Diabetic retinopathy among patients with type 2 diabetes mellitus at Moi Teaching and Referral Hospital, Eldoret, Kenya

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ABSTRACT

Background: Diabetic Retinopathy (DR) accounts for 5% of the 39 million causes of blindness occurring worldwide and is estimated to contribute 3% of blindness in Kenya. Dyslipidemia, poor control of sugar, hypertension and obesity increase the risk of DR in patients with diabetes. This study addresses the gap in information on the magnitude of DR and its associated factors in patients with type 2 diabetes at Moi Teaching and Referral Hospital (MTRH).

Objectives: To determine the prevalence and severity of DR and its associated factors in patients with type 2 diabetes mellitus.

Methods: This cross sectional study was conducted amongst patients with type 2 diabetes mellitus in MTRH. Randomly selected participants underwent anthropometric, laboratory and visual acuity testing. Direct ophthalmoscopy was used to assess DR and macula edema. Grading of DR was done using international clinical diabetic retinopathy severity scale. A univariate and multivariate logistic regression model was used to assess associations of the variables with DR.

Results: Of the 329 participants enrolled, 187 (57%) were female with a mean age of 56.8 (10.99) years. One hundred and three (31%) had diabetic retinopathy and 39 (12%) had diabetic macula edema. Mild to moderate non proliferative diabetic retinopathy was the most prevalent grade at 79 (25%). One hundred and eighty four (56%) of participants had hypertension (133/80; IQR 120/70-150/89) mmHg and 158 (48%) had glycated haemoglobin between 7-10%. The median for the other assessed factors were as follows: duration of diabetes 5 (9) years, total cholesterol 4.6 (1.3) mmol/l and low density lipoprotein 3.0 (1.5) mmol/l. Increase in duration of diabetes by 5 years {OR 2.02(95% CI 1.11-3.69); p 0.02}, glycated haemoglobin > 6.5% {OR 2.13(95% CI 1.02-4.42); p 0.04}, systolic hypertension >160 mmHg {OR 1.02(95% CI 1.01-1.03); p 0.01} were associated with increased risk of diabetic retinopathy while male gender and body mass index did not. Only 15% of the participants in this study reported having had previous eye check-up.

Conclusion: A third of patients with type 2 diabetes on follow up at MTRH have DR. Systolic hypertension, increased duration of diabetes and high glycated haemoglobin were positively associated with increased risk of developing DR.

Key words: Diabetic retinopathy, Type 2 diabetes mellitus

INTRODUCTION

Diabetes Mellitus (DM) affects about 350 million people worldwide and results in considerable morbidity and mortality. There is significant increase in developing countries; thought to be the result of population growth, ageing, obesity, and sedentary lifestyles[1]. The International Diabetes Federation (IDF) has estimated the number of adults with DM in Africa will double in 20 years from 12 million in 2010 to 24 million in 2030[2]. Diabetes Retinopathy (DR) is a leading cause of vision loss in middle-aged and elderly people globally. Early detection and prompt treatment allow prevention of diabetes-related visual impairment[3].

Diabetes has many manifestations in the eye, of which cataracts and Diabetic Retinopathy (DR) are the most significant causes of visual impairment and blindness. People with diabetes are 25 times more likely than the general population to become blind with DR reported as the sixth leading cause of global visual impairment[4]. In developed countries, diabetic eye disease represents the leading cause of blindness in adults aged less than 75 years. Visual impairment as a result of DR has a significant impact on patients' quality of life and can compromise their ability to manage their disease, which can in turn have a negative impact on the incidence of other diabetic complications and overall life expectancy[4,5].

Diabetic retinopathy is estimated to contribute about 3% of blindness in Kenya. In Nairobi, it is estimated

that 50% of patients diagnosed with diabetes have DR, while 20% of patients in rural central province had DR[5]. Majority of patients diagnosed with DR have never undergone any eye examination[5,6]. Long duration of diabetes, hyperglycemia, hypertension, dyslipidemia, obesity, proteinuria and low socioeconomic status play important roles for development of retinopathy. Long duration of diabetes and inadequate glycemic control are most important[7]. Loss of productivity and quality of life for the patient with diabetic retinopathy will lead to additional socio-economic burdens on the community. Many cross sectional studies have been done on the prevalence as well as the associated risk factors for developing diabetes retinopathy in other parts of the world as well as Kenya. Moi Teaching and Referral Hospital does not have data on the prevalence of diabetic retinopathy and the particular risk factors associated with the condition hence this research work aims at addressing this gap. Identification of risk factors associated with diabetic retinopathy is essential if effective preventative measures are to be developed. It is hoped that publishing of such data at the hospital level will stimulate interest in development of programs aimed at prevention through early diagnosis, management of risk factors and treatment of advanced cases.

MATERIALS AND METHODS

Study design and setting: This was a cross-sectional study conducted at the Moi Teaching and Referral Hospital which is a referral hospital for Western Kenya and Rift valley.

Study participants: The participants were persons with type 2 diabetes mellitus recruited from the diabetes clinic and in-patient adult wards.

Sampling technique: This study employed simple random sampling technique. There are approximately 3000 patients with diabetes mellitus on follow up in diabetes clinic in Moi Teaching and Referral Hospital. About 30 to 70 patients are attended to during the clinic days. Patients were recruited during the clinic days (Tuesday, Thursday and Friday). The attendance list which had names of patients booked on a particular clinic day was used as a sampling frame. The participants were then randomly selected from the attendance list using a sampling table. The patients in the wards were enrolled on Monday and Wednesday. The admission list of the patients in the wards was used as the sampling frame. A sampling table was used to randomly select the participants.

Variables: The main exposure variable was Type 2 DM which was derived from the patients chart. The main outcome variable was diabetic retinopathy. Other covariates of interest were glycated haemoglobin, blood pressure, body mass index, age, lipid profile, previous eye check up and gender.

Inclusion criteria: Available documentary evidence (medical chart/file) of diagnosis of type 2 diabetes mellitus.

Exclusion criteria: Ocular diseases precluding slit lamp examination/ophthalmoscopy; Inability of a participant to consent.

Study procedures: Clients with type 2 diabetes mellitus on follow up in the diabetes clinic and those admitted in the adult wards were recruited into the study upon meeting all the inclusion criteria. The research assistant collected the participant's bio data, a comprehensive medical history and anthropometric measurements (weight and height). Blood pressure was recorded in the sitting position in the right arm using a mercury sphygmomanometer. Blood samples for glycated haemoglobin and lipid profile were drawn by the researcher/research assistant from patients who had fasted for >8 hours. Direct ophthalmoscopy was performed to assess diabetic retinopathy and diabetic macula edema. The findings were confirmed by an ophthalmologist before grading the participant degree of diabetic retinopathy using the international clinical diabetic retinopathy disease severity scale.

Data analysis: Data was explored for missing values, errors and inconsistencies. Descriptive statistics were summarized means (standard deviation) or medians (interquartile range). Univariate and multivariate logistic regression models were used to assess associations of clinical, biochemical and anthropometric variables with diabetic retinopathy. Odds ratios were calculated for the associations between covariates and the outcome. The univariate analyses that showed significant relationships ($p < 0.20$) between exposure variables and diabetic retinopathy were included into the multivariate analysis.

Study limitations: The performance of examinations through a dilated pupil by direct ophthalmoscopy is 50-70% that of the gold standards (color fundus photography) meaning some early cases of diabetic retinopathy could have being missed.

Ethical considerations: Ethical clearance was obtained from the Institutional Research and Ethics Committee (IREC) of MTRH and Moi University School of Medicine and permission from MTRH management. A written informed consent was obtained from all the participants.

RESULTS

Of the 329 participants included in the final analysis, 187 (57%) were female with a mean age of 56.8 years (SD 10.97). Among the in patients; reasons for admission included hyperglycemia and co-morbidities like diabetic foot, renal disease and stroke. The mean Body Mass Index (BMI) was 27 (SD 5). One hundred and eighty four (56%) of participants were hypertensive with the median blood pressure of 133/80 mmHg (IQR 120/70-150/89). The median duration of diabetes mellitus was 5 years (IQR 2-11) with a median glycated haemoglobin and total cholesterol of 8.65% (IQR7.2-11) and 4.48 mmol/l (IQR 3.59-5.37) respectively (Table 1).

Table 1: Overall participant characteristics and comparing those with and without diabetic retinopathy

Characteristics		Total n=329	With diabetic retinopathy (n= 103)	Without diabetic retinopathy (n = 226)
Age (years)	Mean (SD)	56.8 (11.0)	59.2 (9.4))	55.8 (11.5)
Gender	Male	140 (42.6%)	46 (44.7%)	94 (41.6%)
	Female	189 (57.4%)	57 (55.3%)	132 (58.4%)
Duration of DM in years	Median (IQR)	5 (9)	8 (11)	4 (9)
Hypertension	Yes	184 (55.9%)	72 (69.9%)	112 (49.6%)
	No	145 (44.1%)	31 (30.1%)	114 (50.4%)
Systolic BP (mm/hg)	Mean (SD)	135.6 (23.0)	143.7 (22.9)	131.8 (22.1)
Diastolic BP (mm/hg)	Mean (SD)	79.7 (13.2)	81.4 (14.2)	78.9 (12.7)
Hba1c (%)	< 7%	60 (18%)	4 (4%)	56 (25%)
	7 – 10%	158 (48%)	47 (46%)	111 (49%)
	> 10%	110 (34%)	52 (50%)	58 (26%)
BMI (kg/m^2)	Mean (SD)	27.1 (5.1)	27.0 (4.5)	27.2 (5.4)
Total cholesterol (mmol/l)	Median (IQR)	4.6 (1.3)	4.9 (1.3)	4.4 (1.3)
Triglycerides (mmol/l)	Median (IQR)	1.7 (1.4)	2.0 (1.3)	1.7 (1.4)
HDL-C (mmol/l)	Median (IQR)	1.0 (0.5)	1.0 (0.5)	1.0 (0.4)
LDL-C (mmol/l)	Median (IQR)	3.0 (1.5)	3.8 (1.6)	2.7 (1.4)
Previous eye check	Yes	73 (22.2%)	35 (34.0%)	38 (16.8%)
	No	256 (77.8%)	68 (66.0%)	188 (83.2%)

In the univariate model of risk factors associated with diabetic retinopathy (Table 2), every increase in age by a year (OR 1.12 (95% CI 1.03-1.22; p 0.001); presence of hypertension (OR 2.36 (95% CI 1.44-3.87; p 0.001) or elevated systolic blood pressure (OR 1.02 95% CI 1.01-1.03; p 0.0001) were associated with diabetic retinopathy. Other risk factors that were statistically significant in this model include every point increase in glycated haemoglobin, total cholesterol and low density lipoprotein levels.

Table 2: Univariate analysis showing unadjusted OR for the relationship between participant characteristics and diabetic retinopathy

Characteristics		UOR	95% CI	P value
Age (years)	(Increase in 10 years)	1.12	1.03 to 1.22	0.001
Gender	Female	ref		
	Male	1.13	0.71 to 1.81	0.602
Duration of DM in years	5 year increase in duration	1.15	1.25 to 1.82	0.001
Hypertension	No	ref		
	Yes	2.36	1.44 to 3.88	0.001
Systolic BP (mm/hg)	Mean (SD)	1.02	1.01 to 1.03	0.001
Diastolic BP (mm/hg)	Mean (SD)	1.01	1.00 to 1.03	0.113
Hba1c (%)	<6.5%	ref		
	>6.5%	4.62	2.12 to 10.05	0.001
BMI (kg/m^2)	Increase by a unit	0.99	0.95 to 1.04	0.780
Total cholesterol (mmol/l)	Mean (SD)	1.41	1.16 to 1.71	0.001
LDL-C (mmol/l)	< 3.2	ref		
	3.2 to 4.2	2.56	1.43 to 4.59	
	>4.2	7.53	3.98 to 14.21	0.001
Previous eye check	No Yes	ref 2.54	1.49 to 4.35	0.001

In the multivariate model (Table 3), longer duration of diabetes (OR 2.02; 95% CI 1.11-3.69); higher glycated haemoglobin (OR 2.13; 95% CI 1.02-4.42); and higher systolic blood pressure (OR 1.02; 95% CI 1.01-1.03) were positively associated with diabetes retinopathy. Higher LDL cholesterol (OR 1.14, 95% CI 0.59 to 2.26) and advancing age (OR 2.72, 95% CI 0.86 to 8.63) were not significantly associated with diabetic retinopathy in the final model.

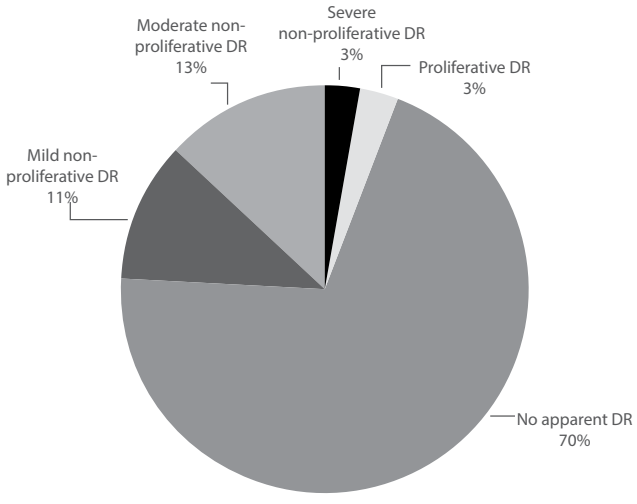

Figure 1: Distribution of the different stages of diabetic retinopathy

Table 3: Multivariate analysis showing adjusted Odds ratios for the participant characteristics and diabetic retinopathy

Characteristics	AOR	95% CI	P value
Age group (increase by 10 years)	1.03	0.92 to 1.15	0.57
Increase in duration of diabetes by 5 years	2.02	1.11 to 3.69	0.02
Systolic blood pressure >160mmHg	1.02	1.01 to 1.03	0.01
HBA1C > 6.5%	2.13	1.02 to 4.42	0.04
LDL cholesterol >3.2mmol/l	1.14	0.59 to 3.05	0.23
Previous eye check	1.52	0.76 to 1.35	6.28

DISCUSSION

This study found high prevalence of diabetic retinopathy among patients with type 2 diabetes at MTRH, with majority having mild to moderate non proliferative diabetic retinopathy. Longer duration of DM, poor glycemic control and higher blood pressure were significantly associated with higher likelihood of diabetic retinopathy.

The prevalence reported in this study (31%) is comparable to a systematic review of African studies on micro and macrovascular related complications in diabetes. The systematic review reported prevalence of diabetic retinopathy of 16 to 77% depending on the duration of diabetes and glycemic control, with severe retinopathy representing 15% of all cases[8]. Kohner *et al*[9] in 1998 through a large systematic review reported prevalence of diabetic retinopathy among patients with type 2 diabetes ranged from 30.2– 31.6% among various African countries. Similar studies done in Kenya in Nakuru and Embu reported a prevalence rate of 35.9% and 41% respectively and almost 50% of diabetics at Kenyatta National Hospital[10-12].

The estimated prevalence of macula edema is 12% which is less than 33.3% as found by Mathenge *et al*[10] in Nakuru. This might be because the study in Nakuru incorporated color fundus photography in diagnosing diabetic retinopathy and macula edema which is more sensitive than slit lamp examination or direct ophthalmoscopy. Generally, the prevalence of diabetic macula edema among patients with diabetes is generally much lower than that of diabetic retinopathy[13]. Among the population-based studies, prevalence of diabetic macula edema among patients with type 2 diabetes was between 1.4 and 12.8%[14].

Gender did not attain a statistical significance as a risk factor for diabetic retinopathy. This is in contrast to other studies which have shown varying results when predicting sex as a risk factor for developing diabetic retinopathy. Male preponderance in diabetic retinopathy has been shown in India[15,16]. Body mass index was not a risk factor for development of diabetic retinopathy. The evidence supporting a relationship between high body mass index and increased risk of diabetic retinopathy is inconclusive. Some studies have demonstrated a positive relationship between higher body mass index and diabetic retinopathy whereas others have reported conflicting results[9,17,18].

Increasing age was positively associated with increasing risk of diabetic retinopathy. This apparent association between older age and diabetic retinopathy might be due to collinearity between old age and longer duration of diabetes. Furthermore, it is believed that undiagnosed type 2 diabetes mellitus may occur 4 – 12 years before its clinical diagnosis and that diabetes may be present for five years before the onset of retinopathy thus the preponderance of diabetic retinopathy in old age[19, 20].

Duration of diabetes above 10 years, glycated haemoglobin > 10%, systolic blood pressure 160-179 mmHg and low density lipoprotein >3.4mmol/l were independently associated with diabetic retinopathy. The duration of diabetes has consistently been shown to be one of the most important determinants of diabetic retinopathy. It has been suggested that the duration reflects total glycemic control, a risk factor that involves cumulative damage[21].

High glycated haemoglobin was associated with diabetic retinopathy. This findings compares with the United Kingdom Prospective Diabetes Study Group (1998) and the Diabetes Control and Complications Trials (1993) which provided strong evidence that tight control of glycemia (glycated haemoglobin <7%) reduces the risk of development and progression of diabetic retinopathy in both type 1 and type 2 diabetes[16]. Hypertension is recognized as a risk factor for the development and progression of diabetic retinopathy as was evidenced in the present study. Multiple epidemiologic studies have identified hypertension as a risk factor for diabetic retinopathy and diabetic macula edema[22].

Univariate analysis of the lipid profile data showed total cholesterol and low density lipoproteins as risk factors associated with diabetic retinopathy but not on multivariate logistic model. No single lipid measure has been consistently found to be associated with diabetic retinopathy or diabetic macula edema[23]. In recent cohort studies, only the Madrid Diabetes Study[24] found an association between low density lipoprotein cholesterol and incidence of diabetes.

Previous eye check-up as used in this study meant that since diagnosis of diabetes mellitus whether the client has had his/her eyes screened. Only 15% of the participants in this study reported having had previous eye check-up. The most common eye symptom given was poor/hazy vision. Njambi *et al*[11] reported 71% of the patients had never had an eye examination before done by an ophthalmologist.

CONCLUSION

A third of patients with type 2 diabetes mellitus on follow up at Moi Teaching and Referral Hospital have diabetic retinopathy. There is need to restructure the existing diabetic eye screening programs to enhance prevention through early diagnosis. The health workers managing patients with diabetes should intensify efforts aimed at controlling hypertension and high glycated haemoglobin.

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