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Prevalence and risk factors associated with retinopathy in diabetic patients at Parirenyatwa Hospital outpatients' clinic in Harare, Zimbabwe

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ABSTRACT

Diabetic retinopathy is the fifth leading cause of blindness worldwide accounting for nearly 5% of all blindness. However, most of the prevalence and incidence data is from developed countries, with very limited information from sub-Saharan Africa. The study sought to determine the prevalence of, and factors associated with, retinopathy in diabetic patients. Diabetes mellitus patients attending the outpatients' clinic at Parirenyatwa Group of Hospitals between October 2013 and July 2014 were recruited into this analytical cross-sectional study. Demographic information was collected. A nurse carried out anthropometric measurements. An ophthalmologist using slit lamp indirect ophthalmoscopy with a 20-diopter and a 90-diopter lens diagnosed retinopathy. Blood samples were collected and analysed for triglycerides, total cholesterol, HDL cholesterol, glycosylated hemoglobin and serum creatinine. A total of 340 patients were enrolled into the study, of whom 73.2% were female. Mean (SD) age was 57.5 (14.9) years and there was no difference in age between females [57.6 (14.1) years] and males [57.2 (16.8) years]. The overall prevalence of diabetic retinopathy was 28.4%. Using multivariate logistic regression analysis retinopathy was associated with longer duration of diabetes mellitus (OR 1.06, 95% CI 1.03-1.09, p value < 0.001) and lower serum creatinine (OR 0.99, 95% CI 0.97-1.00, p value 0.025). The prevalence of diabetic retinopathy was 28.4%. Longer duration of diabetes mellitus and lower serum creatinine, which is a marker of renal damage, were independent risk factors of diabetic retinopathy.

KEY WORDS: ***Diabetes mellitus; Diabetic retinopathy; Complications; Blindness; Prevalence; Risk factor***

INTRODUCTION

Diabetic retinopathy is the fifth leading cause of blindness globally and is estimated to cause nearly 5% of all blindness.[1] Diabetic retinopathy can be divided into two clinical categories, namely non-proliferative and proliferative diabetic retinopathy. Pathophysiology of non-proliferative diabetic retinopathy is characterized by abnormal permeability of retinal capillaries causing retinal edema and closure of capillaries leading to

retinal non-perfusion and ischemia. Proliferative diabetic retinopathy occurs when retinal ischemia is sufficiently severe to cause formation of new vessels.[2]

In proliferative diabetic retinopathy visual loss occurs when vessels bleed or tractional retinal detachment ensues from fibrovascular proliferation. Without treatment 50% of patients with proliferative diabetic retinopathy become blind within 5 years.[2] Visual impairment and blindness in patients with proliferative diabetic retinopathy can be reduced by laser photocoagulation treatment and anti-vascular endothelial growth factor medicines.[1]

Diabetic retinopathy has been associated with factors such as poor glycemic control, hypertension[1], duration of diabetes mellitus, presence of diabetic nephropathy and dyslipidemia.[3] In developed countries the prevalence and incidence of sight threatening diabetic retinopathy is well documented whereas there is little published data on prevalence of diabetes retinopathy in sub-Saharan Africa.[1] Clinic based surveys in Africa report a prevalence range of diabetic retinopathy of 7.0 to 62.4%.[2] In Zimbabwe the last study on diabetic retinopathy was done two decades ago (October 1995 to April 1996) in which an overall prevalence of 27.5% was reported.[4]

Standard treatment guidelines on diabetes mellitus recommend annual eye examination; however, studies have documented limited use of ophthalmic services in Africa.[5-6] Thus, even though diabetic retinopathy is an important complication of diabetes mellitus, it is usually identified at a late stage when it is too late to save the sight of patients. Therefore it is critical that a study be carried out on prevalence and risk factors of diabetic retinopathy in a Zimbabwean population. This study sought to determine the prevalence of, and risk factors associated with, retinopathy in diabetic patients attending an out-patients clinic at Parirenyatwa Hospital, Harare.

METHODOLOGY

Study Population

An analytical cross-sectional study was carried out amongst adult diabetic patients (18 years and above) attending the out-patients clinic at Parirenyatwa Group of hospitals in Harare, Zimbabwe between October 2013 and July 2014. Parirenyatwa Group of hospitals is a tertiary referral teaching hospital in Harare, the capital city of Zimbabwe. All diabetic patients aged 18 years and above attending the outpatients' clinic at Parirenyatwa Group of hospitals in Harare, Zimbabwe during the study period (October 2013 and July 2014) who were willing and able to give an informed consent for participation into the study were consecutively enrolled.

Ethics

Ethical approval was obtained from the Joint Parirenyatwa hospital and College of Health Sciences ethics committee and Medical Research Council of Zimbabwe.

Ethnobiological Survey

Demographic data was collected using a questionnaire. A nurse performed anthropometric measurements: an analogue scale was used to measure the patient's weight to the nearest kilogram whilst a stadiometer was used to measure height to the nearest centimeter. The weight and height were used to calculate the body mass index. A manual mercury sphygmomanometer was used to measure the systolic and diastolic blood pressure after at least ten minutes in a sitting position. An average of two readings of blood pressure was used. Using the vacutainer method, two 4 ml blood samples were collected in each of plain and

ethylenediaminetetraacetic acid (EDTA) tubes by the nurse.

Retinopathy was diagnosed by an ophthalmologist using slit lamp indirect ophthalmoscopy with a 20-diopter and a 90-diopter lens. Diabetic retinopathy was diagnosed by the presence of a minimum of one microaneurysm in the examined field. Diabetic retinopathy was classified according to presence or absence of abnormal new vessels as non-proliferative (background/preproliferative retinopathy) and proliferative retinopathy. The presence of macular edema/maculopathy and cataracts were also recorded.[7]

The Zimbabwe national guidelines were used to categorize diabetes mellitus into type 1 and type 2 diabetes mellitus. Type 1 diabetes mellitus was defined as disease diagnosed usually before the age of 30 years and treated with diet and insulin. Type 2 diabetes mellitus was defined as disease diagnosed after 30 years of age, treated with diet and oral hypoglycemic agents. However, some of the type 2 patients may eventually require insulin.[5]

Laboratory investigations

Blood in the plain tubes was centrifuged at 3000 revolutions per minute for five minutes on the day of collection and the serum harvested was used for analysis of triglycerides by the glycerokinase peroxidase-peroxidase method, total cholesterol by the cholesterol oxidase-peroxidase method, HDL cholesterol by the direct method and serum creatinine by the modified Jaffe method. The blood in the EDTA tubes was used for glycosylated hemoglobin analysis by the enzymatic method. All the biochemical measurements were made using a BS120 Mindray analyzer, Shenzhen, China. Before samples were analyzed, the analyzer was calibrated according to the manufacturer's instructions using standards and two sets of controls supplied by the manufacturer. Creatinine clearance was calculated using the Chronic Kidney Disease Epidemiology Collaboration [CKD-EPI] equation.[8]

Data Analysis

STATA version 13.1 was used for statistical analysis. The Student's t-test was used to compare all normally distributed data. Mann-Whitney U test was used to compare skewed data. The chi-square test was used to compare proportions. Quantitative data was expressed as mean ± standard deviation whilst skewed data was indicated as median and inter-quartile range. Age, body mass index, systolic blood pressure, diastolic blood pressure, total cholesterol, HDL cholesterol and serum creatinine clearance were normally distributed. Duration of diabetes mellitus, triglycerides and glycosylated hemoglobin were skewed. A $p<0.05$ was considered significant. Univariate and multivariate analysis using logistic regression were performed. The multivariate analysis was performed for variables that were significant (p value=0.25) in univariate analysis whilst adjusting for type of diabetes mellitus.

RESULTS

A total of 340 patients were enrolled into the study, of whom 249 (73.2%) were female. Overall mean (SD) age was 57.5 (14.9) years. There was no difference in age between females [57.6 (14.1) years] and males [57.2 (16.8) years] (p=0.810). The majority of the patients [75.6%] had type 2 diabetes mellitus.

There were five patients who could not be classified due to lack of fundus view caused by mature cataracts. Thus, overall, prevalence of retinopathy was 28.4% (95/335). Retinopathy was not classified in 13 (13.7%) of the 95 retinopathy patients. Of the 82 who were classified, 44 had non-proliferative retinopathy, 31 proliferative retinopathy and 7 had clinically significant macular edema giving overall prevalences

(N=335) of 13.1%, 9.3% and 2.1% respectively.

The prevalence of retinopathy was slightly higher in type 1 diabetes mellitus (27/80, 33.8%) than in type 2 diabetes mellitus (68/255, 26.7%) but the difference was not statistically significant (p=0.220). Cataracts were found in 40.6% (138/340) and glaucoma in 5.9% (20/340) of the diabetic patients.

Table 1 shows characteristics associated with diabetic retinopathy in type 1 diabetes mellitus patients. Longer duration of diabetes mellitus [OR 1.09 CI (1.03 – 1.15)], higher total cholesterol [OR 1.37 CI (1.02-1.84)], higher HDL cholesterol [OR 3.00 CI (1.04-8.55)] and lower creatinine clearance [OR 0.98 CI (0.97 – 0.99)] were significantly associated with diabetic retinopathy in univariate analysis.

As shown in **Table 2**, prevalence of retinopathy was significantly higher in type 2 patients with longer duration of diabetes mellitus [OR 1.05 CI (1.02 – 1.08)], higher systolic blood pressure [OR 1.02 CI (1.00 – 1.03)] and lower creatinine clearance [OR 0.98 CI (0.97 – 0.99)].

Table 3 shows overall factors associated with diabetic retinopathy. In multivariate analysis only longer duration of diabetes mellitus [OR 1.06 CI (1.03 – 1.09)] and lower serum creatinine [OR 0.99 CI (0.97 – 1.00)] remained significant predictors of diabetic retinopathy. The median duration in patients with diabetic retinopathy was 3.5 times more than in patients without diabetic retinopathy.

Table 1: Univariate analysis of characteristics of type 1 diabetes mellitus patients with and without diabetic retinopathy

	Diabetic retinopathy		**Univariate analysis**	
	Yes (N= 27)	No (N = 53)	Odds ratio (95% CI)	p value
Sex Female Male	20 (37.7%) 7 (26.0%)	33 (62.3%) 20 (74.0%)	0.58 (0.21-1.61)	0.293
Age/ years	52.7±13.3	45.0±18.2	1.03 (1.00-1.06)	0.058
Duration of diabetes mellitus/ years	14.8 (11.8-22.6)	4.3 (1.6-12.9)	1.09 (1.03-1.15)	<0.001
Body mass index/Kg/m^2	26.1±5.4	25.8±5.2	1.01 (0.93-1.11)	0.802
Systolic blood pressures/mmHg	151.0 (142.0-177.0)	141.0 (128.0-161.0)	1.02 (1.00-1.04)	0.067
Diastolic blood pressure/mmHg	84.0 (77.0-90.0)	80.0 (73.0-88.0)	1.01 (0.98-1.05)	0.540
Triglyceride/mmol/L	0.88 (0.66-1.86)	0.99 (0.66-1.44)	1.18 (0.55-2.50)	0.673
Total cholesterol/ mmol/L	5.1±2.0	4.2±1.4	1.37 (1.02-1.84)	0.035
HDL cholesterol/mmol/L	1.44±0.54	1.19±0.45	3.00 (1.04-8.55)	0.043
Glycosylated hemoglobin /%	8.5 (7.6-9.7)	7.6 (6.2-9.9)	1.05 (0.89-1.23)	0.570
Serum creatinine clearance/ml/min/1.73m^2	78.0 (55.0-97.0)	94.0 (69.0-110.0)	0.98 (0.97-0.99)	0.031

Table 2: Univariate analysis of characteristics of type 2 diabetes mellitus patients with and without diabetic retinopathy

	Diabetic retinopathy		Univariate analysis	
	Yes (N=68)	No (N= 187)	Odds ratio (95% CI)	p value
Sex Female Male	51(26.6%) 17 (27.0%)	141(73.4%) 46 (73.0%)	1.02 (0.54-1.94)	0.948
Age/ years	61.8±9.9	60.0±13.4	1.01 (0.99-1.03)	0.310
Duration of diabetes mellitus/ years	13.6 (4.5-22.3)	4.2 (1.3-12.0)	1.05 (1.02-1.08)	<0.001
Body mass index/Kg/m^2	26.2±5.5	27.0±5.3	0.97 (0.92-1.03)	0.320
Systolic blood pressures/mmHg	160.7±24.3	151.4±23.5	1.02 (1.00-1.03)	0.007
Diastolic blood pressure/mmHg	85.9±14.1	82.5±13.1	1.02 (1.00-1.04)	0.078
Triglyceride/mmol/L	1.36 (0.90-1.72)	1.25 (0.89-1.90)	0.85 (0.62-1.16)	0.305
Total cholesterol/mmol/L	5.0±1.6	4.6±1.3	1.18 (0.97-1.44)	0.096
HDL cholesterol/mmol/L	1.20±0.35	1.13±0.34	1.76 (0.82-3.86)	0.159
Glycosylated hemoglobin /%	8.7 (7.5-10.8)	8.1 (6.6-10.4)	1.09 (0.98-1.21)	0.121
Serum creatinine clearance/ ml/min/1.73m^2	67.6±21.1	78.1±23.3	0.98 (0.97-0.99)	0.002

Table 3: Logistic regression analysis of factors associated with overall diabetic retinopathy

	Diabetic retinopathy		Univariate analysis		Multivariate analysis	
	Yes (N =95)	No (N = 240)	Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value
Sex Female Male	71 (29.0%) 24 (26.7%)	174 (71.0%) 66 (73.3%)	0.89 (0.52-1.53)	0.677	N/A	
Age/ years	59.2±11.6	56.7±15.8	1.01 (1.00-1.02)	0.157	0.98 (0.95-1.00)	0.101
Duration of diabetes mellitus	14.7 (5.6-22.4)	4.2 (1.4-12.0)	1.06 (1.03-1.08)	<0.001	1.06 (1.03-1.09)	<0.001
Body mass index Kg/m^2	26.2± 5.4	26.7±5.3	0.98(0.94-1.03)	0.410	N/A	
Systolic blood pressures mmHg	159.6± 24.3	150.2± 23.8	1.02 (1.01-1.03)	0.001	1.01(1.00-1.03)	0.076
Diastolic blood pressure/mmHg	85.3± 13.1	82.4± 13.4	1.02 (1.00-1.03)	0.073	1.00(0.98-1.03)	0.985
Triglyceride mmol/L	1.21 (0.77-1.72)	1.21 (0.83-1.76)	0.87 (0.66-1.14)	0.309	N/A	
Total cholesterol mmol/L	5.0±1.7	4.5 ± 1.3	1.23(1.05-1.45)	0.010	1.05(0.86-1.29)	0.607
HDL cholesterol mmol/L	1.27± 0.44	1.15± 0.37	2.23(1.20-4.10)	0.008	1.34(0.64-2.79)	0.435
Glycosylated hemoglobin %	9.1± 2.41	8.6± 2.7	1.07 (0.98-1.17)	0.113	1.05 (0.95-1.17)	0.341
S creatinine clearance ml/min/1.73m^2	69.5±23.9	81.1±26.7	0.98 (0.97-0.99)	<0.001	0.99 (0.97-1.00)	0.025
Diabetes mellitus Type 1 Type 2	 27 68	 53 187	 1 0.71 (0.42-1.23)	0.220	0.81 (0.42-1.58)	0.541

DISCUSSION

The prevalence of diabetic retinopathy in this study was high and similar to that reported in a study conducted between October 1995 and April 1996 at the same hospital. This was despite the exclusion of diabetic patients below the age of 30 years in the previous study.[4] The similarity in prevalence between the current study and the previous study could be explained by the fact that even though age 18 years and above was the inclusion criteria in the current study, the mean age was 57.5 years and median duration of diabetes mellitus was 14.7 years, indicating that most of the patients were elderly. The prevalence in the current study is within the reported prevalence of diabetic retinopathy in diabetic clinic based surveys in Africa of 7.0 to 62.4%, which is a wide range. The wide range is due to the fact that the studies in Africa were highly heterogeneous in patient selection, method of assessment and classification of retinopathy.[2]

The prevalence of diabetic retinopathy in the current study was higher than the 21% reported in Mekelle Hospital in Ethiopia. In the Ethiopian study, the patients had a mean diabetes mellitus duration of 7 years[9], which is half of the median diabetes duration in retinopathy patients in the current study. The patients in the current study also had a higher mean age than those in the Ethiopian study. It has been reported that older patients with prolonged diabetes mellitus are more likely to develop retinopathy.[10] The difference in prevalence of diabetic retinopathy can also be attributed to differences in socioeconomic factors which include access to and level of diabetic care, and genetic susceptibility.[3]

The current findings of constant overall prevalence of diabetic retinopathy when compared with a previous study in the same clinic two decades ago is similar to what was reported in United Kingdom where the prevalence of diabetic retinopathy was constant over two decades. This is in spite of global increase in diabetes mellitus prevalence, changing population composition and improved diagnostic criteria and examination techniques. There is no scientific explanation for the constant overall prevalence over two decades.[11] We postulate the reasons for this constant overall prevalence despite better diagnostic capability could be the poor glucose control and health care seeking behavior of the patients which could have remained unchanged over the two decades.

The prevalence of retinopathy in this study was similar in type 1 and type 2 diabetes mellitus patients. The prevalence of retinopathy in type 1 diabetes mellitus patients in the current study is similar to that reported in Queen Elizabeth Central Hospital, Malawi [March 2007–June 2007]. Whilst the prevalence of retinopathy in type 2 diabetes mellitus in the current study is lower than that found in Queen Elizabeth Central Hospital, Malawi (March 2007–June 2007).[1]

Proliferative diabetic retinopathy and clinically significant macular edema are sight threatening.[12] The prevalence of proliferative diabetic retinopathy was higher than the reported prevalence of proliferative diabetic retinopathy in diabetic clinic based studies in Africa of 0–6.9% whilst the prevalence of clinically significant macula edema was within the reported prevalence of 1.2–31.1%. However it is important to note that these studies in Africa were highly heterogeneous in patient selection, method of assessment and classification of retinopathy.[2] The risk factors for the progression to proliferative diabetes retinopathy are duration and poor glycemic control.[10] In the current study poor glucose control amongst patients was observed, which was indicated by glycosylated hemoglobin levels higher than the target of 7% in both patients with and without diabetic retinopathy.

Hyperglycemia does contribute to high prevalence of diabetic complications that include diabetic retinopathy.[9]

In univariate analysis there was an association of systolic blood pressure with diabetic retinopathy, which was not found in a multivariate analysis. Similar findings were reported in Malawi. This demonstrates that the incidence and progression of diabetic retinopathy is reduced by tight control of blood pressure as previously shown in the United Kingdom prospective diabetes study group.[1] Higher total cholesterol and HDL cholesterol were associated with diabetic retinopathy in type 1 diabetes mellitus patients and in overall diabetic retinopathy. The contribution of lipids to pathogenesis of diabetic retinopathy has not yet been fully elucidated.[13]

Diabetic retinopathy was also strongly associated with longer duration of diabetes mellitus and lower serum creatinine in both univariate and multivariate analysis. Duration of diabetes mellitus is a well-known diabetic retinopathy factor.[3] Lower serum creatinine clearance is indicative of renal damage which has been previously associated with diabetic retinopathy in the United Kingdom Prospective diabetes study.[1]

Cataract prevalence was 40.6%, of which 5 of the patients could not be classified due to poor fundus view caused by the cataracts. Glaucoma was also found in 5.9% of the patients. It is also important to highlight that cataracts and glaucoma on their own are also causes of visual impairment. The global principal causes of visual impairment are uncorrected refractive errors (43%), cataracts (33%), glaucoma (2%), age related macula degeneration (1%) and diabetic retinopathy (1%).[3]

Study limitations

This was a clinic-based study, which can be subject to a significant selection bias. However, it is important to note that patients travel long distances to health facilities as evidenced by the addresses of patients recorded in the study register; thus, rural patients are included in this study though the results should be extrapolated with caution.[2] We were unable to carry out fundus photography which is the gold standard for diagnosis of diabetic retinopathy. However, ophthalmoscopic evaluation by an experienced ophthalmologist has been reported to have acceptable sensitivity.[3]

CONCLUSION

The prevalence of diabetic retinopathy in this study was 28.4%. Longer duration of diabetes mellitus and lower serum creatinine, which is a marker of renal damage, were independent risk factors of diabetic retinopathy.

Adherence to annual eye examination in diabetes mellitus patients as documented in the national guidelines to enable early diagnosis and treatment of diabetic retinopathy and other causes of visual disability such as cataracts and glaucoma are recommended. A countrywide survey of diabetic retinopathy is also recommended to confirm these results.

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