clinic-based studies and 11 other hospital-based surveys. Included studies varied considerably in terms of patient selection, method of assessing the eye and retinopathy classification. In population-based studies, the reported prevalence range in patients with diabetes for diabetic retinopathy was 30.2 to 31.6%, proliferative diabetic retinopathy 0.9 to 1.3%, and any maculopathy 1.2 to 4.5%. In diabetes clinic-based surveys, the reported prevalence range for diabetic retinopathy was 7.0 to 62.4%, proliferative diabetic retinopathy 0 to 6.9%, and any maculopathy 1.2 to 31.1%.[6]

A recent study in Northern Tanzania showed a prevalence of 27.9% for DR, 6.1% for maculopathy and 2.9% for PDR[31].

In a study done in Nakuru Kenya, to estimate the prevalence and factors associated with DR among people aged ≥50 years a total of 277 patients were screened for DR by slit lamp biomicroscopy (SLB) and 195 also underwent retinal photography. The prevalence of any DR diagnosed by retinal images among diabetics was 35.9% (95%, CI-: 29.7–42.6%). The most common grades of DR were mild and moderate non-proliferative DR (NPDR; 22.1%, 95% CI 16.1–29.4%), while severe NPDR and proliferative DR were less frequent (13.9%, 95% CI 10.0–18.8%) [18].A study done in 2007 in the diabetic clinic KNH showed a prevalence of 22.6%[40] and another one done in 2011 showed a prevalence of 31.9%[39].

3. JUSTIFICATION

The specificity and sensitivity of the fundus camera in screening for DR has not been validated in our setup. The England national committee guidelines on screening for sight threatening disease describes a good screening tool as one with a sensitivity of above 80%, however there are some studies which have shown the fundus photograph sensitivity to be less than 80%[12].The study was to ensure that the proper method of screening in our set up is recommended so that not to miss patients with diabetic retinopathy and also not to refer patients to posterior segment clinic unnecessarily. Increasing prevalence of DR in Kenya calls for use of an accurate method of screening to identify patients who require treatment.

4. OBJECTIVE

4.1 Broad objective

The broad objective was to assess the accuracy of screening for diabetic retinopathy and macula edema using the fundus camera and optical coherence tomography (OCT) in diabetic patients attending the medical outpatient clinic at KNH.

4.2 Specific objectives

1. To compare grading of DR using fundus photographs by the technician (screener) and ETDRS clinical grading criteria by the ophthalmologist.

2. To compare diagnosis of macula edema using fundus photographs and OCT.

5. METHODS

5.1 Study Design

This was a hospital based, cross-sectional study.

5.2 Study Period

The study was conducted between September 2017 and July 2018.

5.3 Study area

The study was done in the diabetic medical outpatient clinic at KNH. The hospital is located in Nairobi the capital city and it is the main national referral hospital. The diabetic clinic is located in the old outpatient clinic. It run clinic five days a week but Wednesday is mainly an education day for patients and on average 25 patients are seen daily and 60 patients on Fridays. The clinic has a catchment population of about 2500.

5.4Study Population

All type 2 diabetic patients attending the diabetic medical outpatient clinic at KNH were eligible for this study.

5.5 Sample size estimation

Formula for assessment of a diagnostic test used[1];

$$\mathbf{TP+FN} = \boldsymbol{Z^2} \times \frac{\mathbf{[sen(1-sen)]}}{\mathbf{W^2}}$$

$$\mathbf{N\ (sN)} = \frac{\mathbf{TP+FN}}{\mathbf{P}}$$

N=56 patients

Where:

TP=True positive

FN=False negative

Z=Confidence interval normal distribution value i.e. 95%, z=1.96

Sen. =sensitivity of the test, 80%

W =Accuracy, within 17.5%

N (sN) =sample size powered for sensitivity.

P=Prevalence, 35.9%

5.6 Sample Selection methods

Simple random sampling method was used. Patients were allocated numbers on a daily basis. Numbers were then selected at random from the pool.

5.6.1 Inclusion Criteria

Patients with type 2 diabetes attending diabetic medical outpatient clinic in KNH..

5.6.2 Exclusion criteria

Patients with other retinopathies.

Patients with type 1 diabetes.

Patients under 18 years of age (cannot give consent)

5.7 Data Collection, Management and Analysis

5.7.1 Data Collection Procedure

Ethical approval (Appendix IV) was obtained from the Kenyatta National Hospital/University of Nairobi Ethics and Research Committee (KNH/UON ERC) and department of medicine KNH (Appendix V). Informed consent was obtained from each patient in either English or Kiswahili using the informed consent document in AppendixVI, VII and VIII.

Personal information such as age and sex was taken, best corrected visual acuity (BCVA) and a questionnaire filled (appendix VIII) by the principal investigator. The Snellen chart for those who can read was used. Illiterate, E' chart was used for those who could not read. Charts were placed at 6metres.

Patient's fundus photograph findings were recorded according to the ENSC grading (Appendix IX) by the technician. The patient's pupils were dilated using 1.0% tropicamide, 1 drop in each

eye, repeated after every 5 minutes for 15-20minutes if required. A detailed fundus examination was performed and graded using a non- contact fundus examination (+90D) Volk lens with a slit lamp bio-microscope and indirect ophthalmoscope by the principal investigator. The fundoscopy findings were confirmed by the vitreoretinal surgeon. A sketch of the fundus was drawn and changes suggestive of diabetic retinopathy were noted. Eyes were graded according to EDTRS grading system (Appendix II) OCT scanning was performed on the 60 patients to determine the presence or absence of macula edema. Patients found to have clinically significant macula edema were referred to the posterior segment clinic or any facility of their choice for further management and follow up.

5.7.2 Data Instruments

A predesigned questionnaire as used to collect data (Appendix VIII). Snellen chart and E chart were used to assess for vision for the literate and illiterate respectively. A fundus camera was used to take fundus photographs. Tropicamide 1% was then used to dilate patients. Slit lamp and a 78D were used for fundoscopy. Indirect ophthalmology was done with a 20D.Spectral domain OCT was for scanning.

5.8 Data Management and Analysis

Data was collected using structured questionnaires (Appendix VIII) and entered into a password protected Microsoft Access Database. The hard copy data forms were stored in a lockable cabinet in the Principal Investigator's office. Upon completion of data entry, hard copy forms were compared with the entered data to identify errors and corrections made appropriately.

Descriptive statistics were carried out and were summarized with frequencies and percentages while continuous variables were summarized using measures of central tendency such as mean, median, mode and standard deviation.

The sensitivity and specificity of fundus test were estimated using simple proportions. SPSS program was used to analyze data**.**

Table 1: Demographics

Particular	**Response**
Age in years	
Sex	
Male	
Female	

Table 2: Sensitivity, specificity and predictive values

Gold standard (Fundoscopy)				
		Retinopathy present	Retinopathy absent	Total
Fundus Camera	Retinopathy present	A	B	A+B
	Retinopathy absent	C	D	C+D
	Total	**A+C**	**B+D**	A+B+C+D

Where;

Sensitivity: A/ (A+C) × 100

Specificity: D/ (D+B) × 100

Positive Predictive Value: A/ (A+B) × 100

Negative Predictive Value: D/ (D+C) × 100

Prevalence (A+C)/ (A+B+C+D)

5.9 Ethical Considerations

5.9.1 Confidentiality

The identity of the patients was kept anonymous during data collection. No record of the identity of the patient or file number was made. No photocopies of medical records were made. The information of the patient was only available to the statistician and investigator for analysis.

5.9.2 Potential risks and benefits

The study was not made to harm the patient in anyway. Fundoscopy involves shining a bright light into the patient's eyes but the examination has been found to be safe. No adverse events noted with OCT which is safe and non-invasive. Tropicamide, the drug used for pupillary dilation is safe and has no major side effects. Patients were advised that they may experience blurring of vision which won't disappear as the drug wears out in about six hours. Participation in the study was voluntary and one could opt out at any stage of the study. Patients diagnosed of any condition during screening were referred to the appropriate clinic for further management. All the examinations done to the patient were safe.

5.9.3 Approval by Ethics Committees

Written ethical approval to conduct the study was sought from the Ethics and Research Committee of University of Nairobi and Kenyatta National Hospital (Appendix IV).

6.0 RESULTS.

The figure below shows that 99 patients were selected, 60 patients had OCT of both eyes done.

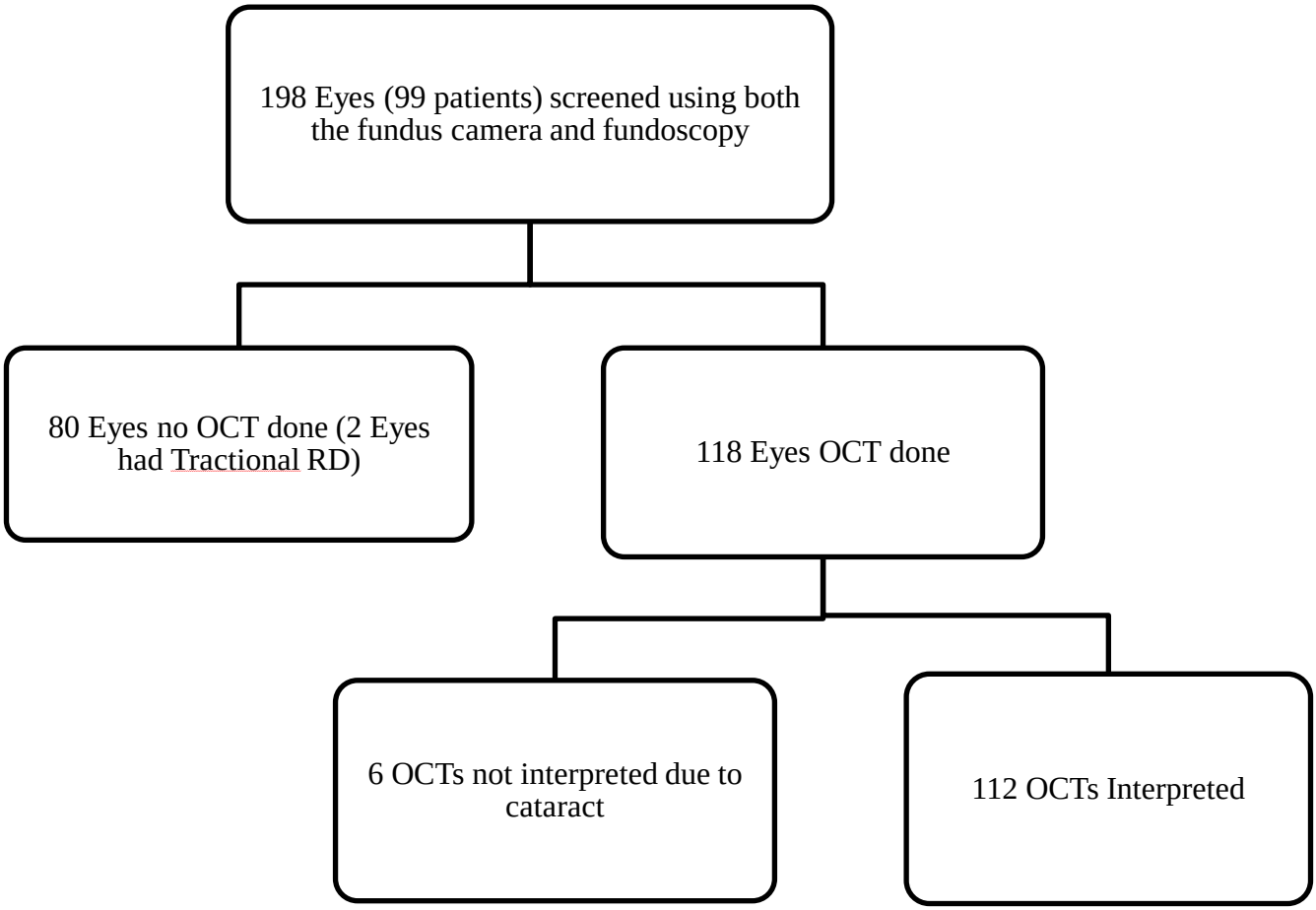

Figure 1: Flow diagram

6.1 Socio-demographic characteristics

6.1.1 Age

The mean age of the patients was 59.4 years with standard deviation of 13.4 years and within the range of 25 and 92 years. The figure below shows population distribution by age.

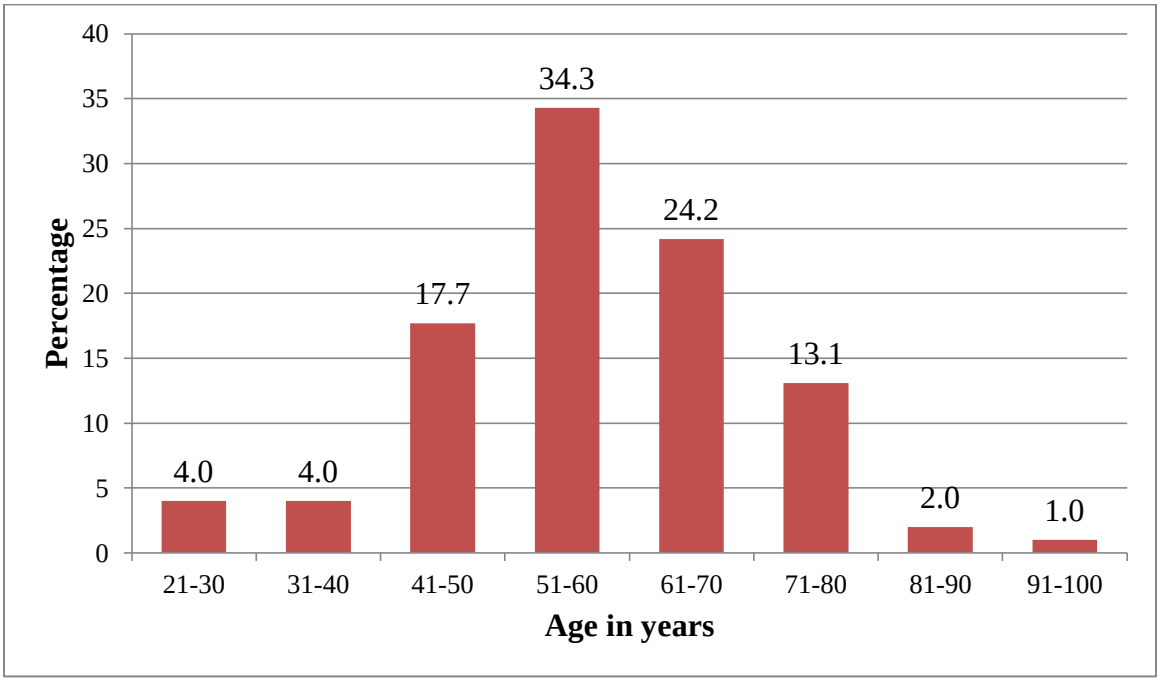

Figure 2: Distribution of the studied patients by age in years (n=99)

6.1.2 Sex

The male to female ratio was approximately 1:2.and this difference was statistically significant (p value=0.01). The figure below shows the distribution of the sample population by sex.

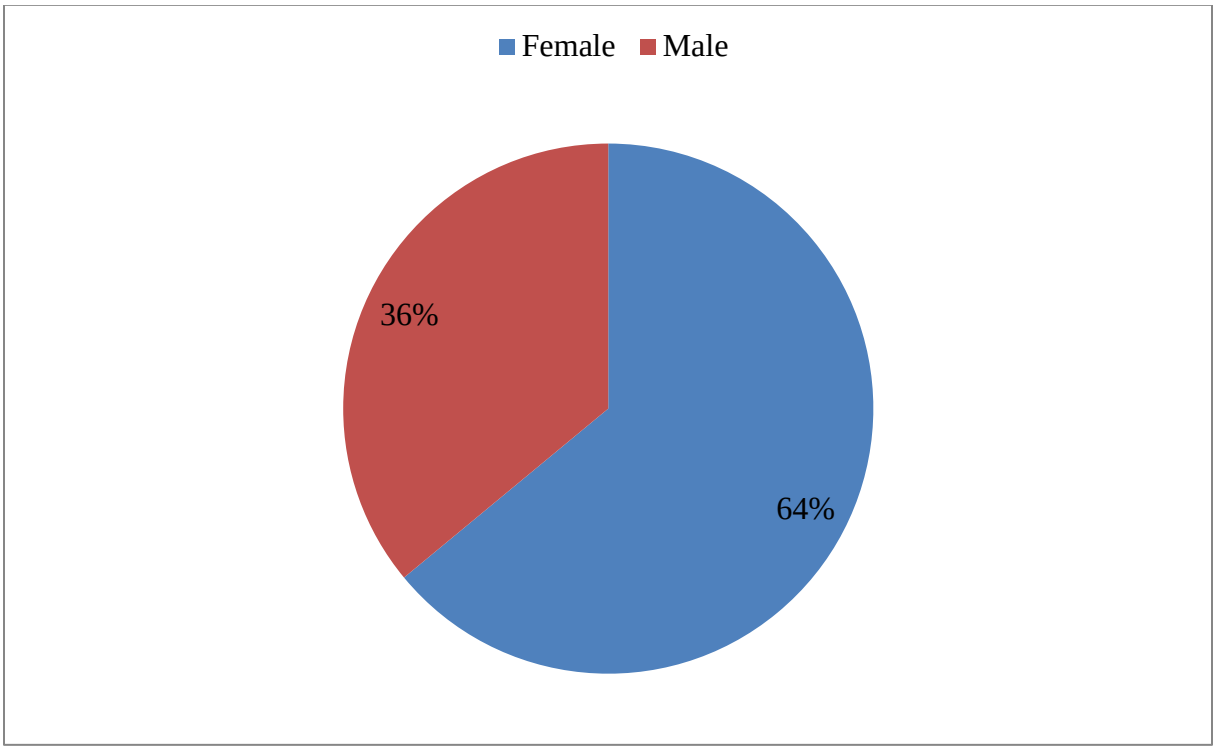

Figure 3: Distribution by sex (n=99)

6.1.3 Best corrected visual acuity

It was noted that most patients had normal vision according to WHO classification. 10.1% of the patient had moderate visual impairment. It was also noted that the patients who had severe visual impairment had age related macular degeneration(ARMD).The table below shows the number of eyes with the best corrected visual acuity in different categories.

Table 3: Grading of visual acuity per eye according to WHO categorization of blindness and visual impairment

Category	Visual Acuity		Right Eye		Left Eye	
	Worse than	Equal to or better than	Number of patients	%	Number of patients	%
Normal		6/18	88	88.9	85	85.9
Moderate Visual Impairment	6/18	6/60	8	8.1	11	11.1
Severe Visual Impairment	6/60	3/60	2	2.0	2	2.0
BLINDNESS)	3/60		1	1.0	1	1.0
TOTAL			**99**	**100**	**99**	**100**

Table 4: Grading of visual acuity in the best eye as per WHO categorization of blindness and visual impairment

Category	<	≥	**No.**	**%**
Normal		6/18	88	88.9
Moderate Visual Impairment	6/18	6/60	10	10.1
Severe Visual Impairment	6/60	3/60	1	1.0
BLINDNESS)	3/60		0	0
TOTAL			**99**	**100**

6.1.4 Duration of Diabetes

The average duration was 10.8 years (SD 7.3) within the range of 2months to 36 years distributed as shown below.

Table 5: Duration of diabetes in years

Age Clusters	**No of patients**	**Percentage**
<1yr	2	2.0
1-5	19	19.2
6-10	27	27.3
11-15	25	25.3
16-20	18	18.2
21-25	2	2.0
26-30	3	3.0
31-35	2	2.0
36-40	1	1.0
TOTAL	**99**	**100**

6.2. Fundus Examination Findings using the fundus camera

6.2.1 DR Grading using the fundus camera

Fifty three percent of the patients had no DR as per the diagnosis made by thefundus camera photographs using the English National Screening program for grading diabetic retinopathy (Appendix X) as shown below.

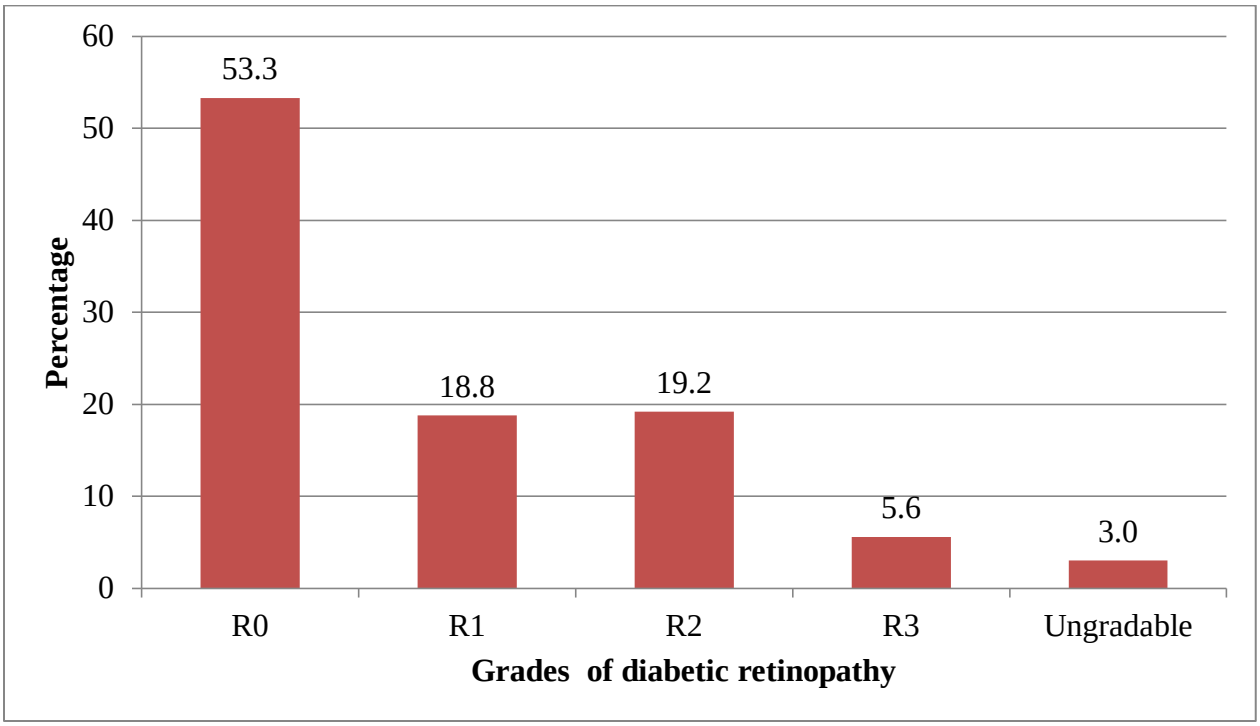

Figure 4: Grades of diabetic retinopathy on fundus photography (n=198)

6.2.2Maculopathy

The pie chart below shows that 16% of the eyes had macula edema as per fundus photography.

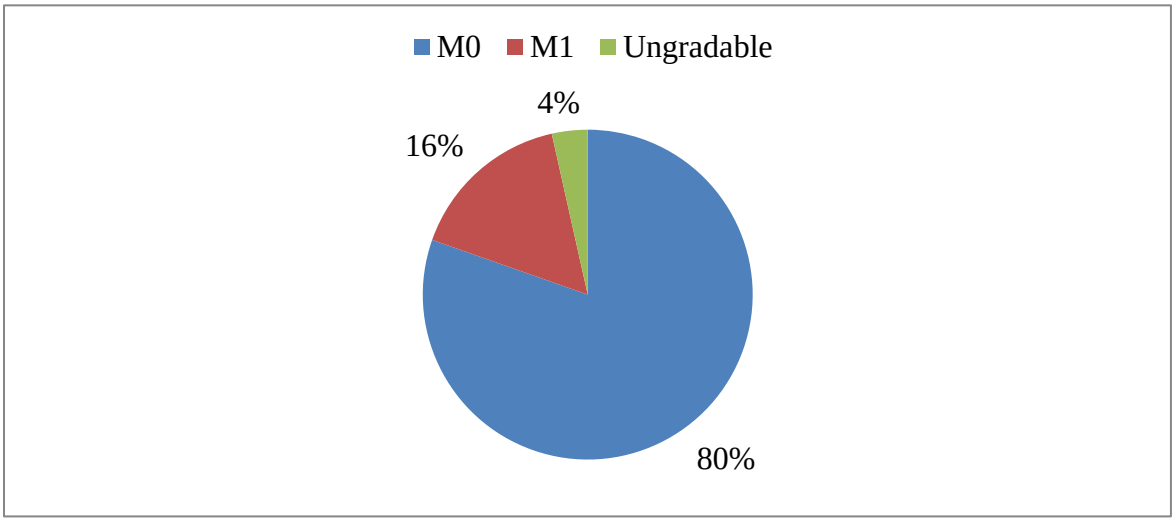

Figure 5: Eyes with maculopathy on fundus photography (n=198).

6.2.3 Photocoagulation

Only 4.1% 0f the patients had had retinal photocoagulation as in the figure shown below

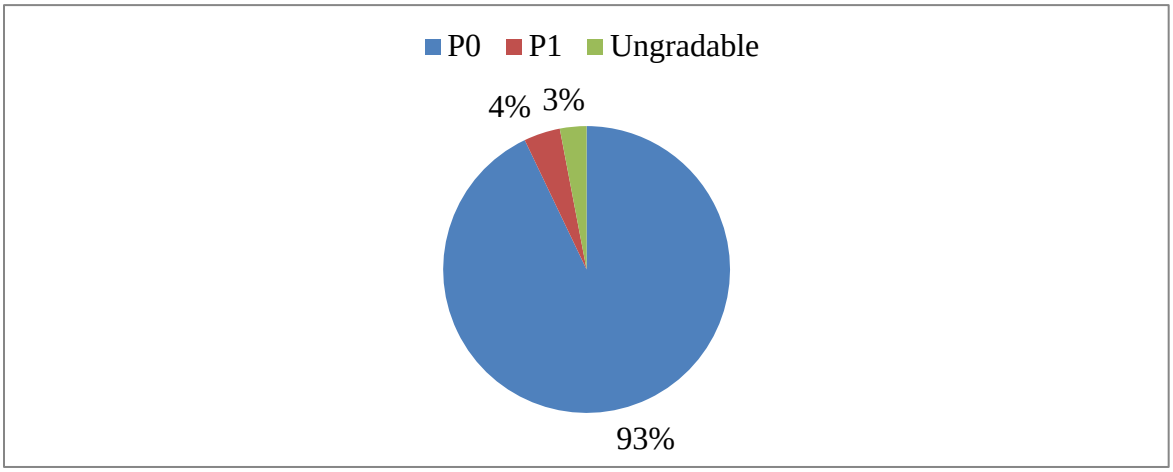

Figure 6: Eyes which had retinal photocoagulation on fundus photography(n=198)

6.3 Fundus Examination using indirect ophthalmoscope

6.3.1 ETDR grading of diabetic retinopathy using indirect ophthalmoscope.

49.7% patients had no diabetic retinopathy. 5.6% had PDR as per the bar chart below.

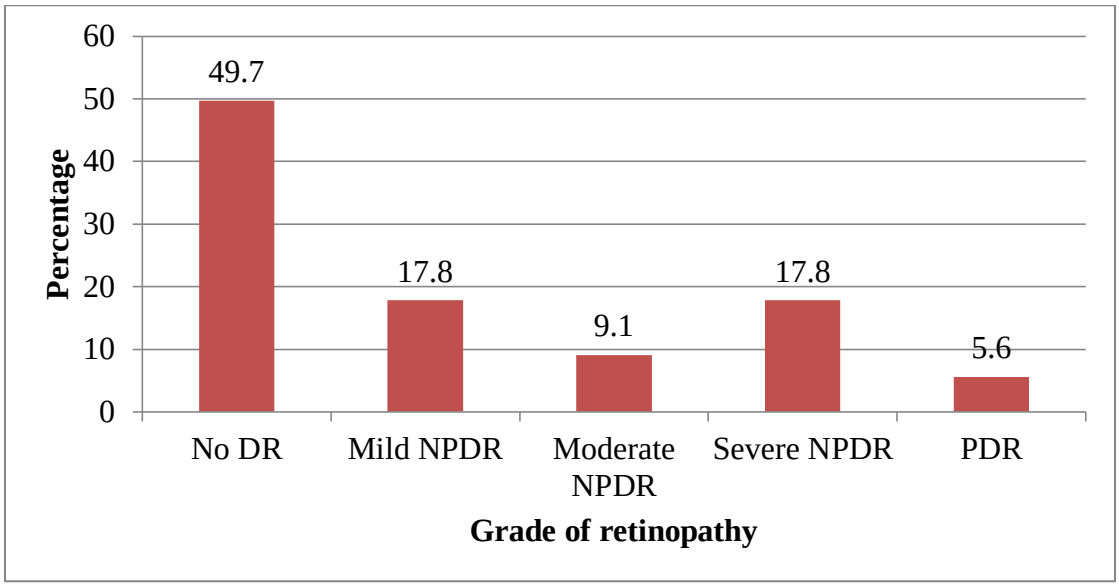

Figure 7: Percentage of eyes which had DR on fundoscopy (n=198)

6.3.2 Grading of clinically significant macula edema by indirect ophthalmoscope

Nineteen percent of the eyes had CSME as shown below.

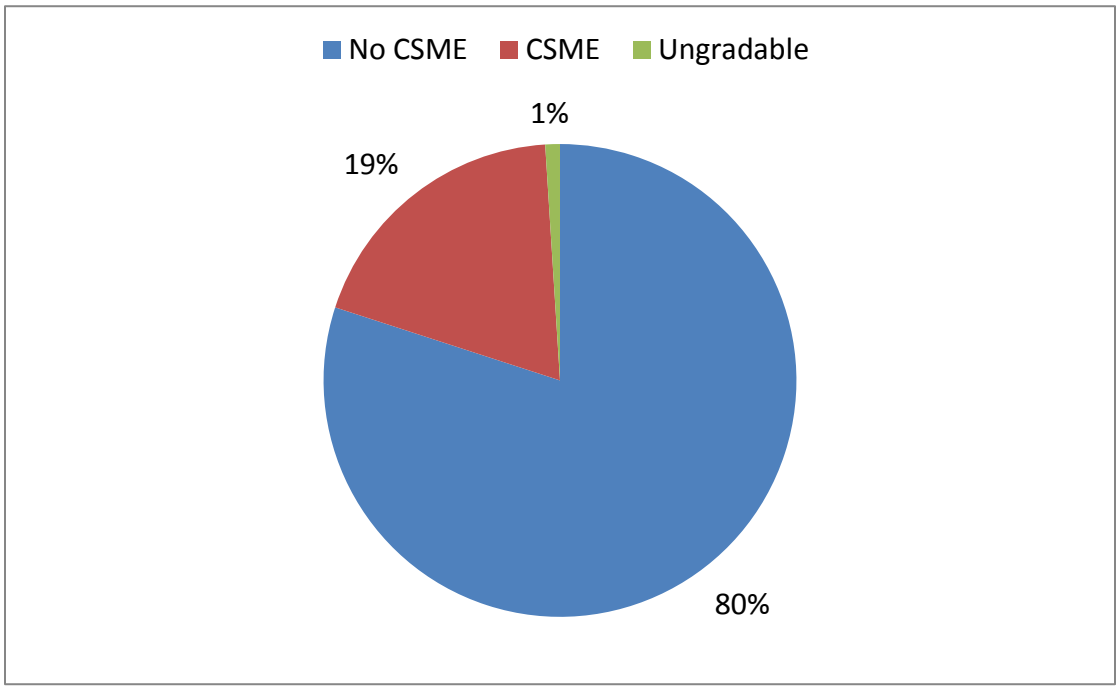

Figure 8:Percentage of eyes with clinically significant macula edema(n=198)

6.4 Sensitivity, specificity and predictive values

6.4.1 Accuracy of Diagnosis for DR (All grades)

Diagnosis for DR had a sensitivity of 86.2% (95% CI: 77.5% - 92.4%) and a specificity of 94.9% (95% CI: 88.4% - 98.3%) as shown below. Eight eyes were ungradable by the fundus camera and so they could not be compared.

Table 6: Accuracy of Diagnosis for All grades of DR (n=94)

		Fundoscopy (Gold standard)		
		Present	Absent	Total
Fundus photography	Present	81	5	86
	Absent	13	92	105
	Total	94	97	191

Statistic	**Value**
Sensitivity	86.2% (95% CI: 77.5% - 92.4%)
Specificity	94.9% (95% CI: 88.4% - 98.3%)
Positive Predictive Value	94.2% (95% CI: 87.3% - 97.5%)
Negative Predictive Value	87.6% (95% CI: 81.0% - 97.5%)

6.4.2 Accuracy of Diagnosis for No DR

Diagnosis for no NPDR had a sensitivity of 94.9% (95% CI: 88.3% - 99.3%) and a specificity of 86.2% (95% CI: 77.5% - 92.4%)

Table 7: Shows accuracy of Diagnosis for No DR(n=97)

Fundoscopy (Gold standard)				
		Present	Absent	Total
Fundus photography	Present	92	13	105
	Absent	5	81	86
	Total	97	94	191

Statistic	**Value**
Sensitivity	94.9% (95% CI: 88.3% - 99.3%)
Specificity	86.2% (95% CI: 77.5% - 92.4%)
Positive Predictive Value	87.6% (95% CI: 81.0% - 92.2%)
Negative Predictive Value	94.1 % (95% CI: 87.3% - 97.5%)
Prevalence	50.8 %(95% CI: 43.5% - 58.1%)

6.4.3 Accuracy of Diagnosis for mild DR

Diagnosis for mild NPDR had a sensitivity of 60.6% (95% CI: 42.1% - 77.1%) and a specificity of89.2% (95% CI: 83.3% - 93.6%)as shown below

Table 8:Showsaccuracy for diagnosis for mild DR

Fundoscopy (Gold standard)				
		Present	Absent	Total
Fundus photography	Present	20	17	37
	Absent	13	141	154
	Total	33	158	191

Statistic	**Value**
Sensitivity	60.6% (95% CI: 42.1% - 77.1%)
Specificity	89.2% (95% CI: 83.3% - 93.6%)
Positive Predictive Value	54.1% (95% CI: 41.0% - 66.6%)
Negative Predictive Value	91.6% (95% CI: 87.6% - 94.3%)

6.4.4 Accuracy of Diagnosis for Moderate and Severe NPDR

Diagnosis for moderate and severe NPDR had a sensitivity of 74.0 % (95% CI: 59.7% - 85.4%) and a specificity of 99.3% (95% CI: 96.1% - 99.9%) as shown in the table below

Table 9:Shows accuracy of Diagnosis for moderate and Severe NPDR

		Fundoscopy (Gold standard)		
		Present	Absent	Total
Fundus photography	Present	37	1	38
	Absent	13	140	153
	Total	50	141	191

Statistic	**Value**
Sensitivity	74.0 % (95% CI: 59.7% - 85.4%)
Specificity	99.3% (95% CI: 96.1% - 99.9%)
Positive Predictive Value	97.4% (95% CI: 84.0% - 99.6%)
Negative Predictive Value	91.6% (95% CI: 87.2 %- 94.5%)

6.4.5 Accuracy of Diagnosis for PDR

Diagnosis for PDR had a sensitivity of 90.9% (95% CI: 58.7% - 99.8%) and a specificity of 99.4% (95% CI: 96.9% - 99.9%) as shown in the table below.

Table10: Table Shows accuracy of Diagnosis for PDR

	Fundoscopy (Gold standard)		
	Present	Absent	Total

Fundus photography	Present	10	1	11
	Absent	1	179	180
	Total	11	180	191

Statistic	**Value**
Sensitivity	90.9% (95% CI: 58.7% - 99.8%)
Specificity	99.4% (95% CI: 96.9% - 99.9%)
Positive Predictive Value	90.9% (95% CI: 58.4% - 98.6%)
Negative Predictive Value	99.4 % (95% CI: 96.5%- 99.9%)

6.5 Optical Coherence Tomography (OCT) findings

6.5.1 Macula edema as per OCT

Eighty two percent of the patients did not have CSME as shown in the pie chart below.

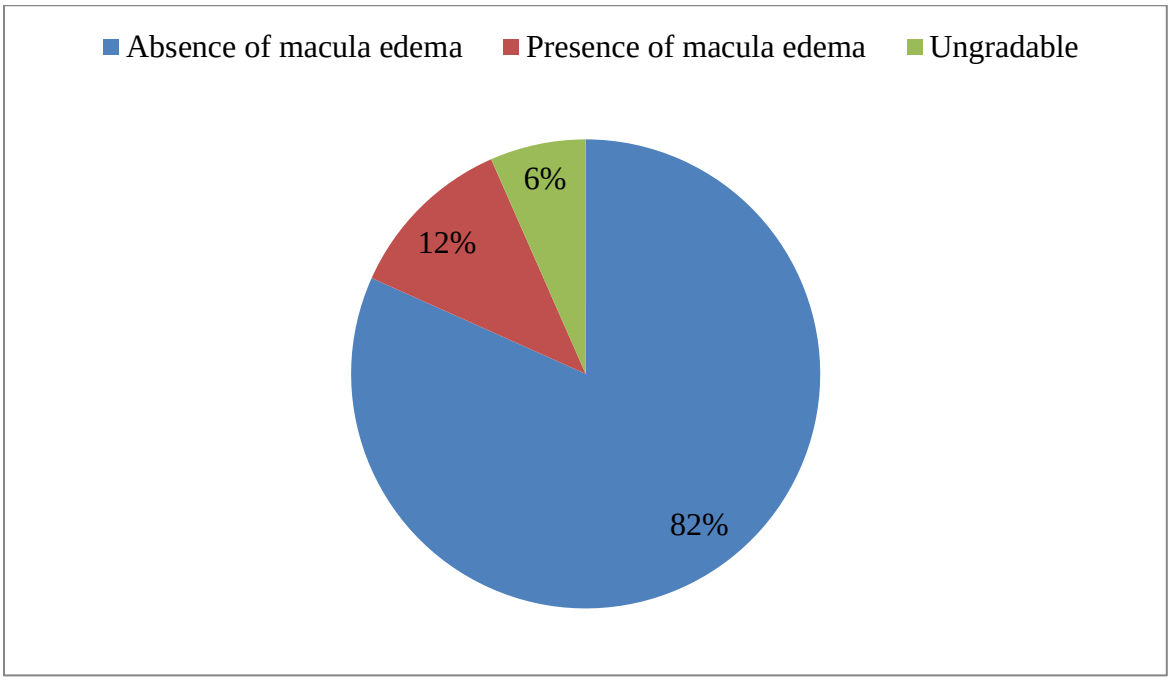

Figure 9: Percentage of eyes with Macula edema after OCT scanning(n=118)

6.5.2Accuracy of diagnosis for macula edema using the fundus photography

The sensitivity of fundus camera in diagnosis for macula edema was found to be 57.1% (95%CI: 28.9% - 82.3%) with a specificity of 89.8% (95%CI: 82.0% - 95.0%).

Table11: Accuracy of diagnosis for macula edema using the fundus photography

	OCT (Gold standard)			
		Present	Absent	Total
Fundus photography	Present	8	10	18
	Absent	6	88	94
	Total	14	98	112

Statistic	**Value**
Sensitivity	57.1% (95%CI: 28.9% - 82.3%)
Specificity	89.8% (95%CI: 82.0% - 95.0%)
Positive Predictive Value	44.4% (95%CI: 27.6% - 62.7%)
Negative Predictive Value	93.6% (95%CI: 88.9 %- 96.4%)
Prevalence	12.5% (95%CI:41.5% t-o 56.0%)

7.0 DISCUSSION

The accuracy of diagnosis for DR had a sensitivity of 86.2% and a specificity of 94.9% and the sensitivity of fundus camera in diagnosis for macula edema was found to be 57.1% and a specificity of 89.8%.

Majority of patients, 63(63.6%), screened were female. This is comparable to many studies done in Africa have shown that majority of patients with diabetes are female. A study in Nakuru showed that 52% were female[38].A study done in 2017 by international diabetic federation (IDF) showed that the global diabetes prevalence in adults aged 20–79 years was estimated at 8.8%. There were differences in the prevalence of diabetes by age group, World Bank income group, and geographical region. Diabetes prevalence peaked at ages 65–69 years for men and ages 75–79 years for women[12].

Diabetic retinopathy is one of the leading causes of irreversible blindness. Most patients (88.9%) in this study had mild or no visual impairment in their best eye as per the WHO guidelines. A small percentage (10.1%) had moderate visual impairment. Only one patient had severe visual impairment. The patient had age related macular degeneration in both eyes. A similar study done in Nakuru in 2015 showed that 79.3% of the patients had no visual impairment[38].

The mean duration of diabetes was found to be 10.8 years with a standard deviation of 7.3 years, within the range of 0.2 to 36 years. The patient with the shortest duration of two months had proliferative diabetic retinopathy and macula edema. This may be attributed to late diagnosis. This is comparable to a study done in Nakuru which found that most patients had duration of over 10 years. A study done in 2014 by Massino et al, to estimate the delay between onset and diagnosis of type 2 diabetes found that type 2 diabetes may arise 4 to 6 years before clinical diagnosis is reached[17].

Fundus photography examination revealed that most patients (53.3) had no diabetic retinopathy. Majority of the patients had R1 (18.8%) and R2 (19.2%).5.6% of the patients had R3.A small percentage (3%) of photographs was ungradable. The major reason for photographs being ungradable was unclear ocular media and miotic pupil. Nonmydriatic fundus photographs have been reported to be of decreased quality compared with mydriatic fundus photographs. The rate of upgradable photographs in prior studies varies from 6% to 36% among those taken without pupillary dilation compared with 2% to 7% of photography performed after pupillary dilatation[7].

Fundus photography diagnosed 16% of the eye with diabetic maculopathy. It was found that 4% of the patients had retinal photocoagulation.

Fundoscopy revealed that majority of the patients (49.7%) had no diabetic retinopathy. Patients with mild and moderate diabetic retinopathy were 26.9%, severe NPDR 17.8% and 5.6% had PDR. This was comparable to the findings in a study done in Nakuru which found 22.1% of the patients to have mild and moderate NPDR and 13.9% to have severe NPDR and PDR[18].it was observed that most patients with severe diabetic retinopathy had been referred to the eye clinic but had not been seen.

The sensitivity for identifying no DR was 94.8% while that of mild NPDR was 60.6%. Moderate and Severe NPDR had a sensitivity of 74.0% and PDR had a sensitivity of 90.9%. The specificity for identifying no DR was 86.2%, mild NPDR was 89.2%, moderate and severe NPDR was 95.5%% and PDR was 99.4%. This study revealed that the ability of the fundus camera to diagnose no DR had a sensitivity of 94.8%.This means that out of 100 people with no diabetic retinopathy 95 were correctly diagnosed by the fundus camera. This showed that the fundus camera had higher sensitivity for diagnosis of advanced disease than mild disease. This is comparable to a study done in Nakuru in 2015 which showed that the fundus camera had a sensitivity of 91%, specificity of 69.9% [21].

The prevalence of DR was 50.7% which is high compared to previous studies. A study done in Nakuru found a prevalence of 35.9%[21].Mwale et al in 2007 found a prevalence of 22.6%[23] at KNH diabetic clinic and Wambugu et al found a prevalence of 31.9%[37] in 2007 at KNH diabetic clinic. During data collection there was a doctor's strike and the number of patients attending the clinic was very low. Among the few patients were patients who had attended the clinic for management of diabetic foot who were also sampled.

It was found that 11.7% of patients who had OCT scanning had macula edema. This is the lowest percentage compared to 16% maculopathy by fundus photography and 19% by slit lamp biomicroscopy though it was not clinically significant. The prevalence of macula edema was 12.5% which is also high. The same reasons for high prevalence of DR above could explain this. A study done by Yu et al, involving 246 eyes found that 48.5% of patients we diagnosed with CSME by the fundus camera compared to 27.2% diagnosed by OCT[42]. Therefore it appears that fundus photography used for screening tends to over-estimate the presence of DME.

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8.0 STUDY LIMITATIONS

This was a hospital based cross-sectional study and the following limitations were encountered:

1. Thirty nine patients did not go for OCT scanning and this resulted in a high dropout rate

of 39.4%.

2. The high prevalence of DR may have affected the sensitivity and specificity.

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9.0 CONCLUSION

1. Fundus photography is an accurate method of screening for diabetic retinopathy.
2. Accuracy of identification of moderate and severe DR was higher than mild DR
3. Fundus camera has a low accuracy in screening for diabetic macula edema compared to OCT.

10.0 STUDY RECOMMENDATIONS

1. Since the fundus photography is accurate for DR, it should be expanded for use as a screening modality.

2. KNH needs an OCT as it has been seen that fundus photography tends to over-estimate DME.

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11.0 APPENDICES

APPENDIX I: The basic principles for disease screening as per the WHO.

The condition sought should be an important health problem.

- There should be an accepted treatment for patients with recognized disease.
- Facilities for diagnosis and treatment should be available.
- There should be a recognizable latent or early symptomatic stage.
- There should be a suitable test or examination.
- The test should be acceptable to the population.
- The natural history of the condition, including development from latent to declared disease, should be adequately understood.
- There should be an agreed policy on whom to treat as patients.
- The cost of case finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.
- Case finding should be a continuing process and not a 'once and for all' project.

APPENDIX II: ETDRS grading of diabetic retinopathy

1.Nonproliferative Diabetic Retinopathy (NPDR)

1.1.Mild NPDR

At least one retinal microaneurysm and one or more of the following:

Retinal hemorrhage, hard exudate, soft exudate, etc.

1.2.Moderate NPDR

Hemorrhages or microaneurysms or both in at least one quadrant and one or more of the following:

Soft exudates, venous beading, and IRMA.

1.3.Severe NPDR

Hemorrhages or microaneurysms or both in all four quadrants. Venous beading in two or more quadrants.

IRMA is in at least one quadrant.

2.Proliferative Diabetic Retinopathy (PDR)

2.1. **Early PDR** (proliferative retinopathy without DRS high-risk characteristics). One or more of the following:

– NVE

– NVD

– Vitreous or preretinal hemorrhage and NVE <1/2 disc area.

2.2. High-risk PDR (proliferative retinopathy with DRS high-risk characteristics). One or more of the following:

– NVD >1/4-1/3 disc area

– NVD; vitreous or preretinal hemorrhage

– NVE >1/2 disc area; preretinal or vitreous hemorrhage.

2.3.Advanced PDR

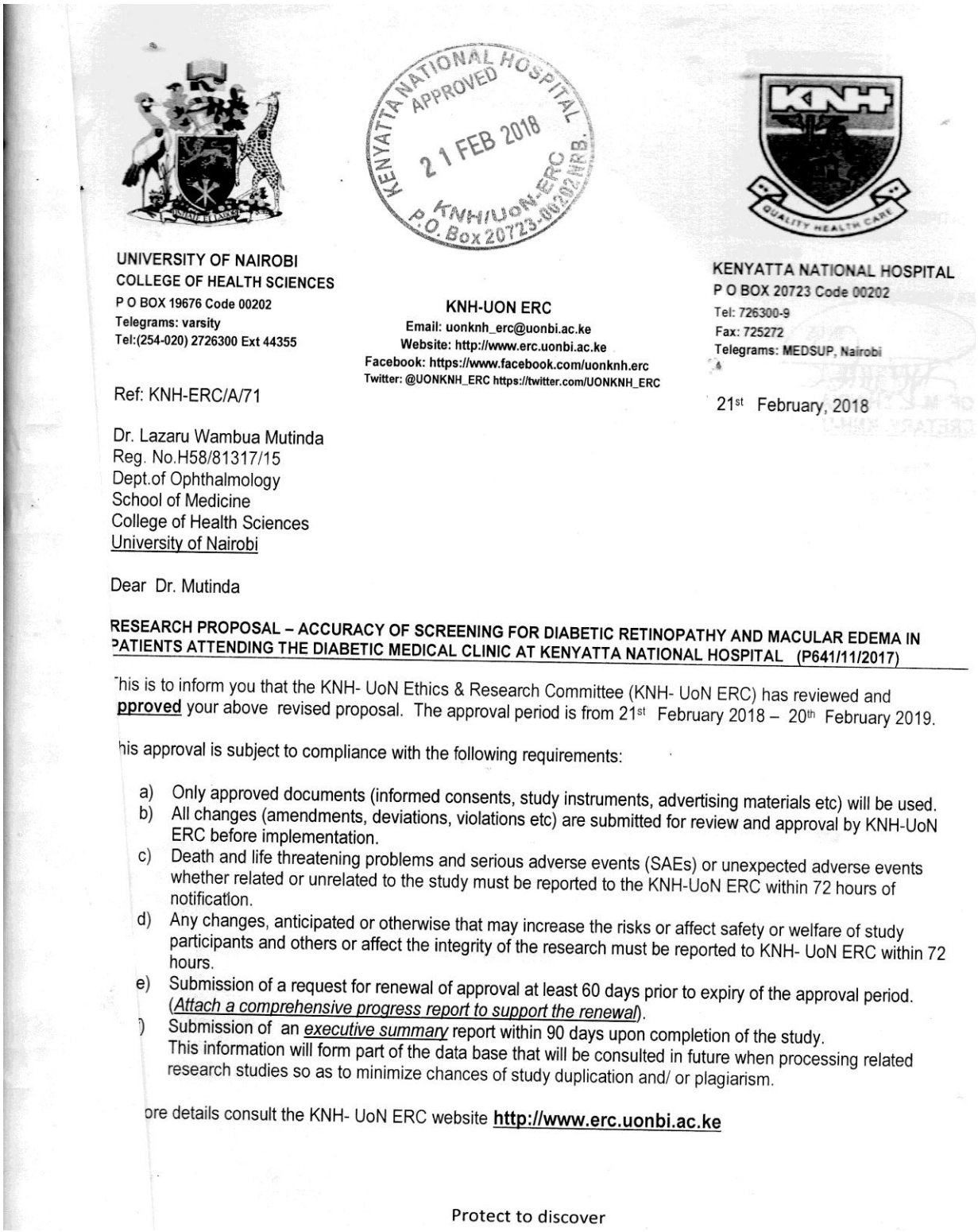
High-risk PDR; traction retinal detachment involving macula or vitreous hemorrhage obscuring ability to grade NVD/NVE.

APPENDIX III: Clinically significant macular edema, as defined by ETDRS.

It includes any one of the following lesions:

1. Retinal thickening at or within 500 microns from the center of the macula
2. Hard exudates at or within 500 microns from the center of the macula, if there is thickening of the adjacent retina
3. An area or areas of retinal thickening at least 1 disc area in size, at least part of which is within 1 disc diameter of the center of the macula

APPENDIX IV: KNH-UoN ERC Approval



UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
Tel:(254-020) 2726300 Ext 44355

KENYATTA NATIONAL HOSPITAL APPROVED 21 FEB 2018 KNH/UON-ERC P.O. Box 20723-00202 KNH-UON ERC

KNH-UON ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/71

21st February, 2018

Dr. Lazaru Wambua Mutinda
Reg. No.H58/81317/15
Dept.of Ophthalmology
School of Medicine
College of Health Sciences
University of Nairobi

Dear Dr. Mutinda

RESEARCH PROPOSAL – ACCURACY OF SCREENING FOR DIABETIC RETINOPATHY AND MACULAR EDEMA IN PATIENTS ATTENDING THE DIABETIC MEDICAL CLINIC AT KENYATTA NATIONAL HOSPITAL (P641/11/2017)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and approved your above revised proposal. The approval period is from 21st February 2018 – 20th February 2019.

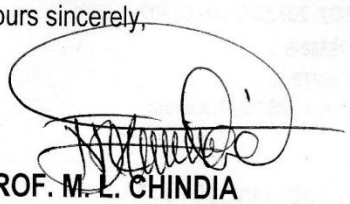
This approval is subject to compliance with the following requirements:

a) Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b) All changes (amendments, deviations, violations etc) are submitted for review and approval by KNH-UoN ERC before implementation.
c) Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
d) Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
e) Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
) Submission of an *executive summary* report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

ore details consult the KNH- UoN ERC website **http://www.erc.uonbi.ac.ke**

Protect to discover

Yours sincerely,



PROF. M. L. CHINDIA
SECRETARY, KNH-UoN ERC

c.c. The Principal, College of Health Sciences, UoN
The Deputy Director, CS, KNH
The Chairperson, KNH-UON ERC
The Assistant Director, Health Information, KNH
The Dean, School of Medicine, UoN
The Chair, Dept.of Ophthalmology, UoN
Supervisors: Dr. Muchai Gachago, Prof. Jefitha Karimurio

APPENDIX V: DEPARTMENT OF MEDICINE KNH APPROVAL FORM

KENYATTA NATIONAL HOSPITAL
P. O. Box 20723, 00202 Nairobi

Tel: 2726300/2726450/2726550
Fax: 2725272
Email: knhadmin@knh.or.ke

Ref: KNH/AD-MED/42B/VOL.I/

Date: 27th February 2018

Dr. Lazarus Wambua Mutinda
Department of Ophthalmology
School of Medicine
College of Health Sciences
University of Nairobi

RE:APPROVAL TO CONDUCT A STUDY IN MEDICINE DEPARTMENT

Following approval of your study by the KNH/UoN ERC and completion of the KNH study registration certificate, permission is hereby granted for you to collect data from Diabetic Clinic to enable you complete your study on ***"Accuracy of screening for diabetic retinopathy and macular edema in patients attending the diabetic clinic"*** ***at*** Kenyatta *National Hospital, Nairobi County, Kenya.*

Kindly liaise with the Assistant Chief Nurse Diabetic Clinic for facilitation.

DR. P.ETAU
HOD - MEDICINE

Copy to: Assistant Chief Nurse - Diabetic Clinic

Vision: A world class patient-centered specialized care hospital

ISO 9001: 2008 CERTIFIED

APPENDIX VI: CONSENT

Consent information

I, Dr. Lazarus Mutinda of the Department of Ophthalmology, University of Nairobi, am conducting a study to access the accuracy of screening for diabetic retinopathy (DR) using fundus camera in patients with diabetes at KNH.DR is one of the potentially vision threatening condition that requires early diagnosis and treatment to prevent blindness. My supervisors for the study are, Dr. Muchai Gachago and Prof. Jefitha Karimurio of the University of Nairobi Ophthalmology department and Dr. Stanley Ngare of KNH, department of Internal Medicine.

The study will be a cross sectional study, eye examination of patients after the fundus photography then OCT scanning and using questionnaires to get data from the patients. Eligible participants for the study are diabetic patients who attend medical outpatient clinic. Informed consent will be sought from participants before any data is collected. Once consent has been obtained, the participants will undergo medical history taking and an eye exam. Information obtained will be captured in a formulated questionnaire. The study period will run from January 2017 to June 2018. Study results will be disseminated to all participants after the study. This study will be beneficial since information obtained will be useful in the screening for DR. Permission and authorization for the study will be sought from all the responsible authorities before commencement of the study and therefore all the risks of data abstraction will be dealt with. Throughout the study, the data obtained will be treated with strict confidentiality.

Any question and concern can be addressed to Lazarus Mutinda at mutindalazarus@yahoo.com /0721157630 or Dr. Muchai at muchaigachago@gmail.com/0722873059 or Prof. Jefitha Karimurio at jkarimurio@gmail.com/0722760121 or Dr. Ngare at stanngare@gmail.com/0722881579. Questions can also be addressed to the University of Nairobi/ Kenyatta National Hospital Review committee. By signing below, you indicate your permission for the data abstraction.

Sign_____ Date_____

APPENDIX VII: INFORMED CONSENT

Title of Study: Accuracy of screening for diabetic retinopathy and macula edema in patients attending the diabetic medical clinic at Kenyatta National Hospital

Sponsor: SELF

Principal Investigator
Dr. Lazarus Mutinda
University of Nairobi

Supervisor
Dr. Muchai Gachago
University of Nairobi

Supervisor
Prof. Jefitha Karimurio
University of Nairobi,

Supervisor
Dr. Stanley Ngare
Kenyatta National Hospital

Introduction

My name is Dr.Lazarus Mutinda. I am doing my postgraduate degree in Ophthalmology at the University of Nairobi. My thesis is on the accuracy of screening for diabetic retinopathy and macula edema using in patients with diabetes at KNH and it is a cross sectional study from January 2017 to June 2018.

The purpose of this consent form is to give you information that might help you to decide whether to participate in the study or not. You are allowed to ask questions related to the study and implications on your part. The consenting process will take place in a private place that is comfortable to you.

Investigator's statement

Diabetic retinopathy is one of the potentially vision threatening condition that requires early diagnosis and treatment to prevent blindness. Blindness can be caused by vitreous hemorrhage, retinal detachment or macula edema. The aim of this study is to evaluate the accuracy of screening for DR and macula edema in patients attending medical outpatient clinic at KNH. Dilated fundoscopy is being used as the gold standard for DR screening.

Purpose of study

The results of this study will enable us to know the accuracy of screening for DR using fundus camera in patients with diabetes at KNH.

Study design and site

The study will be a cross sectional study done at KNH.

Procedures to be followed

The principal investigator together with the vitreoretinal surgeon will evaluate how accurate the fundus camera is able to screen for DR

Study process

Patients will be recruited at the MOPC, taken fundus photograph then taken to the ophthalmology department for visual acuity assessment, pupillary dilatation, slit-lamp biomicroscopy and OCT scanning. The information will be captured in questionnaire.

Benefits

The results of the study will reveal the accuracy of screening for DR and macula edema. This will potentially help in improving the efficiency of screening patients with diabetes for DR

Risks of accessing records

There is no risk if we access the medical records in this study. We will maintain privacy and confidentiality of all information obtained.

Assurance of confidentiality

The information given and records obtained will remain confidential and will not appear when we present this study or publish its results. You will receive a copy of the consent form.

Storage of data

The data will be stored in secure cabinets and computers with password/s and will only be accessible to the investigators.

Range of information desired

Patient demographic data, eye examination findings, OCT scanning and final diagnosis in relation to DR.

Right to refuse or withdraw

It is important that you understand the following general principles that will apply to all participants in the study:

1. Participation is entirely voluntary.
2. You may withdraw from this study at any time without penalty or loss of benefits.

Please feel free to ask any questions that you may have. Do you agree to participate?

I acknowledge that this consent form has been fully explained to me in a language that I understand and had the opportunity to ask questions which have been answered to my satisfaction. I agree voluntarily to participate in this study and understand that I have the right to withdraw at any time without penalty.

Participant's name: _____

Participant's signature or thumb print: _____

Date: _____

Study No:

For participants who are illiterate giving oral consent.

Name of witness: _____

Signature of witness: _____ Date: _____

Investigator's signature: _____ Date: _____

Contact: If you have questions in future, please contact The Secretary, University of Nairobi, College of Health Sciences Ethical Review Committee, P. O. Box 19676-00202, Nairobi, and Telephone: 020-2726300-9 ext. 44355, email uonknherc@uonbi.ac.ke

APPENDIX VIII: Fomu ya Ridhaa

Kuanzishwa

Jina langu ni Daktari Lazarus Mutinda, mwanafunzi katika idara ya Oftalmologia katika Chuo Kikuu cha Nairobi. Mimi ninafanya utafiti juu ya usahihi wa uchunguzi wa ugonjwa wa kisukari katika macho ukitumia kamera ya fundus kwa wagonjwa wa kisukari katika hospitali kuu ya Kenyatta.

Madhumuni ya utafiti

Tunata kakujua usahihi wa kamera ya fundus kuchunguza ugonjwa wa kisukari katika macho. Pia tunataka kutambua usahihi uchunguzi wa wagonjwa walio na selimapafu kutumia machine ya OCT.

Msingi wa kushiriki

Kushiriki katika utafiti huu ni kwa hiari yako.Unaweza kuwachakushiriki wakati wowote wa kipindi cha utafiti huu. Kutoshiriki ama kutoka kwa utafiti huu, hakutadhuru matibabu yako katika hospitali ya Kenyatta kwa njia yoyote.

Utaratibuwa utafiti

Baadaya kupeana idhini, yakushiriki katika utafiti huu, utaulizwa maswali kuhusu shidayako ya jicho, kasha utaangaliwa macho kutumia kamera ya fundus. Baadaye utaangaliwa nyuma ya macho na pia utapigwa picha ya sehemu ya nyuma ya macho na machine ya OCT.

Usiri

Chochote utakachochangi akatika utafiti huu kitawekwa siri. Sitatumia majina yako katika ripoti zozote.

Faida ya utafiti huu.

Matokeo ya utafiti huu yanaweza kuchapishwa katika vitabu vya matibabu au jarida kwa madhumuni ya kufundisha. Pia mtokeo haya yatachangia katika kuelewa zaidi ugonjwa huu, katika jami iyetu.

Utaonyeshwa picha ya maumbile ya sehemu ya nyuma ya jicho, utakayopigwa,ilikujuahali ya macho yako

Hatari na usumbufu

Katika harakati za uchunguzi na picha ya jicho hakuna uvamizi, wala maumivu yoyote. Baadhi ya maswali utakayo ulizwa yanaweza kuwa ya kibinafsi lakini faragha na uaminifu zitazingatiwa wakati wote.

Ombi la taarifa

Unaweza kuuliza maswali zaidi kuhusu utafiti huu wakati wowote. Utafahamishwa kuhusu matokeo ama jambo lolote muhimu kwa afya yako, litakalogunduliwa katika utafiti huu.

Mawasiliano

Unaweza kuwasilianana Daktari Lazarus W. Mutinda, nambari ya simu 0721157630 au Daktari Muchai Gachago (UON idara ya Ofthalmologia) nambari ya simu 0722760121 au Prof Jefitha Karimurio (UON idara ya ofthalmologia), nambari ya simu 0718057138 au Daktari Stanley Ngare (KNH) nambari ya simu 0722881579 au KNH / UON Kamati ya maadili S.L.P. 20723-00202 Nairobi, namba ya simu. +2542726300 Ext 44102 na barua pepe uonknherc@uonbi.ac.ke

Ridhaa

Baada ya kusoma na kuelewa fomu hii ya ridhaa, maswali yangu yote yamejibiwa, sahihi yangu hapa chini inaonyesha nia yangu ya kushiriki katika utafiti huu na idhini yangu kutumia matokeo na kushirikiana na wengine.

Mimi .....(Mgonjwa/mzazi) wa ..... minesoma na nikaelezwa lengo la utafiti huu n aDt Lazarus W. Mutinda. Ninatoa ridhaa ya kushiri kikatika utafiti huu katika hospitalikuu ya Kenyatta.

Sahihi..... ..Tarehe .....

Gumba..... ..Tarehe..... ..

Ninathibitisha ya kwamba nimemueleza mgonjwa nakujibu maswali yake kuhusu utafiti huu.

Sahihi ya mpelelezi..... .....

Dt Lazarus W.Mutinda

Simu 0721157630

APPENDIX IX: Questionnaire

A. Demographics:

1. Hospital patient Number ☐ 2. Patient Code No: ☐

3. Age: ☐ Years 4. Sex: Male ☐ Female ☐

5. Best Corrected Visual Acuity (BCVA) /pinhole Right Eye_____ Left Eye_____

B. **Fundus Examination Findings using the fundus camera**

		Right Eye	Left Eye
1. Retinopathy 0 (R0)	----------	☐	☐
2. Retinopathy 1 (RI)	----------	☐	☐
3. Retinopathy 2 (R2)	----------	☐	☐
4. Retinopathy 3 (R3)	----------	☐	☐
5. Maculopathy 0 (MO)	----------	☐	☐
6. Maculopathy 1 (R1)	----------	☐	☐
7. Photocoagulation 0 (PO)	----------	☐	☐
8. Ungradable	Yes	☐	No ☐

9. Others

C) Grading of diabetic retinopathy using indirect ophthalmoscope

	Right Eye	Left Eye
1. No Diabetic Retinopathy --------	☐	☐

2. Mild Nonproliferative Diabetic Retinopathy -------- ☐ ☐

3. Moderate Nonproliferative Diabetic Retinopathy --------- ☐ ☐

4. Severe Nonproliferative Diabetic Retinopathy ---------- ☐ ☐

5. Proliferative Diabetic Retinopathy ---------- ☐ ☐

6. Advanced Diabetic eye Disease ---------- ☐ ☐

7. Diabetic macula Edema ---------- ☐ ☐

E.Optical Coherence Tomography (OCT) FINDINGS

	Right Eye	Left
Eye	☐	☐
1. Presence of Diabetic Macula Edema		
2. Absence of Diabetic macula Edema	☐	☐
If present;		
3. Centre involving	☐	☐
4. Non Centre involving	☐	☐
5. Central thickness in micrometers ----------	☐	☐

APPENDIX X: English National Screening program for grading diabetic Retinopathy

Retinopathy

Ro – No diabetic retinopathy

R1 – background microaneurysms, retinal hemorrhage and exudates

R2 – (pre proliferative) venous bleeding, venous loop or reduplication intraretinal micro vascular abnormality (IRMA) cotton wool spots and blot hemorrhage

R3 – (proliferative) new vessels at disc and elsewhere, pre-retinal or vitreous haemorrhage, pre – retinal fibrosis and tractional detachment.

Maculopathy

M0- No maculopathy

M1 -Exudates within one disc diameter of fovea or circinate or group of exudates within the macula. Retinal thickening within 1 disc diameter of the centre of the fovea or any microaneuryms or hemorrhage within 1 disc diameter of the centre of the fovea.

Photocoagulation-Evidence of focal/grid laser to macular or evidence of peripheral scatter laser

APPENDIX XI: WORK PLAN

YEAR 2017/2018	Jun	Jul	Aug	Sept	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May
Proposal presentation				■								
Ethics approval					■	■						
Data collection							■					
Data analysis								■				
Report writing								■				
Dissemination of the result									■			

APPENDIX XII: BUDGET

M. Med Thesis Budget

TITLE: ACCURACY OF SCREENING FOR DIABETIC RETINOPATHY AND MACULA EDEMA IN PATIENTS WITH DIABETES AT KENYATTA NATIONAL HOSPITAL

Principal Investigator: Dr Lazarus Mutinda

Item	Quantity	Unit Cost	Total Cost
Proposal/Ethical approval and ministry of Education approval			
Proposal writing & printing	6 copies	Ksh 10 per page	5000
Binding Proposal	6 copies	100	600
Ethics	1	2000	2000
Airtime		Ksh. 3 per minute	2000
		Subtotal	**9600**
Data Collection			
Typing and Printing of Questionnaires		60 per copy	300
Photocopy of questionnaires		18 per copy	10000
Stationary –pens, rubbers etc			2000
Flash Disc 16GB Hp	1	4500	4500
Tropicamide eye drops	5	200	1000
Box files for filing questionnaires	10	450 each	4500
		Subtotal	**22300**

Contracted services			
Statistician	1		50000
Research assistant	1		25000
		Subtotal	**75000**
Printing costs and binding of Final book			
Finished book printing (120 pages approximately)	8 copies- 100 pages	Ksh 10 per page	8000
	8 copies- coloured20 pages	Ksh 30 per page	4800
Binding Finished book	2 copies- marking	100 per book	200
	8 final copy(black cover)	300	2400
		Subtotal	**15400**
TOTAL BUDGET			**122300**

Signature: ---------- Date: …….