Original Article

RISK FACTORS FOR DIABETIC RETINOPATHY IN DIABETICS SCREENED USING FUNDUS PHOTOGRAPHY AT A PRIMARY HEALTH CARE SETTING IN EAST MALAYSIA

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ABSTRACT

Introduction: This study reports on the prevalence of diabetic retinopathy (DR) and risk factors among diabetic patients, who underwent fundus photography screening in a primary care setting of Borneo Islands, East Malaysia. We aimed to explore the preliminary data to help in the planning of more effective preventive strategies of DR at the primary health care setting.

Materials and Methods: A cross-sectional study on 738 known diabetic patients aged 19-82 years was conducted in 2004. Eye examination consists of visual acuity testing followed by fundus photography for DR assessment. The fundus pictures were reviewed by a family physician and an ophthalmologist. Fundus photographs were graded as having no DR, NPDR, PDR and maculopathy. The data of other parameters was retrieved from patient's record. Bi-variate and multivariate analysis was used to elucidate the factors associated with DR.

Results: Any DR was detected in 23.7% (95% CI=21 to 27%) of the patients and 3.2% had proliferative DR. The risk factors associated with any DR was duration of DM (OR =2.5, CI=1.6 to 3.9 for duration of five to 10 years when compared to <5 years) and lower BMI (OR=1.8, CI=1.1 to 3.0). Moderate visual loss was associated with DR (OR=2.1, CI=1.2 to 3.7).

Conclusions: This study confirms associations of DR with diabetic duration, body mass index and visual loss. Our data provide preliminary findings to help to improve the screening and preventive strategies of DR at the primary health care setting.

Key Words: Diabetic retinopathy, epidemiology, screening, primary health care, Malaysia.

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INTRODUCTION

Diabetes mellitus (DM) is a significant public health problem worldwide. The total number of people with diabetes is projected to increase from 171 million in 2000 to 366 million in 2030.[1] The prevalence of DM is expected to reach epidemic proportions with the main burden of disease in developing countries.[2] World Health Organisation (WHO) estimates a 3-fold rise of the disease in Asia.[2]

The prevalence of DM in Malaysia has increased from 0.6% in 1960 to 14.9% in 2006.[3] Reasons for the increase in prevalence includes rapid urbanisation with reduced physical activities, changes in the dietary habits, longevity, reduction in the death rates and increase prevalence of obesity.

Diabetic retinopathy (DR) is a common complication of both type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM).[4] The prevalence of DR increases with the duration of diabetes and the patient's age. Other risk factors are: systemic arteriosclerosis, anaemia, renal impairment and pregnancy.[5-7] DR is the leading cause of blindness in the working-aged people.[8] The prevalence of DR is likely to increase with the projected increase of T2DM in the developing countries,[2] adding to the

already existing burden of preventable blindness diseases like cataract, corneal disease, refractive error and retinal diseases. The prevalence of all DR in Malaysia was 12.3% for T1DM and 22.3% for T2DM.[9] Most published Malaysian data are primarily hospital based.[9-12] This study reports on the prevalence of DR and risk factors among diabetic patients, who underwent fundus photography screening in a primary care setting of Sarawak, East Malaysia. With the limited funding, this study aimed to explore the preliminary data to help in the planning of more effective screening and preventive strategies of DR at the primary health care setting. Sarawak has the largest land area of all the 13 states in Malaysia, situated in the Borneo Islands. The total population is about 2.07 million of which nearly 579,900 people live in the state capital, Kuching.[13]

MATERIALS AND METHODS

This study is a cross-sectional prospective study conducted on all diabetes patients who had undergone screening fundus photography in 2004, in Jalan Masjid Health Centre (KKJM). This clinic is the largest of the three public primary health care clinics in Kuching. Nearly 4500 diabetic patients were registered in the diabetes clinic in KKJM. Fundus photography for the assessment of DR was introduced at KKJM in the year 2004. All patients who were not previously diagnosed to have DR were included for the fundus photography screening at the primary care clinic. Patients who had cataracts for which fundus photography could not be done or those with fundus photographs that were unreadable were excluded. Our study was approved by the Malaysian IRB/IEC MOH Research & Ethics Committee (MREC) (NMRR-10-836-6973). Data was retrieved from the clinic based diabetes cards and the fundus photography assessment forms.

Information obtained included: socio demographic details, type of diabetes, duration of diabetes, compliance to treatment (based on patients' self-report from health provider interview and regularity of follow-up), presence or absence of systemic hypertension, proteinuria or microalbuminuria, coronary heart disease, awareness of DR, any prior review by an ophthalmologist, presence of visual complaints and smoking status. The following parameters were also included in the study: body mass index (BMI), blood pressure (BP), glycosylated haemoglobin (HbA$_{1c}$) and fasting lipid profile (total cholesterol, triglycerides, low density lipoprotein [LDL], high density lipoprotein [HDL]).

The diagnosis of DM was made according to the Malaysian Diabetes Practice guidelines.[14] The target for control of DM and hypertension were based on the recommendations by the International Diabetic Federation (IDF),[15] where HbA$_{1c}$ of <6.5% is optimal, 6.5 to 7.5% is fair and >7.5% is sub-optimal. The BP target for control was categorised into optimal <130/80 mmHg, fair 130/80 to 140/70 mmHg and sub-optimal >140/90 mmHg.

The target for lipid profile was total cholesterol $\leq$4.5 mmol, triglyceride $\leq$1.7 mmol/L, LDL-C $\leq$2.6 mmol and HDL-C $\geq$1.1 mmol/L.[16] The classification of obesity was based on Malaysian guidelines where BMI of <18.5 kg/m^2 is underweight, 23.0-27.4 kg/m^2 is overweight and $\geq$27.5 kg/m^2 is obese.[17] Smokers were defined as those who have a history of cigarette smoking in the past one month.

Eye examination consists of visual acuity testing by Snellen chart followed by fundus photography for DR assessment. Fundus photography was performed by a trained medical assistant using Topcon TRC-50VT camera (Topcon Corporation, Tokyo, Japan). Each eye was subjected to two non-stereoscopic 45° photographs; macula-centred and optic disc centred photograph. The photographic fields were equivalent to Diabetic Retinopathy Study (DRS) standard fields 1 and 2. The fundus pictures were reviewed by a family physician and an ophthalmologist. When there was disagreement, the ophthalmologist made the final decision. The eye with the more severe DR was taken into analysis. Visual loss was classified as mild (6/9 to 6/12), moderate (6/18 to 6/60) and severe (worse than 6/60). Fundus photographs were graded as having no DR, NPDR, PDR and maculopathy. The international clinical DR severity scale adopted by the American Academy of Ophthalmology (AAO)[18,19] were used to classify patients into non-proliferative diabetic retinopathy (NPDR), proliferative diabetic retinopathy (PDR) and maculopathy. NPDR was defined as present of any or more of the following: micro-aneurysms, intraretinal hemorrhage, venous beading, or intraretinal microvascular abnormalities (IRMAs) AND no signs of proliferative retinopathy. PDR was defined as neovascularization or vitreous or preretinal haemorrhage. Diabetic macular oedema (DME) was present when any retinal thickening or hard exudates were present in the posterior pole.

Data entry, cleaning and analysis was done using SPSS version 17.0 for windows. Socio-demographic characteristics of the study sample were analysed and presented using appropriate descriptive statistics. The Chi-square tests and Fischer exact test were used for bivariate analysis. Multiple logistic regressions were used to elucidate the various risk factors influencing the presence and the severity of DR. Variables with a *p* value of <0.05 was included in a multivariate model. All hypotheses tests were based on two-sided test and *p* value <0.05 was considered statistically significant.

RESULT

Characteristic and Health Profile of the study population

Our study consisted of 738 eligible patients. T2DM accounted for 97% of cases (n=720). The age of our study population ranges from 19 to 82 years with the mean of 54±10 years. Almost all cases (98.7%) were aged above 30. The mean duration of DM among our patients was 5.52 (SD 5.8 years). More than half

(55.8%) had DM for less than five years as summarised in Table 1.

Systemic hypertension was the most common co-morbidity found in our study population where 51.5% (n=380) has hypertension. About one third of the patients had sub-optimal control of hypertension (Table 1). In terms of glycaemic control, 75% (n=554) of the patients had sub-optimal HbA_{1c} level (Table 1). Majority of the patients did not achieve the targeted level of control for total cholesterol, LDL-cholesterol and triglyceride level (Table 1). Majority of patients, 85.6% (n=632) did not have proteinuria.

Table 1: Characteristic and Health Profile of the respondents (n=738)

Variables	Frequency, n (%)
Total cholesterol	
≤4.8 mmol/L	226 (30.6)
>4.8 mmol/L	512 (69.4)
TGL	
≤1.7 mmol/L	345 (46.7)
>1.7 mmol/L	393 (53.3)
LDL	
≤2.6 mmol/L	145 (19.6)
>2.6 mmol/L	593 (80.4)
HDL	
>1.1 mmol/L	490 (66.4)
≤1.1 mmol/L	248 (33.6)
Present of coronary artery disease	
Yes	12 (1.6)
No	726 (98.4)
Smoker	
Yes	6 (0.8)
No	732 (99.2)
Visual loss	
Normal 6/6	298 (40.4)
Mild 6/9 to 6/12	334 (45.3)
Moderate 6/18 to 6/60	106 (14.3)
Severe visual loss <6/60	0 (0)

Most of the patients (89.4%, n=660) had visual complaints, however, there were no patient with severe visual loss and blindness. 91.5% (n=675) were aware of DR. We found 175 out of the 738 cases (23.7%) to have DR changes. The majority of these, 86.2% (n=151) had non-proliferative retinopathy changes. Proliferative retinopathy changes were noted in 3.2% of the total patients screened. Maculopathy was seen in 2.7% (n=20).

Factors associated with diabetic retinopathy

Table 2 shows the present of DR and its association with different factors. Duration of diabetes, BMI, hypertension control and visual loss were found to be significantly associated with present of DR

in the bivariate analysis. Factors like gender, ethnicity, glycaemic control, present of proteinuria and lipid profiles were not significantly associated with the present of DR. Statistical analysis was not done for age, present of coronary artery diseases, anaemia and smoking status, as the number of patients were too small for those with DR. Significance levels of the variables by multivariate analysis are presented in Table 3. The odds of developing DR was 2.5 times higher for a patient with duration of diagnosis between five to 10 years when compared to a patients with <5 years of diabetes. The odds of developing DR were increasing as the duration of diabetes increases. Patients who were lean were more likely compared to obese and overweight to develop DR (OR=1.8). Moderate visual loss was associated with DR (OR=2.1). Multivariate logistric regression models for control of hypertension and separate analysis of systolic and diastolic BP found no significant association with the presence of DR.

Table 2: Prevalence of diabetic retinopathy and its association with different factors (Bivariate analysis between DR and non-DR)

Variables	Non-DR Frequency (N=563) (%)	DR Frequency (N=175) (%)	*p* value
Gender			
Male	249 (78.5)	68 (21.5)	NS
Female	314 (74.6)	107 (25.4)	
Ethnicity			
Sarawak native	116 (80.0)	29 (20.0)	NS
Non-native	447 (75.4)	146 (24.6)	
Duration of DM			
<5 yrs	354 (85.9)	58 (14.1)	<0.001*
5-10 yrs	117 (70.9)	48 (29.1)	
11-15 yrs	62 (62.0)	38 (38.0)	
16-20 yrs	15 (50.0)	15 (50.0)	
>20 yrs	15 (48.4)	16 (51.6)	
Age in interval			
19-29	9 (100.0)	0 (0)	
30-39	34 (87.2)	5 (12.8)	
40-49	139 (78.5)	38 (21.5)	
50-59	217 (73.3)	79 (26.7)	
60-69	118 (76.1)	37 (23.9)	
70-79	46 (74.2)	16 (25.9)	
BMI			
<22.9	72 (64.9)	39 (35.1)	0.002*
≥23.0	491 (78.3)	136 (21.7)	
HT control (mm/Hg)			
Optimal <130/80	157 (80.1)	39 (19.9)	0.026*
Fair 130/80 to 140/90	221 (78.9)	59 (21.1)	
Sub-optimal >140/90	185 (70.6)	77 (29.4)	
HbA_{1c} (%)			
Optimal <6.5	69 (85.2)	12 (14.8)	NS
Fair 6.5-7.5	83 (80.6)	20 (19.4)	
Sub-optimal >7.5	411 (74.2)	143 (25.8)	
Protein in urine			
Nil	491 (77.7)	141 (22.3)	NS
Microalbuminuria	14 (66.7)	7 (33.3)	
Proteinuria	58 (68.2)	27 (31.8)	
Total cholesterol			
≤4.8 mmol/L	170 (75.2)	56 (24.7)	NS
>4.8 mmol/L	393 (76.8)	119 (23.2)	

TGL			
≤1.7 mmol/L	268 (77.7)	77 (22.3)	NS
>1.7 mmol/L	295 (75.1)	98 (24.9)	
LDL			
≤2.6 mmol/L	115 (79.3)	30 (20.7)	NS
>2.6 mmol/L	448 (75.5)	145 (24.5)	
HDL			
>1.1 mmol/L	376 (76.7)	114 (23.3)	NS
≤1.1 mmol/L	187 (75.4)	61 (24.6)	
Present of coronary artery disease			
Yes	11 (91.7)	1 (8.3)	–
No	552 (76.0)	174 (24.0)	
Smokers			
Yes	4 (66.7)	2 (33.3)	–
No	559 (76.4)	173 (23.7)	
Visual loss			
Normal 6/6	241 (80.9)	57 (19.1)	0.001*
Mild 6/9 to 6/12	256 (76.6)	78 (23.4)	
Moderate 6/18 to 6/60	66 (62.3)	40 (37.7)	

* *p*-value significant from bivariate analysis   NS= not significant

Table 3: Adjusted[1] Odds Ratio for Factors associated with diabetic retinopathy

Variables	DR Multivariate value adjusted OR (95% CI)	*p* value
Duration of DM		
<5 yrs	1.0	<0.001
5-10 yrs	2.5 (1.6 to 3.9)	
11-15 yrs	3.7 (2.2 to 6.1)	
16-20 yrs	5.6 (2.5 to 12.3)	
>20 yrs	6.0 (2.8 to 12.9)	
BMI		
≥23.0	1.0	0.013
<22.9	1.8 (1.1 to 2.8)	
HT control (mm/Hg)		
Optimal <130/80	1.0	0.121
Fair 130/80 to 140/90	1.1 (0.7 to 1.8)	
Sub-optimal >140/90	1.6 (1.0 to 2.5)	
Visual loss		
Normal 6/6	1.0	0.009
Mild 6/9 to 6/12	1.0 (0.7 to 1.5)	
Moderate 6/18 to 6/60	2.1 (1.3 to 3.5)	

[1]Each odds ratio is adjusted for all other variables in the table

DISCUSSION

As about 20% of the patients were Sarawak native (Bidayuh, Iban and other natives) of which very little data were available for this ethnic group, our study found that the prevalence of retinopathy of the native were comparable to the other ethnic group.

The proportion of patients with DR in our study was 23.7%. This was much lower than the prevalence found in other hospital based studies[11,12] and some community base studies[20-22] in Malaysia, where DR were detected in 31-50% of the patients studied. This could be due to our study reported findings from a primary health care centre where fundus photography was done for screening of asymptomatic patients with diabetes. This group of patients might have less complication as patients with complications might have been referred to referral centres in hospitals. This figure was comparable with the prevalence range of 10.5-26.2% found in other population based studies in India and United Kingdom,[23-25] but it is lower compared to other community based studies in Singapore and China.[26-27] The Singapore study[26] were on patients being referred from the primary health care centres to the hospital, this group of patients may have been screened earlier before being referred, so the possibility of DR is higher. Secondly, the differences of the racial composition in these studies[26,27] where majority were Chinese whereas in our study, there were almost equal combination of Chinese, Malay and native, may have contributed to the differences. Although it was not statistically significant, the proportion of natives found to have DR were lower in our study. Further study is needed to explore these differences. NPDR was the commonest form of DR seen in our study which is consistent with other studies.[25-28]

Previous studies had found that patients with a longer duration of diabetes has a higher risk of developing DR.[26-27,29-34] We also found association between the duration of DM and the presence of DR. The odds of developing DR was 2.5 times higher for a patient with duration of diagnosis between five to 10 years when compared to a patients with <5 years of diabetes and the odds of developing DR increased 1.2 to 1.9 times with each increase of five years. Another local study[12] and studies from Singapore, Thailand and China found similar trend in association of duration of DM with the risk of developing DR.[26,27,34] However, Thailand's study[34] shown much lower odds ratio of DR development at the similar interval of disease duration. Better control of diabetes among patients in tertiary centres in the Thailand study[34] may be the contributing factor for the differences.

We found an inverse relationship between BMI and DR. Patients with lower BMI were more likely compared to obese and overweight to develop DR. Similar inverse relationship was reported in other studies in India.[23,35] However, the association of BMI and DR has not been consistently demonstrated in all studies. Study in China found no significant association of BMI and DR.[27] In some studies conducted in developed countries, higher BMI is associated with DR subjects with T2DM.[36,37]

Visual loss was associated with higher risk of DR in our study. Study in India also showed higher percentage of moderate to severe visual loss among patients with PDR.[28]

In our study, the control of systemic hypertension and separate analysis of systolic and diastolic BP was found not significantly associated with the presence of DR in the multivariate analysis.

This is inconsistent with another local hospital base study where hypertension were reported to be associated with higher risk of DR.[12] The low proportion of patients with BP at >140/90 mmHg (35.5%) in this study may have contributed to the differences in our findings.

Other studies found association of renal impairment, cardiovascular diseases and anaemia with DR.[5-7] The small number of patients reported with these risk factors from our study could have contributed to the negative findings.

Other studies reported higher HbA_{1c} levels positively associated with NPDR, PDR and macular oedema.[29,30] The disproportionately low numbers of patients with optimal HbA_{1c} may have contributed to the insignificant association of HbA_{1c} to the presence of DR in this study. Serum lipids have been found inconsistently associated with DR in various studies.[38-41] Although majority of our patients had dyslipidemia, but we could not find any significant association of serum lipids with DR. The negative findings of this association found from our study add further evidence to the inconsistency of this association.

There were some limitations in our study. Firstly, the cross-sectional nature of the study cannot provide temporal information for the significant associations reported. Secondly, we did not have the information of the blood glucose level in our patients. Thirdly, socio economic and psychosocial factors, health care access and utilisation factors which was not assessed in this study, may modified the relationship between the known risk factors and risk of having DR.[42] Fourthly, our fundus photography included only the standard 2-fields out of the standard 7-fields. These could have underestimated the actual prevalence of DR. Finally, the relatively small number of people with proliferative DR and macular oedema limits our ability to assess associations with these subtypes of DR.

In summary, this study provides data on risk factors associated with DR in a mixed ethnic population including native in Borneo Islands at a primary health care setting. We confirm associations of DR with diabetic duration, BMI and visual loss. Our data provide preliminary findings to help to improve the preventive strategies at the primary health care setting. Ideally, according to the guideline,[16] all patients with diabetes should have screening fundus examination done at least once a year. However, data from the latest National Health Survey found that more than half of patients with known DM had never undergone an eye examination.[43] In the constraint of time and facilities, a selection of patients with higher risk factors like longer duration of disease, lower BMI and those who had moderate visual loss for priority of earlier screening may be a better strategy to enable the detection of patients with DR earlier.

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