VISION-RELATED QUALITY OF LIFE AMONG PATIENTS WITH DIABETES ATTENDING THE MEDICAL AND RETINA CLINICS IN KENYATTA NATIONAL HOSPITAL

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DECLARATION

I declare that this thesis proposal is my original work and has not been presented for the award of a degree in any other university

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TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF ABBREVIATIONS

CSME	Clinically Significant Macular Oedema
DM	Diabetes Mellitus
DME	Diabetic Macular Oedema
DR	Diabetic Retinopathy
ETDRS	Early Treatment Diabetic Retinopathy Study
HbA1c	Glycosylated Haemoglobin
ICD	International Classification of Disease
IDF	International Diabetic Federation
KNH	Kenyatta National Hospital
NPDR	Non-Proliferative Diabetic Retinopathy
PDR	Proliferative Diabetic Retinopathy
PRP	Pan-Retinal Photocoagulation
STDR	Sight-Threatening Diabetic Retinopathy
VEGF	Vascular Endothelial Growth Factor
VFQ-20	Visual Function Questionnaire-20
VRQoL	Visual related Quality of Life
WHO/PBD-VF 20	World Health Organization/ Programme for the Prevention of Blindness and Deafness- Visual function 20

OPERATIONAL DEFINITIONS

a) Diabetes Mellitus (DM):

A subject was said to be diabetic if any of the criterion below was present:

(i) a history of diabetes reported and had been on anti-diabetic medications

(ii) a fasting glucose level ≥ 126 mg/ dl

(iii) a random blood sugar level ≥ 200mg/100ml

b) Diabetic Retinopathy:

All patients with diabetes who had retinopathy consistent with diabetic eye disease as confirmed by the Vitreo-retinal surgeon in the Retina Clinic during dilated slit lamp biomicroscopy.

c) Clinically Significant Macular Oedema:

Patients with diabetes with any retinal thickening within 1/3-disc diameter (DD) of the centre of the macula, hard exudates within 1/3DD of the centre of macula with adjacent thickening and retinal thickening ≥1DD of the centre of the macula.

ABSTRACT

Introduction: The quality of life among patients living with diabetes mellitus (DM) and diabetic retinopathy (DR) can be affected by visual impairment, patient‘s anxieties and lifestyle changes.

Objective: We compared the vision-related quality of life (VRQoL) among diabetics with DR and those without DR, and assessed whether there was a trend of worsening VRQoL with increasing severity of DR.

Design & Methods: Hospital-based analytical cross-sectional study conducted among patients with DM attending the medical and retina clinics in Kenyatta National Hospital in December 2020. Patients living with DM for at least five years and aged ≥18 years were studied. VRQoL was assessed using the World Health Organization / Prevention of Blindness and Deafness Vision Function-20 Questionnaire and the higher the mean score, the worse was the QoL. Diabetic retinopathy was graded using the Early Treatment of Diabetic Retinopathy Study. Student t-test and ANOVA were conducted using SPSS software.

Results: We enrolled 100 participants; 50 without DR and 50 with DR. Patients with DR had a higher VRQoL mean score than those without DR in all domains; overall self-rating (2.6 vs 2.2, $p<0.001$), general functioning (18.0 vs 14.7, $p=0.005$), psychosocial (6.7 vs 5.3, $p<0.001$), and visual symptoms (6.1 vs 4.8, $p<0.001$). VRQoL was worse with increasing severity of DR in all domains. Overall self-rating (mild NPDR 2.2, moderate NPDR 2.5, severe NPDR 3.5 and PDR 3.3); visual symptoms (mild NPDR 5.6, moderate NPDR 5.6, severe NPDR 7.5 and PDR 7.4); psychosocial (mild NPDR 5.7, moderate NPDR 6.5, severe NPDR 6.0 and PDR 8.8); and general functioning (mild NPDR 15.7, moderate NPDR 16.9, severe NPDR 17.5 and PDR 23.6).

Conclusion: Patients with DR had poorer VRQoL than those without DR. VRQoL reduced with increasing severity of retinopathy. These findings underscore the need for interventions for early detection and management of DR to prevent developing more advanced DR and its associated deterioration of VRQoL.

1.0 INTRODUCTION

1.1. Diabetes Mellitus

World Health Organisation (WHO) defines diabetes mellitus as a metabolic disorder of multiple aetiology characterised by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both (1). The recommended classification for diabetes mellitus (DM) encompasses both the clinical descriptive criteria and the etiological classification of diabetes. Type 1 DM results from autoimmune disorders(2). Type 2 DM comprises for about 90% of diabetics and is due to disorders in insulin secretion. Impaired glucose tolerance is a stage of altered glucose regulation which can occur in any hyperglycaemic disorder, but it is not a type of diabetes (3). In the American 2020 edition of ICD-10 for diabetes mellitus, DM was classified as inadequately controlled, out of control and poorly controlled (4). Diabetes mellitus (DM) has been associated with lesions to the eyes such as reduced corneal sensation and tear production, cataract, transient lenticular myopia during hyperglycaemia, iris neovascularization, retinal vascular occlusions, and diabetic retinopathy. DM causes a reduction in visual acuity and diabetic maculopathy also causes severe loss of contrast sensitivity (5).

1.2. Diabetic Retinopathy

Diabetic retinopathy (DR) is a chronic retinal disorder characterized by gradually progressive alterations in the retinal microvasculature in patients with diabetes mellitus. Diabetic retinopathy (DR) damages the retina microvascular system because of prolonged hyperglycaemia.

i) Classification of Diabetic Retinopathy

The ETDRS grading system is an excellent tool in clinical research because it is simple to use and easy to recall (6). It encompasses five different stages including:

1. Mild non-proliferative diabetic retinopathy (NPDR): at least one microaneurysm but no other findings.
2. Moderate NPDR: retinal haemorrhages or microaneurysm in one to three retinal quadrants and/or cotton wool spots, hard exudates, or venous beading.

3. Severe NPDR: based on the 4:2:1 rule that is severe retinal haemorrhages in all 4 quadrants, ≥2 quadrants with venous beading and ≥1 quadrant consisting of IRMA.
4. PDR: includes any or all neovascularization of the following: the disc, retina, iris or anterior chamber angle, as well as vitreous haemorrhage or pre-retinal haemorrhages.

ii) Screening for Diabetic Retinopathy

It is paramount to screen patients for DR because patients with early eye disease are usually asymptomatic. Screening for DR helps to become aware of early sight-threatening retinopathy, permitting remedy in a timely style and for that reason heading off expensive, superior treatment or save you development of blindness (7). Fluorescein angiography is the gold standard for detecting DR but due to its side effects it is less desirable for screening. According to the Kenyan Guideline for management of DR, screening must be conducted by skilled health personnel and should comprise retinal examination or retinal photography, as well as distant and near visual acuity testing. Furthermore, patients with ocular symptoms, visual acuity worse than 6/12, where retinal findings are unclear and where the retinal examination cannot be done should be referred to an ophthalmologist (8). In Kenya, a DR screening project was launched in 2016 and the introduction of this screening program using a fundus camera has augmented the proportion of patients with diabetes referred to an Ophthalmologist (9). The sensitivity and positive predictive values of fundus photography in KNH diabetic clinic were found to be significantly high than that proposed by the British Diabetic Association proposed that any screening programme for DR (10).

1.3. Quality of Life

The term Quality of Life (QoL) may be understood in the context of the World Health Organization wider definition of health that is, ―A state of complete physical, mental, and social well-being not merely the absence of disease‖ (11). Therefore, measurements of health status must not only include the physical dimensions of diseases but also people's state of mental and social well-being. The latter two fall in the psychosocial domain which is where QoL focuses on. WHO defined Quality of existence as an individual's notion of their role in life in the context of the way of life and values structures wherein they stay and the relationship with their goals, expectations, requirements and concerns (12) .

2.0 LITERATURE REVIEW

2.1. Diabetes Mellitus

Between 1990 and 2010, the prevalence of diabetes mellitus (DM) has tripled and the incidence doubled (13). Between 2025 and 2030, it is foreseen that the proportion of diabetics in developed countries will augment by about one third. These speculations of the number of diabetics take into consideration the fact that there will be an increase in the population growth, as well as the ageing population. It also considers the current trends in urbanization, physical inactivity, obesity and decreasing infant mortality (6,9). In low to middle-income countries, mainly subjects in their productive years are prone to developing diabetes mellitus, with over 75% of patients with diabetes aged above 65 years and only 25% being younger than 45 years (14). Following the 2015 Kenyan STEPs Survey, it was published that the nation-wide prevalence of diabetes was 2.4% with a significant proportion (52.8%) of undiagnosed diabetic patients at a higher risk of manifesting complications (15). The national prevalence was found to be close to the 2.2% reported by IDF in the same year (16) but slightly below the estimation (4%) from WHO (17). The possible explanation for the discrepancy between the WHO‘s report and the STEPs Survey was the fact that, the later was a national representation. On the other hand, the former was based on several data and multiple assumptions were introduced to adjust the population estimate. The outcome of the STEPs Survey was more robust because it was a more genuine way of collecting data.

Diabetes mellitus is a significant cause of comorbidity, mortality as well as increased health-system cost and adults with DM have about 50% risk of dying from any aetiology (18). Therefore, the management of patients with diabetes should include educational sessions on DM, dietary control, physical exercises, anti-diabetic agents and control of associated conditions (19,20). As reported in the Kenyan National Guideline for the management of Diabetes Mellitus, the global objective is to ameliorate the quality of life and productivity of diabetics (21). Patients‘ glycaemic levels are monitored using HbAlc tests or an amalgamation of fasting and random plasma glucose.

2.2. Diabetic retinopathy

i) Epidemiology

Diabetes-related complications are mainly as a result of an increment in the incidence of DM worldwide and the high life expectancy (22). Worldwide, diabetic retinopathy (DR) is the foremost aetiology of visual impairment in working-force age groups and it represents an important socio-economic burden for patients with diabetes and the healthcare systems (23). A review in 2015 by the International Diabetes Federation (IDF) accentuated the significant heterogeneity in proportion of patients with DR worldwide and by regions (24). In the United States of America, there is a broad range of any DR, both in type1 DM (ranging from 36.5% to 93.6%) as well as in type2 DM (from 28.5% to 40.3%). Globally, about one-third of patients with DM aged 50 years and above have DR while about 10% have vision-threatening DR (25,26). A population-based study conducted in 2007-2008 in Nakuru, Kenya among adults aged ≥50 years reported a prevalence of 36% (27). A follow-up study of the same cohort in 2013 found that the cumulative incidence of DM among previously non-diabetic participants aged ≥50 years was 61 per 1000 while that of DR was 15.8 per 1000 among those without DM before and 224.7 per 1000 among those with known DM before (11). As reviewed by the IDF between 2015 and 2018, of the 5 studies of African countries, the prevalence of any DR in Ethiopia was 21.1%, in South Africa it was 24.9% and in Tanzania, it was 27.9% (28–30). Vision loss from DR continues to increase while there are improvements from other causes. The Global Burden of Disease Study estimated that between 1990 and 2020 the number of people aged 50 years and older who were blind from DR increased by 15% while the age-standardized prevalence of blindness due to DR increased by 15% (31). In sub-Saharan Africa the corresponding figures were 17% and 26% respectively. During the same period the number of cases from other leading causes of blindness such as cataract, under-corrected refractive error and glaucoma globally increased by 55%-70% while the age-standardized prevalence reduced by 28%-32%. Similar changes were also observed in sub-Saharan Africa. The Wisconsin epidemiology study of diabetic retinopathy concluded that the advancement of DR was more probable with lower grades of DR, male sex, higher HbA1c and an increase in diastolic blood pressure. For those with an onset of DM for less than 5 years, 24% of them had some level of severity of DR (32). On the other hand, more than 12% of those who had had the condition for 30 years or more had Sight-Threatening Eye Disease (33).The prevalence of DR in Kenyatta National Hospital has progressively increased from 22.6% in 2007 to 50.3% in 2018 (34,35). It was also reported

that 30.4% of newly diagnosed diabetics had DR whereas 12.5% had blinding conditions at KNH(34).

ii) Management of Diabetic Retinopathy

Risk for loss of vision from diabetic retinopathy (DR) is reduced by:

a) Primary prevention of microvascular complications

This includes optimum glycaemic control with target glycosylated haemoglobin (HbA1c) of less than 7.5% for patients with diabetes (20). Blood pressure control is important in the management of DR and as reported in the UK Prospective Diabetes Study, the _tightly controlled‘ group who received treatment for high blood pressure had a 34% decrease in the rate of development of DR, a 47% lowering in the risk of sight loss and had 35% less requirement for retinal laser compared to the _less tight group‘ (35). In the ETDRS, it was published that high total serum cholesterol levels were linked to a higher risk of sight loss in DR patients (36)

b) Early detection of retinopathy

In developed countries, systematic screening can be cost-effective but it is influenced by the age at onset of diabetes and glycaemic control (8). The Uptake of Retinal Examination in Diabetes mellitus (DURE) mixed-method cluster randomized controlled trial was performed in Kenya with the aim of evaluating the effectiveness of a complex intervention to improve on the DR screening of patients. From the data it was reported that there were more facilitators than barriers to the achievement of this intervention in Diabetic Support Groups (37).

c) Effective treatment of established disease

In the Diabetic Retinopathy Study, it was reported that Pan-retinal photocoagulation decreased the likelihood of visual loss by 50% (48). The Diabetic Retinopathy Clinical Research Network (DRCRnet) and Prompt Panretinal Photocoagulation Versus Ranibizumab + Deferred Panretinal Photocoagulation for Proliferative Diabetic Retinopathy (Protocol S) studies concluded that anti-VEGF drugs were important in the treatment of PDR (20). Vitrectomy can be used to remove vitreous opacity (commonly blood) and/or fibrovascular membranes, relieve tractional detachment, achieve retinal reattachment, and realization of

endolaser. Despite all these treatment modalities, significant gaps are present in the management of patients with DR partly due to inequities in accessibility to these services as well as financial constraints (38). Some of the services are underutilized, while others being delivered are of adequate quality. This inconsistency could be associated with variation in referral practices, screening practices, and level of awareness of DR patients (52–54). Therefore, Kenyan Ministry of Health developed national guidelines for management of DR to address these notable gaps and prevent vision loss from DR (39). In this protocol, one of the recommendations was that the definitive diagnosis and the type of treatment that a patient should receive should be made by the ophthalmologist.

2.3. Quality of Life

i) Epidemiology

About 25% of adults with diabetes are significantly affected with depressive symptoms (40). This can lead to poor compliance, increased tension in the family, worse diabetes control, progression of DR and, further psychosocial stress which can result in deterioration in patients quality of life (41). Recently, researchers have noted the significant role of QoL in the management of patients with diabetes. Different studies from around the world published inconsistent results on the QoL among diabetics. A study assessing the impact of diabetic complications on health-related QoL using the SF-36 QoL questionnaire noted that DR had no effect on patients‘ QoL (42). Nevertheless, in a study aimed at assessing the effect of DR on QoL using the 26-domain Retinopathy Dependent QoL (RetDQoL) questionnaire in 2 centres in UK and Germany respectively, it was reported that vision loss due to DR had a significant impact on patients‘ QoL (43). In a Singaporean study that evaluated the effect of diabetic retinopathy on VRQoL using the Impact Vision Impairment (IVI) questionnaire, it was concluded that Sight-Threatening DR, was associated with emotional and reading difficulties. They concluded that a proper comprehension of the factors underlying the deleterious relationship between DR and VRQoL may ameliorate rehabilitation outcomes for these patients (44). Following a study conducted in India assessing health related and vision related quality of life among patents with DR using the National Eye Institute 25-Item Visual Function Questionnaire (NEI-VFQ-25) it was again concluded that QoL was worse in patients with DR than in those without DR with the greatest effect seen on general health, overall vision and mental status. They emphasized on the fact that QoL worsened as the duration of DR and as its degree of severity increased (45).

In Sub-Saharan Africa, little is known about the QoL of patients with diabetes and specifically those with DR. This emphasizes on the need for more studies to assess the QoL among patients with DM and DR, their features, the effect of complications of diabetes, health care system and social environmental characteristics which could possibly account for a lower quality of life.

ii) Quality of life Scales

This includes health-related and vision-related quality of life (QoL) tools.

a) Health-related quality of life tools

Instruments used to measure health related QoL (HRQoL) generally contain questions divided into domains and are designed to assess specific problems that limit health and well-being. The World Health Organization Quality of Life Assessment (WHOQOL), Medical Outcomes Study 36-Item Short Form (SF-36), and 12-Item Short-Form Health Survey (SF-12) are among the most widely used instruments for assessing HRQoL (46).

b) Vision-related quality of life tools

Visual acuity (VA) charts are usually used to measure visual impairment. The visual acuity (VA) charts used do not require many skills and yield an unbiased method of measuring vision. Nonetheless, VA does not only completely measure visual function, but it does not also provide a subjective estimate of visual impairment. Therefore, the need for a better measurement of visual function has long been recognized because the best corrected vision acuity may not reflect patient‘s daily-life experience and usually over or underestimate the burden of sight impairment (47).

Many study tools have been invented to subjectively estimate the impact of visual impairment on patient‘s QoL. These questionnaires involve asking the patients the difficulties they face while performing certain specific daily activities. These scales are important for populations in low-income countries to guide referral to ophthalmologists, assist in defining different levels of visual impairment, and advocate for surgical intervention to patients. Most studies investigating diabetic retinopathy and vision-related QoL are from developed countries and the questionnaire designed accordingly. They are not usually appropriate for all populations, so several authors attempt to adjust Vision Function Assessment Questionnaires (VFQ) and Vision-related Quality of Life (VRQoL) scales to the situation in developing

countries. The first VFQ used in Sub-Saharan Africa was created by van Dijk and colleagues and applied on a Malawian population (48). The questionnaire contained 13 questions divided into 3 groups: Problem in near vision, problems in distance vision and problems in contrast sensitivity. Although the questionnaire was found to be easy to use and applicable to the study population, it did not include QoL measures. The World Health Organisation has emphasized on the need to develop more comprehensive forms of visual impairment measurements. A visual function questionnaire, invented particularly for the Madurai Intraocular Lens Study was used in some Asian countries (49,50). Another more general, visual function assessment questionnaire developed in India reproduced the robust psychometric methodology used in the National Eye Institute-Visual Function Questionnaire-25.

VRQoL scales reflect a more credible evaluation of the individual effect of visual disabilities rather than VA alone. Following the consultation between WHO and the National Eye Institute in 2003, it was concluded that visual acuity only explains between 20% and 30% of the variations in VRQoL meanwhile VRQoL tools describe the significance of assessing vision in both eyes as well as studies the impact of poor vision on patient‘s QoL (51). Some of these VRQoL tools include:

- Indian Vision Function Questionnaire

India accounts for almost 25% of the global burden of complete vision loss (52). The Indian Vision Function Questionnaire (IND-VFQ-33) was invented as an interview-administered questionnaire and used to measure the impact of sight disability. IND-VFQ-33 has 3 main areas: general functioning, psychosocial impact, and visual symptoms. The questionnaire can be completed in 20-25 minutes, and it can be used in both illiterate and literate individuals. Subsequent studies done in India showed a high grade of test-retest reliability and validity (53).

- National Eye Institute Visual Function Questionnaire-25

The National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25) is described as a genuine and valid study tool that can be administered in 5 minutes. The VFQ-25 was fashioned to be used as a suitable questionnaire for measuring QoL across a wide scale of visual impairment and the effectiveness of treatment. It assesses patient‘s general health, general vision, near, distant vision, driving, peripheral vision, colour vision, ocular pain, vision specifically linked to role difficulties, social functioning, dependency, and mental

health (54). This questionnaire was used in India to describe the QoL of patients with DR. The authors concluded that QoL was lower in patients with DR when compared to non-DR patients. Maximum effect was noted on general health, general vision, and mental health. As the duration of DR and the level of severity increased the quality of life worsened (45). In another study used to determine the effect of microbial keratitis on patients QoL in Uganda using the same questionnaire, microbial keratitis was reported to severely reduce QoL in the early stage. With advanced management of the corneal ulcer, QoL is expected to eventually improve. However, this improvement in the QoL of someone affected by microbial keratitis (even with no visual impairment) was lower than those without microbial keratitis (55).

- Retinopathy-Dependent Quality of Life Questionnaire

Retinopathy-Dependent Quality of Life Questionnaire (RetDQoL) questionnaire was introduced to determine the QoL both quantitatively and qualitatively among patients with DR. The RetDQoL starts with 2 overview-items and 26 domain-specific items. Overview items ask patients to complete a statement about their overall QoL and it also inquiries the gross impact of diabetic retinopathy on their QoL. Domain-specific items analyse the impact and importance of DR on individual QoL. At the end of the interview, an open-ended question that investigates if DR affects QoL in a way not already assessed by the tool(56). A multicentre randomized control trial study aimed at describing the health-related quality of life and VRQoL among patients with diabetic macular edema (DME) who received two different regimens of Ozurdex was conducted in UK using the RetDQoL questionnaire and NEI-VFQ-25. It was reported that there was difference in the RetDQoL score and NEI-VFQ-25 score (57). Unfortunately, this questionnaire needs a user licence and has never been used in Kenya before. However, in a study performed in Iran it was concluded that the RetDQoL mean score among subjects with DR was low (58).

- World Health Organization/Prevention of Blindness and Deafness Visual Function-20 (WHO/PBD VF-20) Questionnaire

This is a refinement of the original IND-VFQ-33 and NEI-VFQ-25 questionnaires. It‘s a 20-item visual functioning study tool which addresses the following aspects of visual function: general vision, distance vision, near vision, colour vision, role limitations, glare, light/dark adaptation, ocular pain/discomfort, social functioning, mental well-being, and dependency (51). The questions are therefore grouped into 11 dimensions and 4 subscales. These 4

subscales include overall self-rating eye-sight (general vision), general functioning, psychosocial and visual symptoms used to interpret patient‘s vision-related QoL.

The WHO/PBD VF-20 questionnaire also known as the VF-20 questionnaire was invented as a suitable questionnaire for measuring QoL across a wide range of visual impairment. A case-control study conducted in Kenya used this questionnaire to determine the impact of cataract surgeries on patients‘ QoL (59). The test-retest validity of the VF-20 questionnaire in this study was good, the results were reproducible and was therefore validated for use in Kenya. They eliminated one question approximately impairment of shiny mild due to the fact they determined it flawed for his or her observe population. This study tool was reported to be superior to most VRQoL questionnaires because it considers the mental and social impact as well as the vision related activities (75). This prompted us to use the WHO/PBD VF-20 questionnaire for our study.

iii) Conceptual & Theoretical Framework

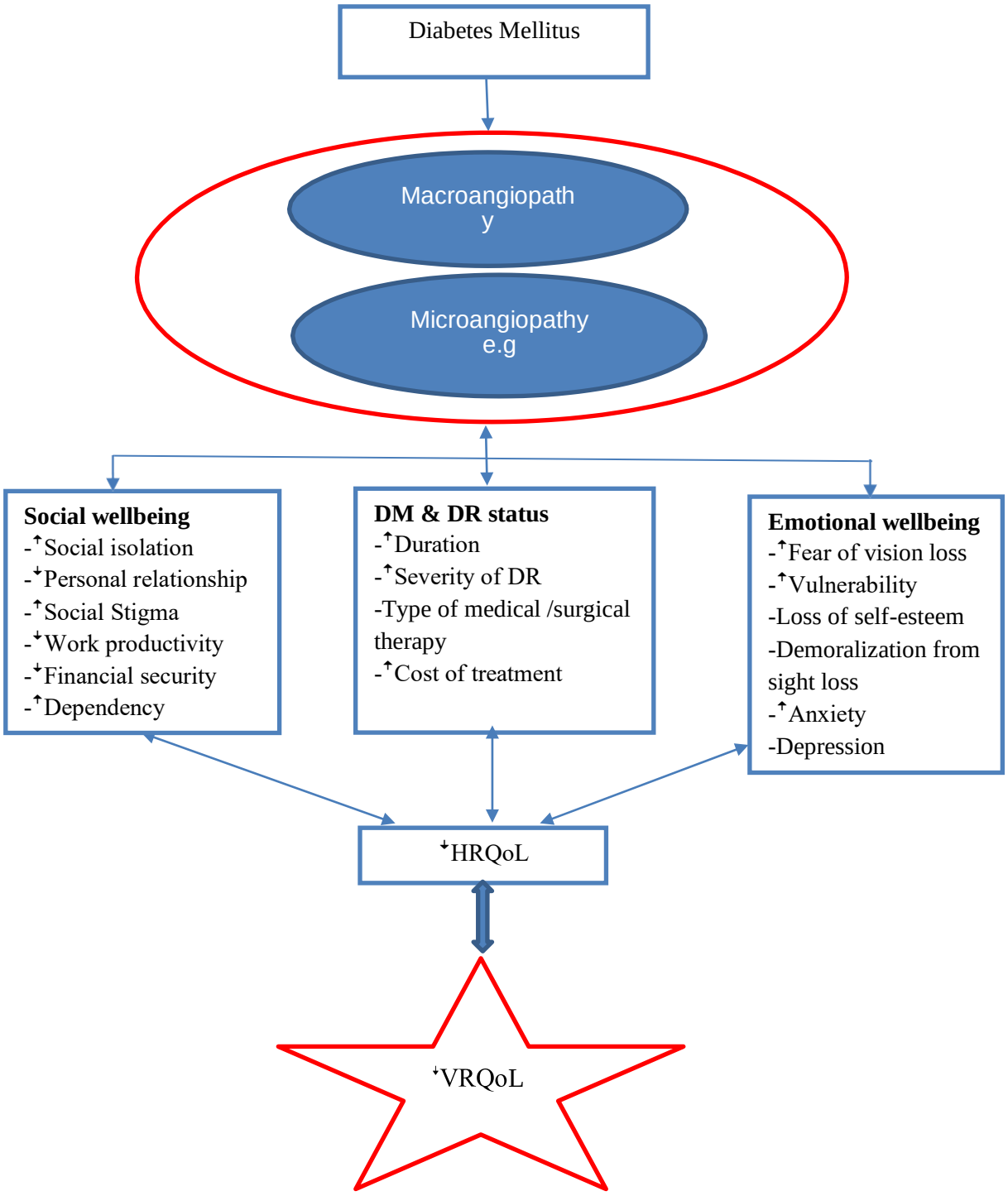

Figure 1: Conceptual Framework illustrating association between Diabetes mellitus, Diabetic Retinopathy and VRQoL

3.0 JUSTIFICATION

The impact of the increasing severity of diabetic retinopathy on visual function, development of new treatments modalities for DM and DR and the associated cost can negatively impact patient‘s quality of life. This will also cause a heavy financial burden on the society. Understanding the VRQoL maybe important in managing patients with DM and DR patients from a holistic point of view as well as guide policy makers and other stakeholders including health care providers/clinicians, patient support groups leaders, in providing comprehensive diabetes care.

Globally, several studies have reported a qualitative and quantitative reduction in the vision-related quality of life in persons with DM and DR, but no such study has been done in the Kenyan population to the best of our knowledge.

4.0 OBJECTIVES

i) General Objectives

Our global aim was to investigate the vision-related quality of life (VRQoL) among patients with diabetes mellitus attending the Medical and Retina clinics in Kenyatta National Hospital.

Our main research question in this context was: Among patients with diabetes attending the Kenyatta National Hospital, is the vision-related QoL different between those with and without diabetic retinopathy?

Null hypothesis: no difference exists in the perception of the visual function between diabetic patients with and without DR.

Alternative hypothesis: perception of visual function among diabetics without DR is different from those with DR.

ii) Specific Objectives

1) To determine the VRQoL in diabetic patients with and those without diabetic retinopathy using WHO/PBD VF20 questionnaire.
2) To determine the trend in VRQoL among patients with different severity of Early Treatment Diabetic Retinopathy Study (ETDRS) grades: mild NPDR, moderate NPDR, severe NPDR and PDR.

5.0 MATERIALS AND METHODS

5.1. Study design

This was a hospital-based analytic cross-sectional study. The study was done in a hospital setting because we needed to evaluate participants for presence of diabetic retinopathy (DR) using the fundus camera located at the Diabetes and Endocrinology Centre of Excellence (Medical clinic) and grading DR using equipment available at the Retina clinic in Kenyatta National Hospital. Also, the Quality of Life (QoL) of patients who had been living with diabetes mellitus (DM) for at least 5 years and on follow up in KNH could be influenced by the diabetes care they received. To reduce the confounding that could be created by receiving care of varying standards from varying health facilities it was best to study participants who attended one health facility. A cross sectional study design was used for meeting our objectives because all our participants had their Vision-related QoL assessed once. The

advantage of this study design is that it is less costly and time saving. It was analytic because we had to determine the VRQoL mean scores among those with DR without DR.

5.2. Study setting

This study was performed at the Diabetes and Endocrinology Centre of Excellence (Medical clinic) as well as in the Eye Clinic 35 (Retina clinic) in Kenyatta National Hospital (KNH). which is the main national referral centre in Nairobi, Kenya.

The Diabetes and Endocrinology Centre of Excellence (Medical clinic) is located in the old outpatient clinic as seen in Figure 2 below. It runs five days a week. Wednesdays are mainly for educative sessions for diabetic patients and on average, 30 patients are seen daily except on Fridays when the average number of patients seen sums to 60. The clinic has a catchment population of over 3000. In the Medical clinic, patients with diabetes are screened for diabetic retinopathy by a well-trained technician who takes fundus photographs of these patients and records them according to the English National Screening program for DR grading in their database. The patients with DR are usually referred to the eye clinic for further management by an Ophthalmologist.

The Eye Clinic 35 runs five days a week and patients with diabetes referred from the Medical clinic is usually reviewed in the Retina clinic on Wednesdays and Fridays. The Eye Clinic 35 has a catchment population of over 300. In the Retina clinic, dilated slit-lamp examination is done for all patients and managed accordingly following review by a Vitreo-retina (VR) specialist.

DM Clinic
(Mon, Tue & Thu)

DR Clinic (Wed
& Fri)

Figure 2: Pictorial illustrations of the Diabetes Medical (DM) and Diabetes Retina (DR) Clinics in Kenyatta National Hospital.

5.3. Study Population

Our target population were patients with DM for at least 5-years at the time of recruitment. Since it takes at least 5 years for a patient with diabetes to develop diabetic retinopathy, we enrolled those who had the disease for at least this period to increase our chances of detecting those with DR. For the two groups to be comparable, we chose those who had DM for at least 5 years as well.

5.4. Study Period

It was conducted from 1st December to 31st December 2020 (1 month). Despite the potential effect of the COVID pandemic on QoL, since we compared those with DR to those without, we assumed the COVID effect equally affected both groups and did not introduce significant bias.

5.5. Sample Size Estimation

To determine the minimum sample size for this study, our calculations were derived from the overall VRQoL mean scores of a previous study conducted in Nakuru, Kenya using WHO/PBD VF20 questionnaire (59). This is the same study that validated the same questionnaire in the Kenyan population. This was a case-control study in which the VRQoL of people with vision impairment from cataract (cases) was compared to that of people without vision impairment (controls). Cases had a mean score of 3.9 (95%CI 3.9-4.1) on the overall self-rating eyesight while controls had a mean score of 2.1 (95%CI 2.0-2.3) on the same domain. The standard deviation in both groups was about 1.0.

In our study we hypothesized that patients without DR had somewhat worse VRQoL scores than the controls in the previous study (2.8 instead of 2.1). This is because they live with a chronic disease and the effect of occasional poor blood sugar control causes a fluctuating vision. We also assumed that patients with DR had a similar VRQoL mean scores to cases (3.9) in the previously mentioned study because patients with diabetes often have cataract. We expected more variability (higher standard deviation) in our study than the previous study because of differing degrees of diabetic retinopathy severity (1.75 instead of 1.0).

Therefore, using the command below in Stata version 15, we obtained the following:

power two means 2.8 3.9, sd (1.75)

That is sample size needed to compare two-sample means (Student t-Test), mean score VRQoL for patients without DR, mean score VRQoL for patients with DR and the standard deviation from previous study (81).

Study parameters:
mean score for DR=3.9
mean score for no DR= 2.8
standard deviation, sd=1.75
power= 0.80
Estimated sample size, N= 82
Adjusted 10% for those who may not give consent to participate means we need **90** participants (45 with DR and 45 without DR).
Based on preliminary findings from previous studies in KNH and the case load in the Medical and Retina clinics, this sample size is achievable.

5.6. Sampling method

All diabetics seen during data collection in the KNH Medical and Retina clinics who consented to participate were enrolled using the purposive consecutive sampling method.

i) Inclusion criteria
- Participants aged 18 years and above
- Patients with either type1 or type 2 diabetes mellitus

ii) Exclusion criteria
- Diabetic with mental illness
- Participants with gestational diabetes
- Patients with other ocular morbidities such as glaucoma, retinal vascular occlusions as well as optic neuritis.

5.7 Data Collection Procedure

Ethical approval was obtained from the Kenyatta National Hospital / University of Nairobi Ethics and Research Committee (KNH/UoN ERC). Administrative approval was obtained from the departments of Internal Medicine and Ophthalmology. Informed consent was obtained from all eligible patients in either English or Kiswahili using the informed consent

document in appendix 2. We went to the Medical clinic on Mondays, Tuesdays, and Thursdays. Data was collected in the Retina clinic on Wednesdays and Fridays. Only patients without diabetic retinopathy were enrolled in the Medical clinic while those with diabetic retinopathy. In these respective clinics, the following examinations were undertaken by the principal investigator and research assistant and the information collected recorded in the questionnaire:

i) Anthropometric & Biochemical data collection

Participants blood pressure (BP) was measured upon arrival and their medical data on diabetes mellitus recorded from their files (duration of diabetes mellitus and latest glycated haemoglobin). The history of the course of microvascular complications such as presence of hypertension and dyslipidemias were also obtained from the patient.

ii) Visual acuity

Best presenting visual acuity (BPVA) were determined using the E-charts for distant and near vision. The distant E-charts was placed at 6 metres and the Near E-chart at 40cm in a well illuminated room. Visual acuity measurements were recorded for both eyes and the vision in the better eye was used to categorize patients using the International Classification of Diseases-11 for vision impairment published by WHO in 2018 (60).

iii) Ophthalmic examination

In the Retina clinic, a slit-lamp examination was performed for all eligible participants to assess for the presence of cataract. Pharmacologic dilation of the participant‘s pupil was done using one drop of tropicamide 1%. Slit-lamp biomicroscopy with a 90 diopter lens, was used to diagnose diabetic retinopathy and diabetic macular oedema which was then confirmed by the Vitreo-retina specialist. The presence of dry eye syndrome was also assessed for all participants in the Medical and Retina clinics using Schirmer‘s test strips and artificial tears only (Schirmer‘s test 1).

iv) ETDRS grading

In the Retina clinic, following confirmation of the presence of diabetic retinopathy by the VR specialist, grading for each eye was done using the Early Treatment Diabetic Retinopathy

Study (ETDRS) grading system and recorded in the patient‘s file. We assumed that patients VRQoL will be driven by the worse eye with respect to diabetic retinopathy status.

v) Fundus photography

In the Medical clinic, all eligible participants had two fundus photographs taken per eye by a well-trained technician using a non-mydriatic retinal camera. These images were digitally stored. The assessment of cataract in the Medical clinic was done using the same retina camera.

vi) Interviews

The WHO/PBD-VF-20 questionnaire was interviewer-administered in a private room over a period of 15minutes (appendix 3). For those who did not understand English, a translator was assigned to them. The participants used a pictorial card of scale 1 to 5 to answer the VF20 questionnaire (appendix 4). Using this rating scale, the scoring spectrum for Question1 ranges from 1=very happy to 5=very unhappy with a teardrop. Implying the higher the mean score, the poorer was the patient‘s VRQoL. Information was collected on demographic data (age, sex, marital status), education and employment status. The research assistant was an Ophthalmology resident who was trained on how to conduct the interview using the WHO/PBD-VF 20 guidelines to promote standardization in the interviewing practice and minimize interviewer-bias. We made sure the respondent did not feel intimidated when answering questions and that the interviewer did not deviate from the intended meaning of the question. We ended each interview by counselling the patients on diabetes and diabetic retinopathy.

Due to the outbreak of Covid-19 and the lockdown in Nairobi, the questionnaire was pretested during my elective term rotation in a different health facility. The tool was pilot tested on 15 diabetic patients in the Retina clinic in Tenwek Eye Hospital, and no modifications was required. Therefore, content validity and test-retest reliability of the questionnaire was not required.

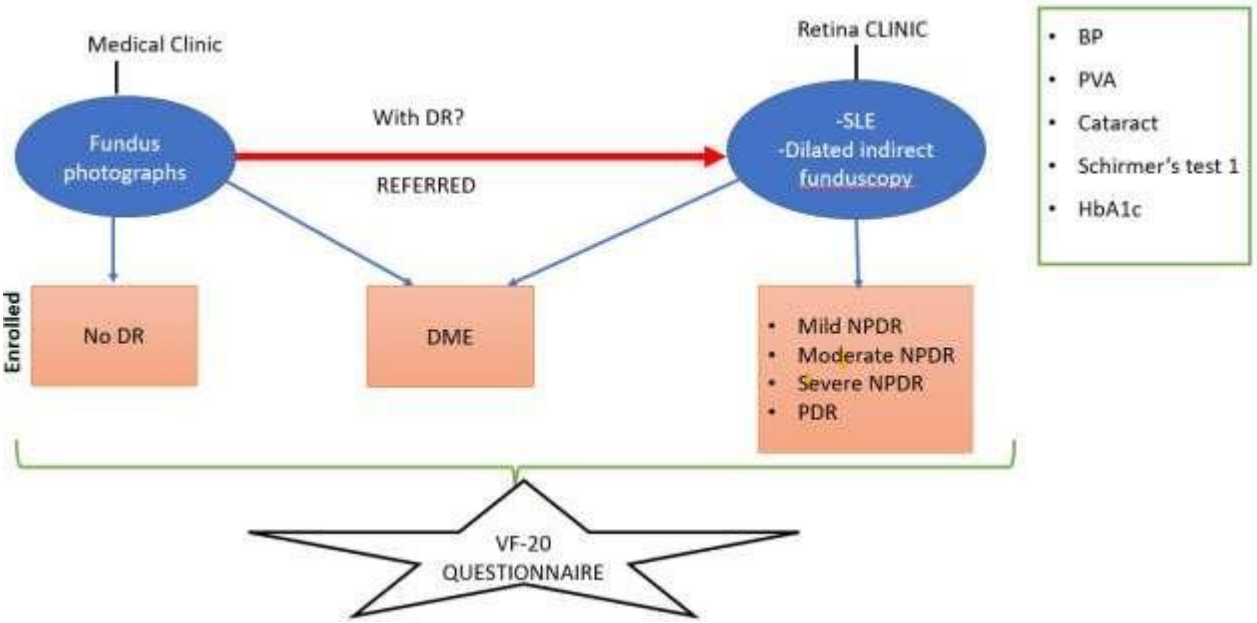

Figure 3: Patient flow at the Medical and Retina Clinics in Kenyatta National Hospital

- Study Materials

1) Patients‘ files (Blood pressure, HbA1c, ETDRS grade)
2) Distant and Near E-charts (for presenting visual acuity with patient‘s correction if available)
3) WHO/PBD/VF20 Questionnaire (VRQoL assessment)
4) Schirmer Tear test strips (to assess dry eye syndrome)

5.8 Ethical Consideration

i) Confidentiality

The anonymity of each participant was ensured by using numbers on each questionnaire. No record of the patient‘s identity or file number was done. We did not make photocopies of their medical records. Participants personal information were made available only to the statistician and investigator for analysis.

ii) Approval by Ethics Committee

Before collecting our data, a written ethical approval was obtained from the KNH/UON ERC as well as the Kenyatta National Hospital administration. We obtained a written informed

consent for all the participants. Patient safety was ensured by adhering to the COVID-19 measures and ensuring that patients with advance DR are urgently referred to VR specialist for treatment on the same week of data collection.

5.9 Data Management and Analysis

After collecting the data, the information extracted was entered in a Microsoft Access Database. All answered questionnaires were cautiously kept in a lockable cupboard and after completing the data entry, hard copy forms were compared with the data entered to identify any mistake and rectify them accordingly. Data was backed up in portable hard discs stored in a separated place off-site from the hospital. Statistical analyses were performed using SPSS software.

Descriptive statistics was displayed using tables and figures. Most tables had 3 columns showing all patients with diabetes, those with DR and those without DR. Figures such as bar charts and pie charts were used. The descriptive data included the demographic, medical data, and VRQoL mean scores. Where data approximated a normal distribution, means were reported with standard deviations. Frequencies were reported with percentages and confidence intervals were appropriate.

For Objective 1, the results of the student t-test, and one-way analyses of variance comparing those with DR to those without DR was displayed in the same table reporting both the 95% confidence intervals and p-values. P-value<0.05 was considered statistically significant.

For objective 2, we stratified the participants by degree of DR severity (using the ETDRS system) with no DR as the baseline group and test if there was a linear trend of worsening VRQoL scores from baseline to the more advanced degrees of DR. In this study, we expected that the overall VRQoL score of DR patients would be mainly determined by the eye with more advanced DR (and therefore worse ETDRS grade). Therefore, for analysis of objective 2, we classified each patient according to the grade of the eye with the worse ETDRS grade then assessed if those with worse ETDRS grades had a higher mean QoL score than those with milder DR. Since we had data for both eyes, we also did a sensitivity analysis by repeating the same analysis this time classifying each patient using the better ETDRS grade and determined if there was a difference.

We conducted a multivariate binomial logistic regression using general vision for all participants as our dependent variable. The criteria used for explaining for good overall eyesight (mean score <3) and low overall eyesight (mean score ≥3) was based on the cut-off points for question 1 from the VFQ-20 questionnaire. We adjusted for possible confounders:

age, sex, presence of diabetic macula oedema, cataract, and dry eye syndrome which could also affect the VRQoL among patients with and without DR. Using the forward selection, a threshold of p=0.10 from univariate analysis was considered.

- Quality Control of Data

To ensure reproducibility of this study a few techniques were carried out, this included: Clearing documentation on any changes within the data collection protocol, handling of collected data, and data entered and stored in spreadsheets.

- Precautions against COVID-19 during data collection

Elderly patients with debilitating illnesses such as diabetes mellitus appear to have a higher likelihood of becoming severely ill with the COVID-19 virus because their immune system has been compromised (61). Therefore, during the data collection, COVID-19 policies for screening of DR patients was strictly followed. We ensured Personal Protective Equipment (PPE) were made available prior to collection of data. Hand sanitizers were used before and after interviewing each patient. Social distancing of about 1.5metres was instituted and patients face-masked prior to data collection.

6.0 RESULTS

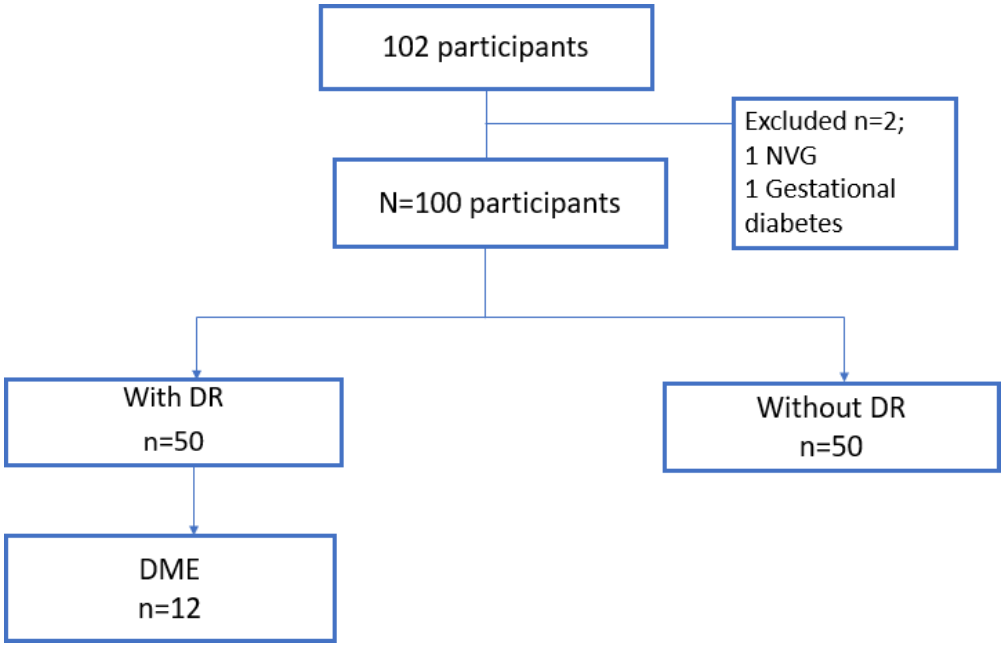

Figure 4: Results flow chart

The study participation rate was high (98%). We excluded the patient neovascular glaucoma and gestational diabetes respectively because these ocular comorbidities are potential confounders of vision-related quality of life (VRQoL).

i) Socio-demographic Characteristics

a) Age

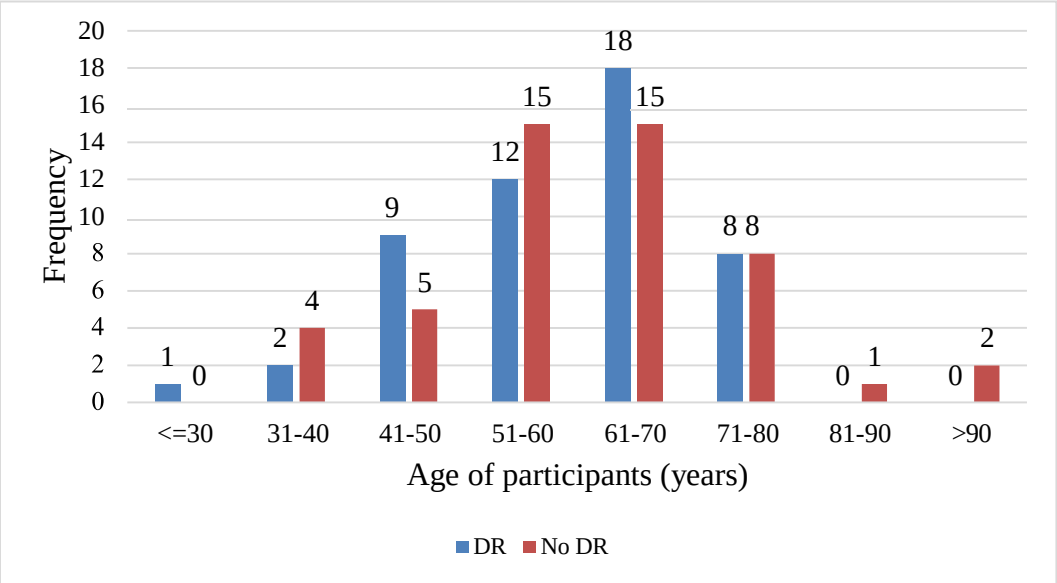

Figure 5: Distribution of patients attending the Medical and Retina clinics by age (N=100)

Patients with diabetic retinopathy were aged between 19 and 80 years (mean 58.7, SD 12.3 years) and this was different from those without diabetic retinopathy who were aged between 33 to 93 years (mean 61.1, SD 14.4 years). This difference was not statistically significant.

b) Sex

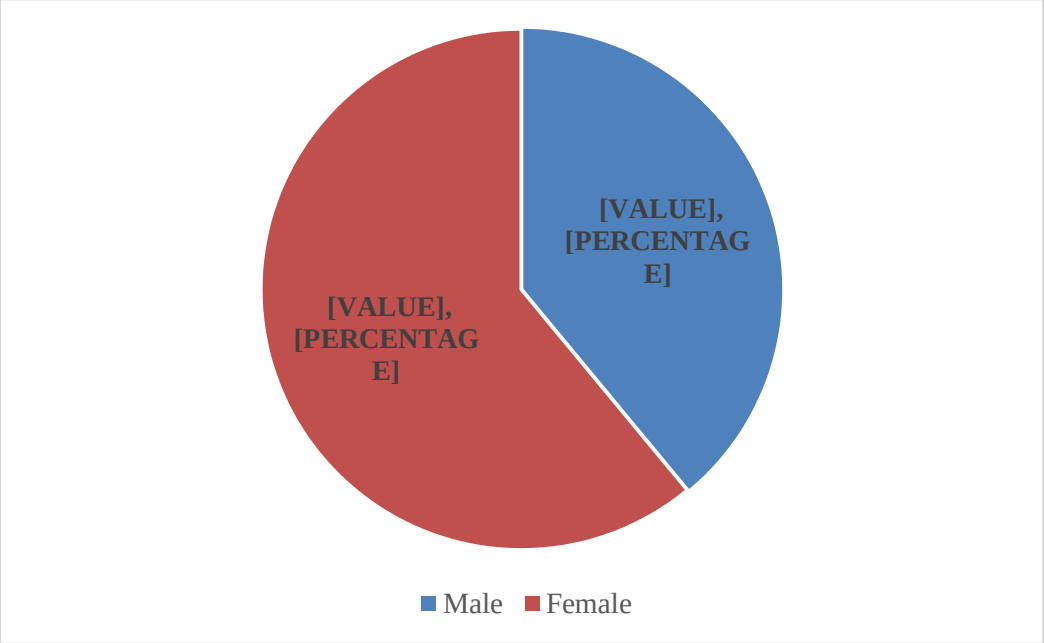

Figure 6: Distribution of patients attending the Medical and Retina clinics by sex (N=100)

Table 1: Socio-demographic characteristics of the participants attending the Medical and Retina Clinics in KNH (N=100)

Characteristics	N (%)	People with DR (N=50)	People without DR (N=50)	Odds ratio (95% CI)	p-value
		n (%)	n (%)		
Age (years)					
≤30	1 (1.0)	1 (2.0)	0 (0.0)	-	0.605
31-40	6 (6.0)	2 (4.0)	4 (8.0)	0.7 (0.1 – 4.7)	
41-50	14 (14.0)	9 (18.0)	5 (10.0)	2.5 (0.6 – 10.3)	
51-60	27 (27.0)	12 (24.0)	15 (30.0)	1.1 (0.3 – 3.6)	
61-70	33 (33.0)	18 (36.0)	15 (30.0)	1.7 (0.5 – 5.2)	
>70	19 (19.0)	8 (16.0)	11 (22.0)	(Reference)	
Sex					
Male	39 (39.0)	17 (34.0)	22 (44.0)	0.7 (0.3 – 1.5)	0.306
Female	61 (61.0)	33 (66.0)	28 (56.0)	(Reference)	
Marital status					
Single	10 (10.0)	9 (18.0)	1 (2.0)	14.1 (1.5 – 137.3)	0.023
Married	72 (72.0)	34 (68.0)	38 (76.0)	1.4 (0.5 – 1.0)	
Divorced	18 (18.0)	7 (14.0)	11 (22.0)	(Reference)	
Education					
No formal schoooling	9 (9.0)	4 (8.0)	5 (10.0)	0.6 (0.1 – 4.3)	0.927
Primary school	21 (21.0)	12 (24.0)	9 (18.0)	1.2 (0.4 – 3.9)	
Secondary	41 (41.0)	19 (38.0)	22 (44.0)	0.8 (0.3 – 2.1)	
Tertiary school	29 (29.0)	15 (30.0)	14 (28.0)	(Reference)	
Employment					
Salaried	24 (24.0)	9 (18.0)	15 (30.0)	0.6 (0.03 – 10.8)	0.122
Self-employed	46 (46.0)	21 (42.0)	25 (50.0)	0.8 (0.05 – 14.2)	
Retired	14 (14.0)	11 (22.0)	3 (6.0)	3.7 (0.2 – 77.6)	
Unemployed	16 (16.0)	9 (18.0)	24 (48.0)	(Reference)	

In our study, most of the patients had type 2 diabetes mellitus (93%). Among those with DR in our study, the male to female ratio was 1:1.9 compared to 1:1.3 among those without DR. There was a statistically significant difference only in marital status between those with DR and those without DR.

ii) Ocular Characteristics/ocular comorbidities

Table 2: Ocular characteristics among patients attending Medical and Retina Clinics, KNH (N=100)

Characteristics	All n(%)	People with DR (N=50)	People without DR (N=50)	p-value
		n (%)	n (%)	
Best Presenting visual acuity, ICD-11, 2018				
Normal (better than or equal to 6/12)	63 (63.0)	31 (62.0)	32 (84.0)	0.031
Mild visual impairment (worse than 6/12 to 6/18)	13 (13.0)	10 (20.0)	3 (6.0)	
Moderate visual impairment (worse than 6/18 to 6/60)	10 (10.0)	5 (10.0)	5 (10.0)	
Severe visual impairment (worse than 6/60 to 3/60)	1 (1.0)	1 (2.0)	0 (0.0)	
Blindness visual impairment (worse than 3/60)	3 (3.0)	3 (6.0)	0 (0.0)	
Near vision, ICD-11, 2018				
Normal	17 (17)	8 (16.0)	9 (18.0)	1.000
Vision impairment (worse than N6)	83 (83)	42 (84.0)	41 (82.0)	
Presence of cataract (n=43)				
Unilateral	6 (14.0)	03 (50.0)	03 (50.0)	0.008
Bilatearal	37 (86.0)	25 (67.6)	12(32.4)	0.024
Presence of DES				
Yes	81 (81.0)	47 (94.0)	34 (68.0)	0.002
No	19 (19.0)	3 (6.0)	16 (32.0)	

Among the ocular characteristics, there was statistically significantly difference between patients with DR and those without DR only with respect to distant visual acuity at presentation, presence of cataract and dry eye syndrome. The patients without DR had better visual acuity than those with DR when using mean logMAR visual acuity score for the better eye (0.25 vs 0.56) and this difference was statistically significant.

iii) Medical comorbidities and biochemical indices

Table 3: Comorbidities and Biochemical indices among patients attending Medical and Retina Clinics, KNH (N=100)

Variables	People with DR Mean ± SD	People without DR Mean ± SD	p-value
Duration of Diabetes (in years)	13.6 ± 6.9	13.7 ± 6.2	0.928
Latest HbA1c (g/dl)	9.1 ± 3.5	7.5 ± 3.0	0.072
Duration of hypertension (in years)	12.4 ± 7.4	14.0 ± 8.4	0.378
Latest Systolic BP (mmHg)	150 ± 19	142± 22	0.084
Latest Diastolic BP (mmHg)	84 ± 14	81 ± 13	0.288

Among all biochemical indices, HbA1c was available for only 60% of participants. This is because HbA1c levels were not well documented for all patients. Commonest medical comorbidity was hypertension (79%).

iv) State of Diabetic Retinopathy

Table 4: Severity of Diabetic retinopathy and Diabetic macular oedema among patients with DR attending the Retina Clinic, KNH (N=50)

Variables	Patient's Better Eye n (%)	Patient's Worse Eye n (%)	DME, n=12 n (%)
ETDRS grade			
No apparent DR	2 (4.0)	-	-
Mild NPDR	25 (50.0)	22 (44.0)	5 (41.7)
Moderate NPDR	12 (24.0)	14 (28.0)	4 (33.3)
Severe NPDR	2 (4.0)	2 (4.0)	1 (8.3)
PDR	9 (18.0)	12 (24.0)	2 (16.7)
Ophthalmic treatment			
Yes	22 (44.0)	22 (44.0)	-
No	28 (56.0)	28 (56.0)	
Type of treatment given			
Anti-VEGF	8 (36.4)	8 (36.4)	-
Laser photocoagulation	8 (36.4)	8 (36.4)	
Laser photocoagulation + Vitrectomy	4 (18.1)	4 (18.1)	
Anti-VEGF + laser photocoagulation	2 (9.1)	3 (9.1)	

Most of the patients had mild NPDR; findings were similar when the ETDRS was used to classify based on the better eye (50%) or the worse eye (44%). Only 2 patients had both PDR and DME and were treated using anti-VEGFs + laser photocoagulation (9.1%). We did not encounter any patient with tractional retinal detachment (advanced PDR).

v) General description of VRQoL scores among participants

Table 5: Detailed scores for the 20 items in the VF-20 questionnaire among patients attending Medical and Retina Clinics, KNH (N=100)

20 Items of VF20 questionnaire	All (N=100) Mean (SD)	People with DR (n=50) Mean (SD)	People without DR (n=50) Mean (SD)	p-value
Overall, how would you rate your eyesight using both eyes – with glasses or contact lenses if you wear them?	2.39 (0.65)	2.62 (0.75)	2.16 (0.42)	<0.001
How much pain or discomfort do you have in your eyes (e.g. burning, itching, aching)?	1.76 (0.53)	1.96 (0.49)	1.56 (0.50)	<0.001
Because of your eyesight, how much difficulty do you have in going down steps or stairs?	1.26 (0.71)	1.46 (0.93)	1.06 (0.24)	0.005
How much difficulty do you have in noticing obstacles while you are walking alone (e.g. animals or vehicles)?	1.23 (0.62)	1.36 (0.80)	1.10 (0.30)	0.036
How much difficulty do you have in seeing because of glare from bright lights?	1.77 (0.72)	1.94 (0.79)	1.60 (0.60)	0.018
Because of your eyesight, how much difficulty do you have in searching for something on a crowed shelf?	1.39 (0.70)	1.60 (0.83)	1.18 (0.44)	0.002
How much difficulty do you have in seeing differences in colours?	1.07 (0.43)	1.14 (0.61)	1.00 (0.00)	0.109
Because of your eyesight, how much difficulty do you have in recognizing the face of a person standing near you?	1.28 (0.59)	1.38 (0.70)	1.18 (0.44)	0.089
How much difficulty do you have in seeing the level in a container when pouring?	1.11 (0.45)	1.16 (0.55)	1.06 (0.31)	0.266
Because of your eyesight, how much difficulty do you have in going to activities outside of the house (e.g. sporting events, shopping, religious events)?	1.25 (0.64)	1.46 (0.84)	1.04 (0.20)	0.001
Because of your eyesight, how much difficulty do you have in recognizing people you know from a distance of 20	1.92 (0.72)	2.10 (0.76)	1.74 (0.63)	0.012

metres?				
How much difficulty do you have in seeing close objects (e.g. making out differences in coins or notes, reading newsprint)?	1.68 (0.72)	1.82 (0.83)	1.54 (0.58)	0.052
How much difficulty do you have in seeing irregularities in the path when walking (e.g. potholes)?	1.23 (0.62)	1.36 (0.78)	1.10 (0.36)	0.036
How much difficulty do you have in seeing when coming inside after being in bright sunlight?	1.93 (0.76)	2.22 (0.76)	1.64 (0.63)	<0.001
How much difficulty do you have in doing activities that require you to see well close up (e.g. sewing, using hand tools)?	1.58 (0.76)	1.70 (0.86)	1.46 (0.61)	0.112
Because of your eyesight, how much difficulty do you have in carrying out your usual work?	1.34 (0.70)	1.46 (0.84)	1.22 (0.51)	0.087
Because of your eyesight, how often have you been hesitant to participate in social functions?	1.26 (0.61)	1.46 (0.79)	1.06 (0.24)	0.001
Because of your eyesight, how often have you found that you are ashamed or embarrassed?	1.07 (0.38)	1.14 (0.54)	1.00 (0.00)	0.070
Because of your eyesight, how often have you felt that you are a burden on others?	1.16 (0.53)	1.30 (0.71)	1.02 (0.14)	0.008
Because of your eyesight, how often do you worry that you may lose your remaining eyesight?	2.49 (1.10)	2.80 (1.09)	2.18 (0.98)	0.004

The composite VRQoL mean score (SD) among DR patients was higher (mean 33.4, SD 11.5) than that among patients without DR (mean 26.9, SD 4.7), implying they had an overall worse VRQoL. Patients with DR had a higher overall eyesight rating (mean 2.62, SD 0.75) than patients without DR (mean 2.16 SD 0.42). Thus, they perceived their general vision as being poorer than those without DR. Patients with DR were more worried about losing their vision when compared to those without DR (mean 2.80, SD 1.09 vs mean 2.18, SD 0.98).

vi) Comparison of VRQoL scores among patients with and without Diabetic retinopathy

Table 6: Description of VRQoL scores using domains of VF-20 questionnaire among patients attending Medical and Retina Clinics, KNH (N=100)

Domains of VF20 questionnaire	People with DR (N=50)	People without DR (N=50)	p-value
	Mean (95% CI)	Mean (95% CI)	
Overall self-rating	2.6 (2.4-2.8)	2.2 (2.0-2.3)	<0.001
Visual symptoms			
Ocular pain/discomfort	1.9 (1.7-2.2)	1.6 (1.4-1.8)	<0.001
Light/dark adaptation	2.0 (1.8-2.1)	1.6 (1.4-1.7)	<0.001
Glare	2.2 (1.0-2.4)	1.6 (1.5-1.8)	0.018
Psychosocial function			
Dependency	1.3 (1.1-1.5)	1.0 (0.9-1.1)	0.008
Mental well-being	1.5 (1.2-1.7)	1.1 (1.0-1.2)	0.002
Social functioning limitations	3.9 (3.5-4.3)	3.2 (2.9-3.5)	0.001
General functioning			
Role limitation	1.2 (1.0-1.3)	1.1 (0.9-1.2)	0.087
Colour vision difficulty	1.5 (1.2-1.7)	1.2 (1.1-1.4)	0.109
Near vision difficulty	7.7 (6.8-8.5)	6.4 (5.9-6.9)	0.014
Distance vision difficulty	7.7 (6.7-8.7)	6.0 (5.6-6.4)	0.002

Patients with DR had a higher VRQoL mean score than those without DR in all domains; overall self-rating (2.6 vs 2.2, p<0.001), visual symptoms (6.1 vs 4.8, p<0.001), psychosocial (6.7 vs 5.3, p<0.001), and general functioning (18.0 vs 14.7, p=0.005). Implying patients with DR had a poorer VRQoL.

vii) Trend in VRQoL scores among patients with diabetic retinopathy

Table 7: VRQoL mean scores for all domains by ETDRS grade using the worse eye among patients attending the Retina Clinics, KNH (N=50)

VF20 domains	Mild NPDR n=26 Mean (95 %CI)	Moderate NPDR n=11 Mean (95% CI)	Severe NPDR n=2 Mean (95% CI)	PDR n=11 Mean (95% CI)	p-value
General Vision	2.2 (2.1-2.5)	2.5 (2.2-3.1)	3.5 (1.2-4.8)	3.3 (2.8-3.9)	<0.001
Visual Symptoms	5.6 (5.1-6.0)	5.6 (5.2-6.8)	7.5 (2.2-12.9)	7.4 (6.4-8.7)	0.002
Psychosocial Symptoms	5.7 (5.3-6.4)	6.5 (5.4-7.6)	7.0 (3.0-8.7)	8.8 (6.3-11.7)	0.004
General Functioning	15.7 (14.4-17.8)	16.9 (13.7-19.4)	17.5 (3.3-28.7)	23.6 (15.8-32.9)	0.014

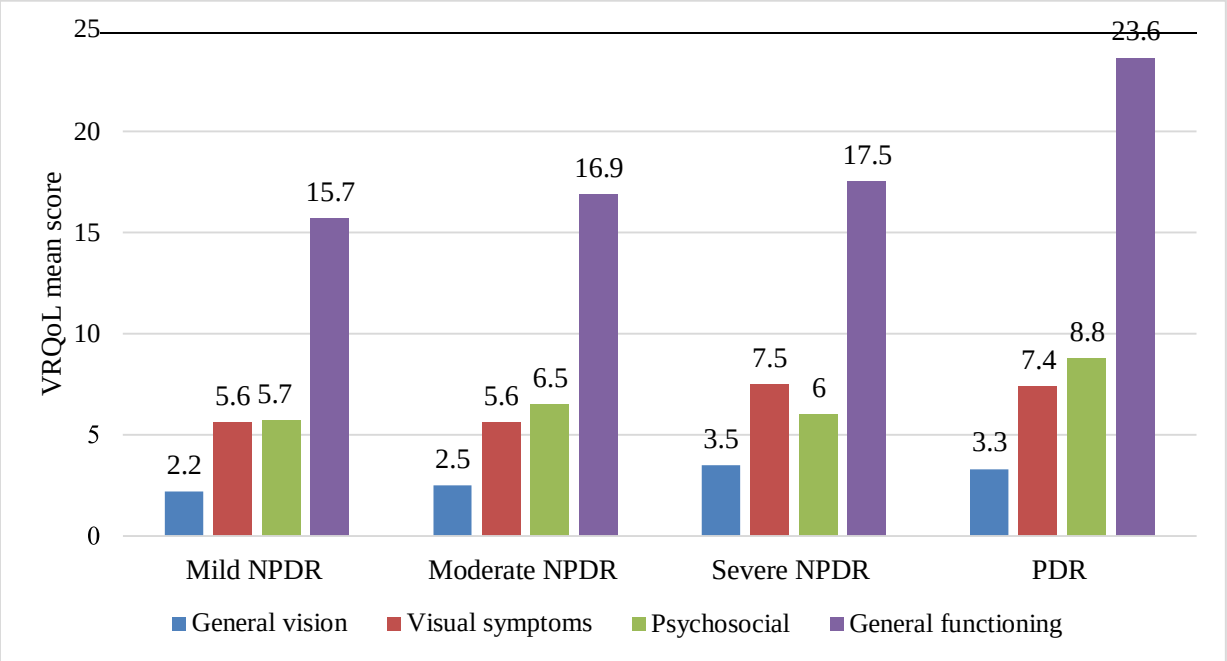

Figure 7: VRQoL mean scores by ETDRS grades using the worse eye among patients attending Retina clinic (N=50).

VRQoL mean scores increased with increasing severity of DR and the higher the scores the lower was the patient‘s QoL. When using the patient‘s worse eye, those with mild NPDR were noted to have lower mean score (SD) in all domains: general vision 2.2 (0.5), visual symptoms. 5.6 (1.2), psychosocial status 5.7 (1.4) and general functioning 15.7 (3.8). Patients with PDR had the highest mean scores (SD) in all domains: general vision 3.3 (0.8), visual symptoms 7.4 (1.7), psychosocial status 8.8 (3.9) and general functioning 23.6 (12.4).

Table 8: VRQoL mean scores for all domains by ETDRS grade using the better eye among patients attending the Retina Clinics, KNH (N=50)

VF20 domains	No apparent DR n=2 Mean (95 %CI)	Mild NPDR n=25 Mean (95% CI)	Moderate NPDR n=12 Mean (95% CI)	Severe NPDR n=2 Mean (95% CI)	PDR n=9 Mean (95% CI)	p-value
General Vision	2.5 (-3.9-8.9)	2.3 (2.0-2.5)	2.7 (2.3-2.8)	3.0 (-2.9-9.9)	3.4 (2.8-4.0)	0.001
Visual Symptoms	6.0 (-19.4-31.4)	5.6 (5.2-6.2)	6.2 (5.0-6.4)	6.5 (1.2-13.9)	7.4 (6.0-8.7)	0.031
Psychosocial Symptoms	7.5 (-24.3-39.3)	5.8 (5.2-6.3)	6.8 (5.7-7.7)	7.0 (-6.7-18.7)	8.9 (5.6-11.8)	0.039
General Functioning	19.0 (-70.0-107.9)	16.1 (14.2-17.3)	17.1 (14.6-19.9)	16.0 (11.2-23.9)	24.8 (14.0-33.6)	0.085

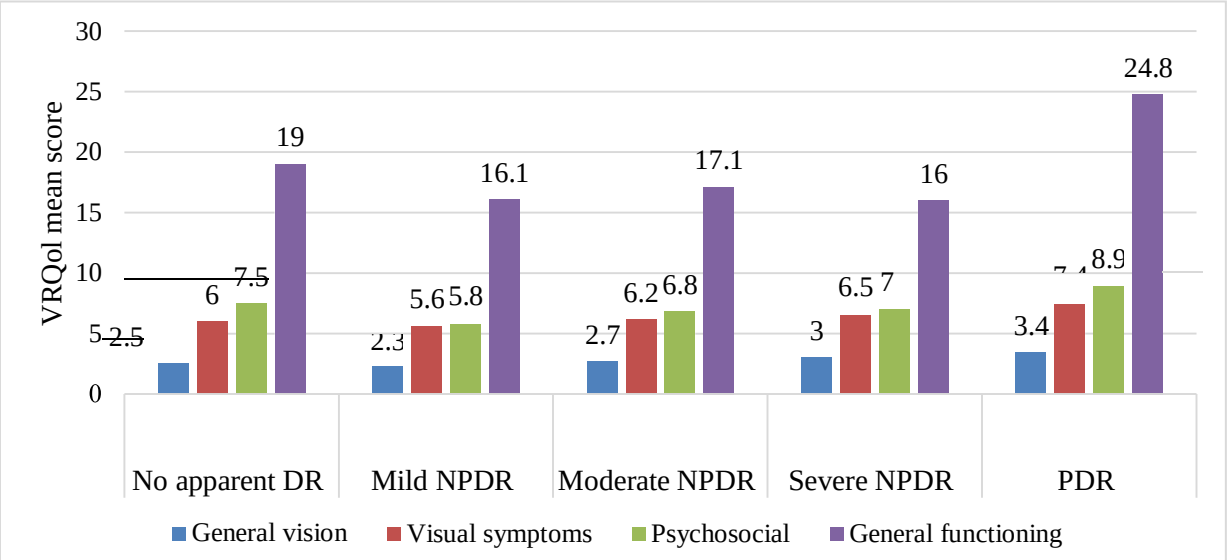

Figure 8: VRQoL mean scores by ETDRS grades using the better eye among patients attending Retina clinic (N=50).

When conducting the sensitivity analysis using the patient's better eye, VRQoL mean scores increased with increasing severity of DR thus patients with mild NPDR had the best VRQoL meanwhile those with PDR had the worse VRQoL in all domains. Two patients with no apparent DR had a high mean score (SD) for all 4 domains: overall self-rating eyesight 2.5 (0.7), visual symptoms 6 (2.8), psychosocial status 7.5 (3.5) and general functioning 19 (10.0).

viii) Multivariate analysis

Table 9: Multivariate binomial logistic regression of VFQ-20 General vision domain for all participants (N=100)

Variables	Low Overall QoL (n, %)	Good Overall QoL (n, %)	Crude Odds ratio (95% CI)	p-value	Adjusted Odds ratio (95% CI)	p-value
DR						
Yes	26 (78.8)	24 (35.8)	6.6 (2.29-19.37)	0.0001	5.8 (2.1-15.9)	0.001
No	7 (21.2)	43 (64.2)	Reference		Reference	
Age in years *(mean, sd)*	60.1 (2.19)	59.8 (1.70)	-	0.938	-	-
Sex						
Female	22 (66.7)	39 (58.2)	1.4 (0.6-3.5)	0.457	-	-
Male	11 (33.3)	28 (41.8)	Reference			
Distance vision impairment						
Yes (VA worse than 6/12)	22 (66.7)	19 (28.4)	5.1 (1.9-13.3)	0.0003	4.3 (1.6-11.2)	0.003
No (VA better or equal to 6/12)	11 (33.3)	48 (71.6)	Reference		Reference	
Diabetic macula oedema						
Yes	10 (30.3)	2 (4.5)	9.3 (2.1-40.8)		4.8 (1.1-21.3)	0.037
No	23 (69.7)	67 (95.5)	Reference		Reference	
Cataract in any eye						
Yes	19 (57.6)	22 (32.8)	2.8 (1.1 – 6.7)	0.018	2.6 (0.9 – 8.1)	0.109
No	14 (42.4)	45 (67.2)	Reference		Reference	
Dry eye syndrome						
Yes	30 (90.9)	51 (76.1)	3.1 (0.8 – 11.7)	0.078	-	-
No	3 (9.1)	16 (23.9)	Reference			
Systemic comorbidity						
Yes	24 (72.7)	55 (82.1)	0.6 (0.2-1.6)	0.282	-	-
No	9 (27.3)	12 (17.9)	Reference			

VA: visual acuity

In this analysis low overall QoL refers to a low overall assessment of eyesight which corresponds to question 1 in the VFQ-20 questionnaire. There was a significant association between the DR grade in the worse eye and low QoL. There was a trend where those with

worse DR had lower QoL than those with less severe DR (p=0.002). If a person had low QoL they were 1.4 times more likely to be female, but this difference did not reach statistical significance. About two thirds of people with a low QoL had distance vision impairment. Therefore, a person with low QoL was 5 times more likely to have distance vision impairment compared to one with no distance visual impairment. Again, a person with low QoL was 2 times more likely to have cataract in any eye when compared to a person with no cataract and this was statistically significant. About a third of people with a low QoL had DME. Thus, a person with low QoL was 9 times more likely to have DME compared to one without DME.

In the multivariate binomial logistic regression, there was a significant association between DR grade, distance vision impairment, presence of DME and low overall QoL. Adjusting for confounders, the odds for a person with DME to perceive his general vision as low QoL significantly dropped to 4 times when compared to one without DME.

7.0 DISCUSSION

The study had adequate power to estimate the vision-related quality of life among patients with diabetic retinopathy as well as those without diabetic retinopathy since the predetermined minimum sample size was achieved. Participants in our study population were aged between 19 and 93 years. The mean age of the patients with DR was lower than those without DR and this difference was not statistically significant. The mean age among DR and no DR patients were also lower that those reported in the EUROCONDOR study (62). This discrepancy was attribute to the difference in study design and study setting. The proportion of female with diabetes in this study of 56% was more than males which was 44.0%. Although the proportion of females with DR (66%) was higher than males (34%) the difference again did not reach statistical significance (p-value< 0.05). Our results were different from those reported in a study conducted in Japan (63). In this study, females were diagnosed with diabetes mellitus at an older age and had a higher prevalence of hypertension and dyslipidaemia than males. In Kenya, most studies on diabetic retinopathy demonstrated similar results. Females consisted 52% in Nakuru; 63% in KNH and 54% in KNH (11,39,40). The mean duration of DM among patients with diabetic retinopathy was comparable to those without diabetic retinopathy but this was not statistically significant. Our results were higher than those reported in a study conducted in India (45) and this difference was due to the fact that only patients with type2 diabetes were enrolled. Using HbA1c to assess diabetes mellitus control, we had close to have of the participants with no documented reports. That notwithstanding, we were able to establish that patients with diabetic retinopathy had a poorer control of their diabetes when compared to those without diabetic retinopathy. Our results were comparable to the study conducted in an Indian population (45).

Vision plays an important role in allowing people to process information from their environment and to participate in activities such as reading, working, walking, driving, and interacting with others. People with visual impairment face challenges in completing these activities, which may lead to depression, social isolation, and difficulties at home, in school or at work. In general, the more advanced a society is the higher are the peoples‘ expectations of good sight. This might be due to a higher level of literacy, wide utilization of modern media which require a good vision. Regional and cultural differences in the perception of visual impairment have been reported by several authors (64). Using the ICD-11 classification for visual impairment, patients without DR had a better presenting VA when

compared to those with DR and this difference was statistically significant. Among DR patients, we noted that more than half of them had normal presenting visual acuity and a minimum number suffered from severe VI and blindness. These results were comparable to those reported in a study conducted in a Singaporean population (44). Measurement of visual acuity using the Snellen chart lacks information about the effect of reduced sight on an individual. Patients‘ perception about their visual impairment was objectively measured by vision-related quality of life scales. Other tools assessing vision-related quality of life have not been approved in Kenya (53,54,56). VFQ-20 is previously reported to be a good measure of QoL for patients with wide range of visual impairment including diabetic retinopathy as it captures mental and emotional aspects of the disease as well as visual function (51). The test-retest validity of the VF-20 questionnaire in this study was good, the results were reproducible and was therefore validated for use in Kenya (59). The patient gives a ‗difficulty rating‘ for each item and responses are scored e.g. 1-no difficulty to 5-extreme difficulty. The WHO/PBD-20 Questionnaire also known as the VFQ-20 questionnaire was used for this study. Normative data for the WHO/PBD-20 Questionnaire exists from a recent study done by Polack et al (2007). They used the questionnaire on a study population in Nakuru, Kenya. They removed question 5, which asks for difficulties in seeing because of bright light because they found it unsuitable. Comparisons with existing quality of life data from other studies and other societies are difficult to make. There is high heterogeneity in the used QoL scales; several dozens of questionnaires assessing VRQoL exist. Most are adjusted to societies and ask about difficulties in daily life according to the study setup and location. This makes the studies difficult to compare.

In our study, we found that the overall vision-related quality of life (VRQoL) among patients with DR was significantly poorer than those without DR using VF-20 questionnaire. The total mean score for DR patients was 33.4 ±11.5 meanwhile for patients without DR, it was 26.9±4.7. This result was significantly evident in all the four subscales of the VF 20 questionnaire with general functioning being the most affected followed by psychosocial functioning and visual symptoms. Patients‘ general vision perception was the least affected. Answers to items exploring these specific dimensions indicate that although our patients with DR perceived their overall eyesight as good, they still had difficulties in performing some daily activities. As regards patients‘ psychosocial status, some were worried about losing their sight, being a burden to others and being hesitant to participate in social gatherings. Similar results were documented in a previous study in India (45). In contrast to a study by Wolf et al, the DM patients even without DR didn‘t have any significant difficulty in seeing

different colours(65). As regards visual symptoms, we explored perceived ocular discomfort and difficulty seeing because of glare from bright light. This ocular discomfort had a significant impact on DR patients‘ daily life when compared to those with no DR. Contrary to Polack and colleagues, our participants were able to report a significant effect of glare on their vision(59). This discrepancy could be due to variations in study population and settings. To the best of our knowledge, VFQ-20 questionnaire has only been used in the study from Nakuru District and Kwale District Eye Centre assessing VRQoL among patients with cataract. Three subscales were originally proposed: visual symptoms (3 items), psychosocial (4 items) and general functioning (12 items), with one overall eyesight-rating item. As no modifications were made to the questionnaire in our study, rotated exploratory factor analysis was not conducted to determine how items should be grouped for summary scores.

We also found that using the patient‘s worse eye, VRQoL became poorer with increasing severity of the ETDRS grading. Using the better or the worse eye, patients with proliferative diabetic retinopathy had a significantly poorer perception of their general functioning followed by their psychosocial and visual symptoms. A study on the effect of DR and its severity on health-related quality of life in a population-based sample of Latinos with Type 2 DM using the NEI VFQ-25 obtained similar results (66). With the better eye, we noted that although the VRQoL again worsened with increasing severity, patients with no apparent DR had a poorer VRQoL when compared to those with mild NPDR. This unexpected, rare finding could be due to possible confounders such as DME, dry eye syndrome or the presence of cataract.

In the multivariable binomial logistic regression analyses performed using general vision as our dependent variable dichotomised into low and good overall self-rating of vision, higher mean scores were significantly associated with presence of DR, distance vision impairment and presence of DME. These findings were comparable to those reported in a study conducted in India and in the USA respectively using the NEI VFQ-25 questionnaire (45,65,67). In these studies, they emphasized on the importance of early detection of DR to avoid progression which is likely to have a positive impact on a person‘s VRQoL.

8.0 STUDY LIMITATION & STRENGTH

- The effect of patients‘ blood sugars on their QoL couldn‘t be assessed because most of them had missing data on their latest HbA1c.
- Our study was a cross-sectional study thus, the findings cannot be inferred to the general population of Kenya.
- In terms of strengths, we had a high participation rate despite the COVID-19 outbreak which had limited the number of patients visiting our clinics.

9.0 CONCLUSION

- In summary, using the WHO/PBD-VF20 questionnaire, the quality of life among diabetic retinopathy patients was significantly lower than those without diabetic retinopathy with maximum effect seen on overall eyesight, general functioning, psychosocial function, and visual symptoms.
- The vision-related quality of life reduced with increasing severity of ETDRS grades using the patient‘s worse eye.
- Presence of DR, distance vision impairment and presence of DME were significantly associated with patients having a low overall QoL.

10.0 RECOMMENDATION

- Understanding the VRQoL among patients with and without diabetic retinopathy should form an initial evaluation of their QoL health status. This may guide policymakers, health care providers, patient support group leaders in strengthening patient centered care.
- Our findings underscore the need for interventions aimed at early detection and management of DR to prevent progression to more advanced DR and its associated deterioration on VRQoL.
- All DM patients with VA worse than 6/12 should have an ocular examination done at least once in a year by an Ophthalmologist to delay diabetes-related loss of vision.

- The latest HbA1c and fasting blood sugars among all patients with DM should be documented in their files to monitor their glycaemic levels as well as conduct analyses aimed at developing service improvement strategies.

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12.0 APPENDICES

Appendix 1: Research Budget

Item	Quantity	Unit cost (KSH)	Total (KSH)
Proposal development/ Ethical Approval			
Printing (75 pages)	4 copies-70 pages	10 ksh per page	2,800
	4 copies-5-coloured pages	30 ksh per page	600
Binding	4	500	2,000
Ethics committee fee	1	2,000	2,000
Plagiarism Check	-	2,000	2,000
Internet	-	3000	3,000
Subtotal=			**12,400**
Pilot study			
Questionnaire (3 pages)	6 copies- 18 pages	10	180
Consent forms	6 copies- 24 pages	10	240
Subtotal=			**420**
Data collection			
Questionnaire (3 pages)	100 copies- 300 pages	10	3,000
Consent forms (5 pages)	100 copies- 500 pages	10	5,000
Printing & lamination of pictorial cards for VF-20 questionnaire	6 copies	60ksh per copy	360
Personal protective equipment kits	60 samples	500ksh per sample	44,000
Box files for filing questionnaires	2	450 each	900
Schirmer Tear Test Strips	1 pack	2,000	2,000
Internet	-	3000	3000
Subtotal=			**76,260**
Contracted Services			
Research Assistant & Interpreter	20 days	7000	140,000
Statistician	-	30,000	30,000

Subtotal=			**170,000**
Printing cost & binding of final book			
Finished book printing (120 pages approximately)	8 copies- 100 pages	10ksh per page	8,000
	8 copies- 20 coloured pages	30ksh per page	4,800
Binding finished book	2 copies -marking	100 per book	200
	8 final copy (Black cover)	300	2,400
Subtotal=			**15,400**
Grand Total			**274,480**

Appendix 2: Consent Form (Statement of Consent)

Participant's statement:

I have read this consent form or had the information read to me. I have had my questions answered in a language that I understand. The risks and benefits have been explained to me. I understand that my participation in this study is voluntary and that I may choose to withdraw any time. I freely agree to participate in this research study.

I understand that all efforts will be made to keep information regarding my personal identity confidential.

By signing this consent form, I have not given up any of the legal rights that I have as a participant in a research study.

I agree to participate in this research study: Yes No

I agree to have my fundus photograph taken: Yes No

I agree to provide contact information for follow-up: Yes No

Participant printed name:

_____

Participant signature / Thumb stamp_____Date _____

Researcher's statement:

I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has willingly and freely given his/her consent.

Researcher's Name: *Nerice F. Emade* Date: _____

Signature

_____

For more information contact *Nerice F. Emade* on telephone number *07574-78659*

Appendix 3: Study Tool

Serial No: _____ Data collection date: _____

Socio-demographics

1. Gender: Male (1) □ Female (2) □
2. DOB: _____
3. Age (years): _____
4. Marital status: Single (1) □
   Married (2) □
   Other (divorced, widowed) (3) □
5. What is your highest level of Education? _____
   Never gone to school + able to read and write (1) □
   Never gone to school + can't read and write (2) □
   Primary school (3) □
   Secondary school (4) □
   Higher education (5) □
6. What is your employment status? : Unemployed (1) □
   Formal Employed (2) □
   Self-employed (3) □
   Retired (4) □
   Others (Specify) (5) □ _____

Clinical History

7. For how long have you had DM? (in years): _____
8. For how long have you had DR? (in years): _____
9. i) When was your last HbA1c? _____
   ii) What was it? _____
10. What is your latest blood pressure? _____
11. i) Any associated comorbidities? _____
    ii) For how long? _____

Ocular Examination

12. Spectacle type:
    None (0) □ Distant only (1) □ Near only (2) □ Bifocal (3) □ Progressive (4) □ Others (5) □_____

13. Visual acuity:

		Right eye	Left eye
Current distant VA	unaided		
	correction		
Current near VA	unaided		
	correction		

14. Cataract:

i) RE: No (0) □ Yes (1) □

ii) LE: No (0) □ Yes (1) □

15. Dry eyes syndrome: No (0) □ Yes (1) □
16. CSME:

i) RE: No (0) □ Yes (1) □

ii) LE: No (0) □ Yes (1) □

17. ETDRS grading: RE _____ LE_____
18. Interventions for DR: _____

None (0) □ Anti-VEGF (1) □ Retinal laser (3) □ Vitrectomy □

WHO/PBD-VF-20

The first questions are about your overall eyesight. I will read out a choice of five answers and you will choose the one that describes you best.

		1.Very good	2.Good	3.Moderate	4.Bad	5.Very bad
1.	Overall, how would you rate your eyesight using both eyes – with glasses or contact lenses if you wear them?					
2.	How much pain or discomfort do you have in your eyes (e.g. burning, itching, aching)?	1.None	2.Mild	3.Moderate	4.Severe	5.Extreme

(NOTE: If the responses were "Very good" and "None" to the above two questions, END the interview.)

		1.None	2.Mild	3.Moderate	4.Severe	5.Extreme/ Cannot do
3.	Because of your eyesight, how much difficulty do you have in going down steps or stairs?					
4.	How much difficulty do you have in noticing obstacles while you are walking alone (e.g. animals or vehicles)?					
5.	How much difficulty do you have in seeing because of glare from bright lights?					
6.	Because of your eyesight, how much difficulty do you have in searching for something on a crowed shelf?					
7.	How much difficulty do you have in seeing differences in colours?					
8.	Because of your eyesight, how much difficulty do you have in recognizing the face of a person standing near you?					
9.	How much difficulty do you have in seeing the level in a container when pouring?					
10.	Because of your eyesight, how much difficulty do you have in going to activities outside of the house (e.g. sporting events, shopping, religious events)?					
11.	Because of your eyesight, how much difficulty do you have in recognizing					

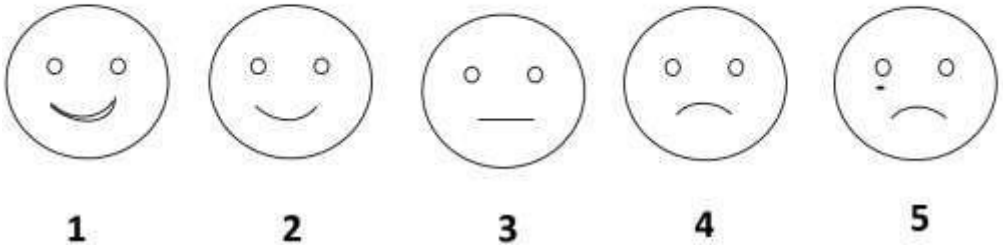
	people you know from a distance of 20 metres?					
12.	How much difficulty do you have in seeing close objects (e.g. making out differences in coins or notes, reading newsprint)?					
13.	How much difficulty do you have in seeing irregularities in the path when walking (e.g. potholes)?					
14.	How much difficulty do you have in seeing when coming inside after being in bright sunlight?					
15.	How much difficulty do you have in doing activities that require you to see well close up (e.g. sewing, using hand tools)?					
16.	Because of your eyesight, how much difficulty do you have in carrying out your usual work?					

In the next section, I am going to ask you how you feel because of your vision problem. I will read out a choice of five answers and you will choose the one that describes you best

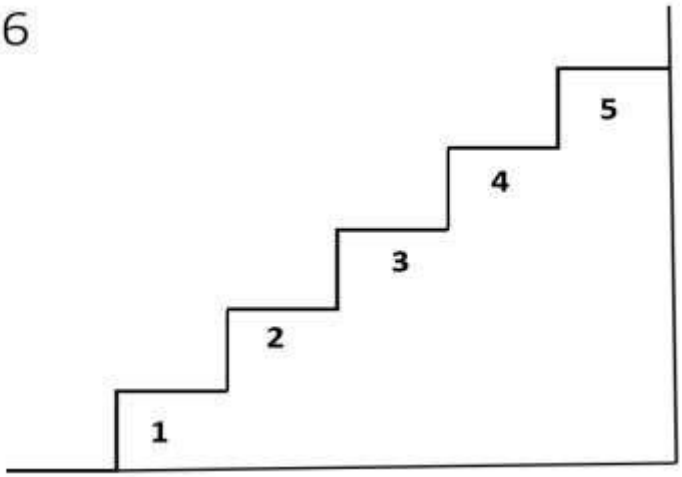
		1.Never	2.Rarely	3.Sometimes	4.Often	5.Very often
17.	Because of your eyesight, how often have you been hesitant to participate in social functions?					
18.	Because of your eyesight, how often have you found that you are ashamed or embarrassed?					
19.	Because of your eyesight, how often have you felt that you are a burden on others?					
20.	Because of your eyesight, how often do you worry that you may lose your remaining eyesight?					

Appendix 4: Pictorial illustrations for WHO/PBD-VF20 QUESTIONNAIRE

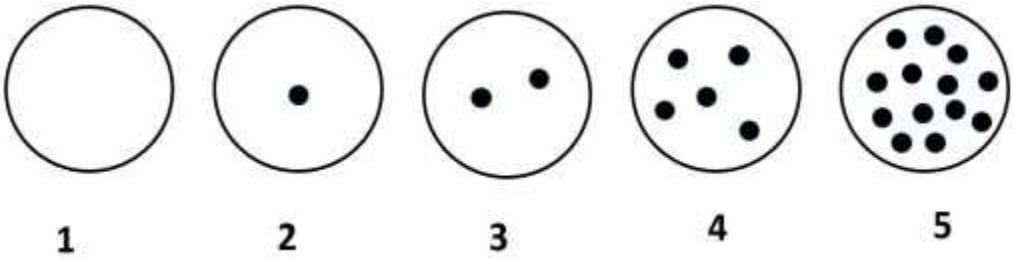
Q1



Q2-16



Q17-20



Appendix 5: Ethical Approval Certificate

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
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Tel:(254-020) 2726300 Ext 44355

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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/364

19 October 2020

Dr. Nerice Francine Emade Ketchemen
Reg. NO.H58/12252/ 2018
Dept.of Ophthalmology
School of Medicine
College of Health Sciences
University of Nairobi

Dear Dr. Ketchemen

RESEARCH PROPOSAL – VISION-RELATED QUALITY OF LIFE AMONG PATIENTS WITH DIABETES ATTENDING THE MEDICAL AND RETINA CLINICS AT KENYATTA NATIONAL HOSPITAL (P356/07/2020)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and **approved** your above research proposal. The approval period is 19th October 2020 – 18th October 2021.

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. Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
f. 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*).
g. 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.

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

Yours sincerely,

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

c.c. The Principal, College of Health Sciences, UoN
The Senior Director, CS, KNH
The Chairperson, KNH- UoN ERC
The Assistant Director, Health Information Dept, KNH
The Dean, School of Medicine, UoN
The Chair, Dept. of Ophthalmology, UoN
Supervisors: Dr. Joseph Nyamori, Dept.of Ophthalmology, UoN
Dr. Margaret Njuguna, Dept.of Ophthalmology, UoN
Dr. Stephen Gichuhi, Dept.of Ophthalmology, UoN