ORIGINAL ARTICLE

Risk Factors for Retinopathy in Diabetes Mellitus in Kelantan, Malaysia

S R Shriwas, MS*, A B Rahman Isa, MPH**, S C Reddy, MS*, M Mohammad, MRCP***, W B W Mohammad, MRCP***, M Mazlan, PhD****, *Department of Ophthalmology, **Department of Community Medicine, ***Department of Medicine, ****Department of Chemical Pathology, School of Medical Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan

Summary

Few attempts have been made to determine the risk factors for diabetic retinopathy which is a major cause of visual impairment and blindness. One hundred and forty patients of diabetes mellitus were studied to determine the prevalence and types of retinopathy, and its relation to various risk factors. Nearly half (48.6%) of the patients suffered from retinopathy. The significant associated risk factors were long duration of diabetes, proteinuria and elevated serum creatinine level. However, there was no significant association between the prevalence of retinopathy and high levels of serum cholesterol, C-peptide levels, associated hypertension, and glycaemic control of diabetes mellitus. An effective screening programme for detection of retinopathy in the patients of diabetes as a regular practice is encouraged.

Key Words: Diabetes mellitus, Diabetic retinopathy, Risk factors for diabetic retinopathy

Introduction

Diabetic retinopathy is a major cause of visual impairment and blindness in economically advanced countries and its prevalence as reported in different surveys varied from 20-79% of the diabetic population[1-6]. Precise quantification of the prevalence of diabetic retinopathy in different communities is important for health services planners. Few attempts have been made to determine the risk factors of diabetic retinopathy in Malaysia. Its relationship to various risk factors such as age, sex, ethnic group, type of diabetes, family history of diabetes, smoking habit, hypertension, socio-economic status, body mass index, serum cholesterol level, serum creatinine level, proteinuria, control of diabetes and duration of diabetes have been reported previously[1-9]. All but one of these studies were done in developed countries. The single study from Malaysia[6] showed that the overall prevalence of retinopathy was comparable with western countries and Japan. However, this study did not consider biochemical parameters such as glycosylated haemoglobin (HbA1), serum creatinine, serum cholesterol, C-peptide, proteinuria or other factors such as body mass index and socio-economic status.

Segato *et al*[1] reported that the prevalence of retinopathy was significantly related to both fasting and post prandial blood glucose levels, blood urea, nitrogen, systolic and diastolic blood pressure. They found no relationship with family history of diabetes, alcohol intake, smoking habits, and blood levels of cholesterol, triglycerides and serum uric acid. Klein *et al*[2] on the other hand found that retinopathy was related to longer duration of diabetes, higher glycosylated haemoglobin levels, higher systolic blood pressure, presence of proteinuria and low body mass index. Adult onset diabetic patients are at risk for the development of vision threatening retinopathies as a result of microvascular changes. This pathological manifestation of diabetes is an important causative factor in the age-related decline in vision that has been reported in population based studies.

Sparrow *et al*[5] reported risk factors for retinopathy to be longer diabetes duration, female sex, higher blood pressure, use of antihypertensive drugs and cigarette smoking. Jerland and Algvere[4] reported a significant correlation of retinopathy with higher levels of glycosylated haemoglobin while a low prevalence of retinopathy was correlated with high body mass index.

It has been reported earlier that diabetes has now become a problem of developing countries[10] and retinopathy is a common complication which may result in blindness. A diabetic survey conducted in two districts of Kelantan state of Malaysia revealed 8.4% diabetes mellitus in the population[11], which is similar to 8.6%[12] and 8.2%[13] reported recently from Singapore and Malaysia respectively. However, it is much higher than 0.65%[14] and 3.5%[15] reported earlier from Malaysia. In view of the high prevalence of diabetes in Kelantan, one wonders if there is a similarly greater percentage of population in Kelantan having diabetic retinopathy. Hence, this study was planned to determine the overall prevalence and types of retinopathy in patients with diabetes mellitus and its relationship to various risk factors.

Patients and Methods

One hundred and forty patients, who attended the diabetic clinic of Hospital Universiti Sains Malaysia, between September 1992 and August 1994, underwent ophthalmic examination during a single visit to the eye clinic. The medical history relevant to diabetes (type, age at onset, duration, parent or relative affected, hypertension and therapy), patient's smoking habit and socio-economic status (monthly income of RM less than 500 as low, 500-1000 as middle and more than 1000 as high) were recorded. The height, weight and body mass index (BMI) were recorded. The BMI was classified as normal if less than 25, overweight if 25-30 and obese if more than 30. Blood pressure was measured in the sitting position after a 5 minute rest. Venous blood (fasting) was collected and analyzed for glycosylated haemoglobin (HbA1) (Eagle's diagnostic, USA), serum cholesterol (Cholesterol enzymatic PAP), serum creatinine (Jaffe method, Bio-Meriexu, France) and C-peptide (Radio Immuno Assay, Inostar Corporation, USA) using commercial kits. The presence of proteinuria was also estimated semi-quantitatively using Albusticks (Boehringer Mannheim, Germany). Patients were considered to be suffering from nephropathy if either serum creatinine level was more than 97 µmol/L or proteinuria was present. Hyperlipidemia was defined as serum cholesterol level more than 6.2 mmol/L and inadequate B-cell reserve as a C-peptide fasting level of less than 0.63 mmol/ml. Patients were divided into non-insulin dependent diabetes mellitus (NIDDM) and insulin dependent diabetes mellitus (IDDM) groups[16]. Duration of diabetes and its treatment was calculated from the age of onset of the diabetes. Glycaemic control was assessed by glycosylated haemoglobin (HbA1) level: good if less than 8%, fair between 8% and 10% and poor control if more than 10% (Eagle's Diagnostic Kit USA).

After recording the ocular history (defective vision, laser treatment, eye operation etc), the best corrected visual acuity was tested on Snellen's distant vision charts. Slit-lamp biomicroscopy was performed to detect cataract or new vessels on the iris. Intraocular pressure was measured with Goldman's applanation tonometer. Direct and indirect ophthalmoscopic examination of the retina was carried out after dilatation of pupils with 1% tropicamide eye drops. Retinopathy was classified[17] as (i) background if microaneurysms, dot and blot haemorrhages or hard exudates were present, (ii) pre-proliferative if cotton wool spots were present, (iii) proliferative if any neo-vascularization was present (iv) maculopathy if hard exudates were present in macula, (v) advanced diabetic eye disease if persistent vitreous haemorrhage, retinal detachment, opaque membrane or neo-vascular glaucoma were present and, (vi) no retinopathy or worse eye if there was a difference in the finding of two eyes. Statistical analysis was computed by using Chi-squared test based on maximum likelihood ratio[18].

Results

One hundred and twenty nine of 140 patients were suffering from NIDDM and 11 from IDDM (Table I). Retinopathy was not significantly related to the age, sex, ethnicity, socio-economic status, body mass index, smoking habits of the patients, family history of diabetes and associated hypertension. The prevalence of retinopathy was found to be higher in the IDDM (63.6%) than the NIDDM (47.3%). The prevalence of retinopathy was

Table I
Association between socio-demographic parameters and retinopathy in diabetes mellitus

Parameter	No. of patients	No. with retinopathy (%)
Sex		
Male	66	32 (48.5)
Female	74	36 (48.6)
Age (years)		
0 - 20	1	- -
21 - 40	23	8 (34.4)
41 - 60	92	45 (48.9)
61 - 80	24	15 (62.5)
Ethnicity		
Malay	116	57 (49.1)
Chinese	23	11 (47.8)
Indian	1	- -
Type of diabetes		
IDDM	11	7 (63.6)
NIDDM	129	61 (47.3)
Socio-economic status		
Low	19	9 (47.4)
Middle	110	54 (49.1)
High	11	5 (45.5)
Body mass index		
Normal	77	42 (54.6)
Overweight	53	20 (37.7)
Obese	8	4 (50.0)
Family history of diabetes		
Present	57	33 (57.9)
Absent	83	35 (42.2)
Smoking habits		
Smoker	45	21 (46.7)
Non-smoker	81	43 (53.1)
Associated hypertension		
Present	65	37 (56.9)
Absent	75	31 (41.3)
Duration of diabetes (years)		
<5	46	12 (26.1)*
5 - 10	53	28 (52.8)
11 - 20	33	21 (63.6)
>20	8	7 (86.5)

** p < 0.005*

significantly associated with the duration of diabetes ($p<0.005$). Retinopathy was not significantly associated with high levels of serum cholesterol, C-peptide levels, and glycaemic control of diabetes mellitus (Table II). However, the prevalence of retinopathy was significantly associated with high serum creatinine ($p<0.007$) and proteinuria ($p<0.04$). Seventy-two patients did not show any changes of diabetic retinopathy (Table III). The overall prevalence of retinopathy in diabetes mellitus was 48.6%, background diabetic retinopathy being the commonest type. Forty- five patients had cataract changes and three had chronic simple glaucoma. Diabetic retinopathy was responsible for gross diminution of vision (6/60 or less) in 21 patients.

The results of one or two parameters were not present in the data forms of some patients at the time of

Table II
Association between biochemical parameters and retinopathy in diabetes mellitus

Parameter	No. of patients	No. with retinopathy (%)
Serum creatinine		
High level	60	37 (61.7)*
Normal level	73	27 (36.9)
Proteinuria		
Present	37	23 (62.2)#
Absent	94	40 (42.6)
Serum cholesterol		
High	62	33 (53.2)
Normal	71	32 (45.1)
C-peptide		
Adequate	22	12 (54.5)
Inadequate	108	48 (44.4)
Glycaemic control (HbA1) of diabetes mellitus		
Good	22	10 (45.5)
Fair	54	25 (46.3)
Poor	62	33 (53.2)

** p < 0.007, # p < 0.04*

analysis, and hence there is a difference in the total number of some risk factors in Tables I and II. However, in these patients at least thirteen out of fifteen variables were covered which justified their inclusion in the analysis of results.

Discussion

In our study, the overall prevalence of retinopathy was 48.6%, which is comparable to the prevalence rate of 44.1% reported from University Hospital, Kuala Lumpur[6]. However, it was lower than the rate of 77.8% reported by Klein *et al*[19]. This may be due to a difference in criteria for selection of subjects in their study. There was no significant association of retinopathy with either of the two types of diabetes mellitus in our study. This shows that the type of diabetes does not influence the development of retinopathy. However, previous studies[1,20] revealed a higher prevalence of retinopathy in individuals receiving insulin therapy than in those taking oral hypoglycaemic agents.

In the present study the retinopathy was equally distributed between the two sexes. Our subjects were drawn largely from Malay population, and is reflected by the number of Malays in our diabetic sample. The prevalence of retinopathy was similar among Malays and Chinese. Influence of ethnic factor in the development of diabetic retinopathy has been reported in Jewish population[9]. In our study, age did not have any relation to the prevalence of retinopathy. Segato *et al*[1] reported that duration of diabetes alone accounts for increasing prevalence of retinopathy, with no influence of age at examination. The prevalence of retinopathy was significantly associated with the duration of diabetes in our study (Table I), which is similar to previous studies[1,2,4-7]. Hence, duration of diabetes plays a more important role in the development of retinopathy than other factors.

There are many publications relating control of diabetes with the prevalence of diabetic retinopathy[21-23]. However, there was no significant relationship between retinopathy and glycaemic control in our study. The probable reasons are that the number of patients in our study was small and glycosylated haemoglobin was measured only once at the time of examination instead of at regular intervals during study. Prevalence of retinopathy was significantly higher in patients with

Table III
Types of retinopathy in diabetes mellitus

Type of retinopathy	NIDDM (n=129) No.(%)	IDDM (n=11) No.(%)	Total (n=140) No.(%)
No retinopathy	68 (52.7)	4 (36.3)	72 (51.4)
Background	37 (28.7)	6 (54.6)	43 (30.7)
Preproliferative	4 (3.1)	-	4 (2.8)
Proliferative	4 (3.1)	1 (9.1)	5 (3.6)
Advanced diabetic eye disease	2 (1.6)	-	2 (1.4)
Maculopathy	14 (10.8)	-	14 (10.0)

NIDDM = Non-insulin dependent diabetes mellitus
IDDM = Insulin dependent diabetes mellitus

high creatinine level as well as in those with proteinuria (Table II). This result supports the findings of previous studies[1,2,8]. Diabetic nephropathy also aggravates retinopathy, especially maculopathy[9]. Hence, proteinuria is predictive of retinopathy and nephropathy.

There was also no significant association between diabetic retinopathy and hypertension. This may be due to antihypertensive treatment of these patients. However, the presence of hypertension has been reported to aggravate the prevalence of diabetic retinopathy[19]. Dodson and Gibson[24] listed hypercholesterolaemia as a risk factor in non-insulin dependent diabetes mellitus in addition to hypertension. However, hyperlipedemia was not associated with retinopathy in the present study (Table II).

Family history of diabetes, smoking and socio-economic status were not associated with retinopathy in this study. However, a positive family history of diabetes in Malays has been reported earlier[25]. The effect of cigarette smoking on macrovascular disease is well recognised but its impact on microvascular disease is not well documented and evidence has not always been consistent[8]. Socio-economic status of a person has been reported to influence development of microvascular complications[9].

Although in our study BMI had no influence on retinopathy, a high BMI has been reported in association with a low prevalence of retinopathy[4]. Level of serum C-peptide is an important indicator of insulin secretion[26]. In the present study, prevalence of retinopathy was not significantly different in those with adequate C-peptide levels compared to patients with inadequate C-peptide levels. Retinopathy of background type was most common (28.7%) in NIDDM patients (Table III). This result is comparable with 24.4% reported by Segato *et al*[1]. The most common cause of blindness was maculopathy in our study which has also been reported by Henkind[27].

The present study demonstrated that nearly half of the diabetic population suffered from retinopathy. The significant associated risk factors were long duration of diabetes, proteinuria and serum creatinine level. There is a high prevalence of retinopathy in this population. Hence, an effective screening programme for detection of diabetic retinopathy is encouraged. Physicians and general practitioners should be able to recognise those patients who have risk factors such as longer duration of diabetes and proteinuria. Such patients should be referred to the ophthalmologist for early detection of retinopathic changes.

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