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Risk Factors for Diabetic Retinopathy in Patients Attending Primary Care Settings

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Objective: To identify risk factors for diabetic retinopathy (DR) among patients with diabetes attending primary care health centers and to assess level of control.

Design: Case control study.

Setting: Twenty-two health centers.

Method: The medical records of patients with diabetes who were screened for retinopathy during the year 2011 were reviewed. The following were documented: age, sex, duration of diabetes, glycated hemoglobin (A1C), blood pressure (BP), lipid profile, smoking status, presence or absence of chronic kidney disease and guardian drugs [Angiotensin Converting Enzyme Inhibitors (ACEi), Angiotensin Receptor Blockers (ARBs), Statins and Aspirin] used. In addition, patients with diabetes who were screened as normal (no DR) from 4 health centers were randomly selected and their medical records were reviewed to compare the above mentioned risk factors between those with and those without DR.

Result: A total of 1,508 retinal screening forms were reviewed, 112 patients were diagnosed with DR. A total of 263 screened but had no DR were reviewed in the selected 4 health centers. In DR, uncontrolled A1C was found in 81 (72.3%) patients, high BP in 69 (61.6%) and Low Density Lipoprotein in 81 (72.3%). There was statistically significant association between A1C ≥ 53mmol/mol (P=0.000), increased diabetes duration (P=0.000), total cholesterol ≥5.2mmol/l (P=0.008), LDL ≥2.6mmol/l (P=0.002) and the presence of DR.

There was no significant association between age, sex, BP, and triglycerides level ≥1.7mmol/l and presence of DR. The use of statins, ARBs, fibrates and aspirin was significantly higher in patients with DR.

Conclusion: Control of the identified modifiable risk factors is suboptimal. The burden of DR can be reduced by more intensive control of these factors through effective use of the currently available guardian drugs.

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Diabetic retinopathy (DR) is one of the most common microvascular complications of diabetes. Worldwide, there are approximately 93 million patients with DR, 21 million with diabetic macular edema and 28 million with vision-threatening DR[1]. The prevalence of DR is likely to increase due to the increasing prevalence of diabetes. For example, it is estimated that the prevalence of DR and vision-threatening DR in the United States will be tripled by the year 2050[2].

Diabetic retinopathy is the leading cause of blindness among age-working adults[3]. Furthermore, an independent association has been found between DR and hypertension, obesity, renal dysfunction and coronary atherosclerosis[4]. Therefore, the presence of DR increases the risk of cardiovascular events and all-cause mortality[5].

Identifying the risk factors for DR is important for several reasons. First, most of the identified major risk factors are modifiable[6-10]. Second, the new modalities for management of DR are comparable to the gold standard of laser photocoagulation[11,12]. Lastly, adherence to annual screening as recommended by the guidelines and referral for ophthalmic evaluation is disappointingly low in family practice[13-15]. Therefore, primary prevention remains the most effective approach to combat this complication which is the main task of primary care providers.

Several studies have been conducted among different ethnic groups and in different settings to identify DR risk factors. Factors identified include duration of diabetes, degree of hyperglycemia and hypertension[1,16-20]. The association of other risk factors, such as dyslipidemia with DR has been inconsistent in various studies[21,22].

In the Kingdom of Bahrain, a recent study found that the prevalence of DR is 20.4%[23]. However, there are no studies conducted about DR risk factors.

The aim of this study is to identify the risk factors of diabetic retinopathy in patients with diabetes attending primary care settings and to assess level of control.

METHOD

Retinal screening using digital cameras is practiced in 6 health centers which cover all regions in Bahrain.

Fundus photos are taken by a trained ophthalmic technician and transferred electronically via Internet to a reading center in the ophthalmology department at Salmaniya Medical Complex; the photos are read and graded by ophthalmologists.

The medical records of patients who were screened and those with DR/maculopathy were reviewed for the year 2011. Data collected include age, sex, duration of diabetes, glycated hemoglobin (A1C), blood pressure (BP), lipid profile, smoking, chronic kidney disease, estimated glomerular filtration (GFR) less than 1 ml/sec/1.73m^2 surface area, and

guardian drugs [Angiotensin Converting Enzyme Inhibitors (ACEi), Angiotensin Receptor Blockers (ARBs), Statins and Aspirin] used.

Four health centers were randomly selected and the forms of patients who were screened as normal (no DR) were reviewed along with their medical records to compare the risk factors in those with and those without DR. We defined controlled A1C, BP, and lipids based on current American Diabetes Association guidelines[13].

Data were analyzed by using SPSS software version 20. Chi-squared test was used to assess the association between DR and each of the following factors: age, gender, level of control of DR risk factors and the use of guardian drugs. Multiple logistic regression model that included all the studied risk factors and DR as the dependent variable was set to determine the independent predictors for DR. P-value less than 0.05 was considered statistically significant.

RESULT

One hundred twelve patients were diagnosed with DR, 108 (96.4%) had type 2 diabetes. Ninety-seven (86.6%) were diagnosed with non-proliferative DR, 19 (17%) had maculopathy, and 7 (6.3%) had proliferative retinopathy. Twenty (17.9%) had both maculopathy and DR. The forms of two hundred and sixty-three patients with diabetes but had no DR were randomly selected from four health centers to represent the control group. Age and sex of the patients with DR and those without DR are presented in table 1.

Table 1: Age and Sex and the Presence or Absence of Diabetic Retinopathy

Personal Characteristics	DR* Present Number & Percentage	DR Absent Number & Percentage	Total Number & Percentage	P value
Age group(years)				
<40	7(6.3)	21(8)	28(7.5)	0.47
40-49	25(22.3)	76(28.9)	101(26.9)	
50-59	58(51.8)	97(36.9)	155(41.3)	
≥60	22(19.6)	69(26.2)	91(24.3)	
total	112(100)	263(100)	375(100)	
Sex				
Male	43(38.4)	121(46)	164(43.7)	0.174
Female	69(61.6)	142(54)	211(56.3)	
Total	112(100)	263(100)	375(100)	

*DR: Diabetic Retinopathy

Table 1 shows that around 70% of patients with DR were ≥50 years and males constitute less than 40% of patients with DR. However, there was no significant statistical difference in age and sex regarding the presence or absence of DR.

The main risk factors of diabetic retinopathy and level of control are presented in table 2 and figure 1.

Table 2: Main Risk Factors for Diabetic Retinopathy

Risk factors	DR present Number & Percentage	DR Absent Number & Percentage	Total Number & Percentage	P value
Diabetes duration(years)				
0-<5	9(8)	96(36.5)	105(28)	0.000
5-<10	24(21.4)	94(35.8)	118(31.5)	
10-<15	39(34.8)	56(21.3)	95(25.3)	
15-<20	14(12.5)	8(3)	22(5.9)	
≥20	19(17)	8(3)	27(7.2)	
No data	7(6.3)	1(0.4)	8(2.1)	
Total	112(100)	263(100)	375(100)	
Glycated hemoglobin(mmol/mol)				
<53*	29(25.9)	148(56.3)	177(47.2)	0.000
≥53	81(72.3)	112(42.6)	193(51.5)	
No data	2(1.8)	3(1.1)	5(1.3)	
Total	112(100)	263(100)	375(100)	
Blood pressure				
Controlled(≤140/80)	39(34.8)	111(42.2)	150(40)	0.265
uncontrolled	69(61.6)	151(57.4)	220(58.7)	
No Data	4(3.6)	1(0.4)	5(1.3)	
Total	112(100)	263(100)	375(100)	
Total cholesterol(mmol/l)				
<5.2	75(67)	209(79.5)	284(75.7)	0.008
≥5.2	37(33)	54(20.5)	91(24.3)	
Total	112(100)	263(100)	375(100)	
LDL**(mmol/l)				
<2.6	28(25)	111(42.2)	139(37)	0.002
≥2.6	81(72.3)	151(57.4)	232(61.9)	
No Data	3(2.7)	1(0.4)	4(1.1)	
Total	112(100)	263(100)	375(100)	
Triglycerides(mmol/l)				
<1.7	42(37.5)	109(41.4)	151(40.3)	0.481
≥1.7	69(61.6)	152(57.8)	221(58.9)	
No Data	1(0.9)	2(0.8)	3(0.8)	
Total	112(100)	263(100)	375(100)	

*equivalent to 7 %(ref.13), **LDL denotes Low Density Lipoproteins

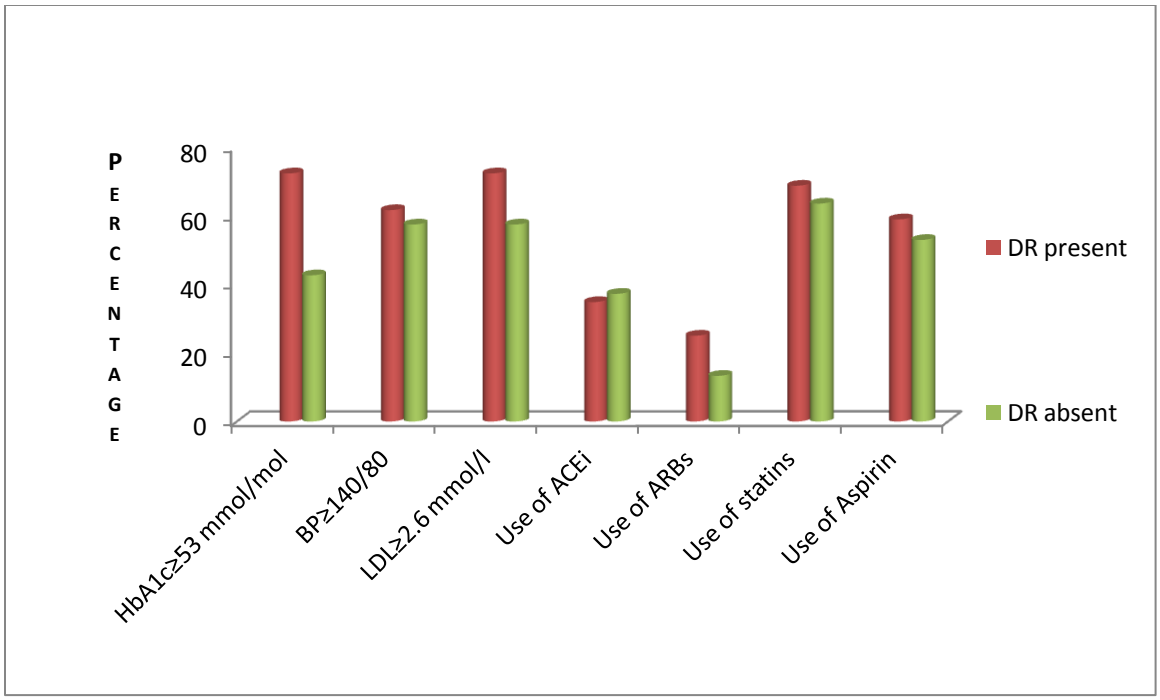

Figure 1: Control of Modifiable Risk Factors and Use of Guardian Drugs

Table 2 shows that patients with DR were more likely to have longer duration of diabetes, worse diabetes control, worse cholesterol and LDL control. However, there was no statistical significant association between blood pressure and triglycerides control and DR.

Seventeen (15.2%) patients with DR were smokers compared to 35(13.3%) without DR (P=0.001).

Estimated glomerular filtration rate was less than 1 ml/s/1.73m^2 surface area in two patients with DR; patients without DR had glomerular filtration rate more than 1.

Guardian drugs used by the patients are shown in table 3 and figure 1.

Table 3: Use of Guardian Drugs

Drug groups	DR present(n=112)			DR absent(n=263)			P value
	Yes Number & Percentage	No Number & Percentage	ND* Number & Percentage	Yes Number & Percentage	No Number & Percentage	ND Number & Percentage	
ACEi	39(34.8)	70(62.5)	3(2.7)	98(37.2)	165(62.8)	0	0.028
ARBs	28(25)	80(71.4)	4(3.6)	35(13.3)	227(86.3)	1(0.4)	0.001
Statins	77(68.7)	32(28.6)	3(2.7)	167(63.5)	95(36.1)	1(0.4)	0.063
Fibrates	8(7.1)	101(90.2)	3(2.7)	14(5.3)	249(94.7)	0	0.022
Aspirin	66(58.9)	36(32.2)	10(8.9)	139(52.9)	124(47.1)	0	0.000

*ND = no data

Table 3 shows patients with DR were more likely to be on ARBs, fibrates, statins and aspirin, but less likely to be on ACEi. The association is statistically significant.

In the multiple logistic regression models, diabetes duration and the degree of diabetes control were found to be significant predictors for diabetic retinopathy as shown in table 4.

Table 4: Multiple Logistic Regressions of Diabetic Retinopathy

Risk factor	P value	Odds ratio(CI)
Duration of diabetes	0.000	2.57(1.89-3.48)
Diabetes control	0.002	2.78(1.45-5.32)

DISCUSSION

The study shows that glycated hemoglobin equal or above 53 mmol/mol, longer diabetes duration, above target LDL and total cholesterol and current smoking were significantly associated with DR. No significant association was found between DR and blood pressure, age, or gender. Patients with DR were less likely to be on ACEi, but more likely to be on ARBs, fibrates, statins and aspirin.

A significant association was found between DR and uncontrolled hyperglycemia and increased diabetes duration, similar to other studies[1,17-20], see tables 2 and 4. DR was found to be common even in patients with newly diagnosed diabetes[19, 24].

No significant association was found between DR and blood pressure control[1,20,16], see table 2. Reduction of elevated pressure is beneficial in the prevention and progression of DR, blood pressure control per se does not prevent the incidence of DR in type 2 diabetes[7,10,16].

While only around 35% were having controlled BP, a large percentage of patients with DR were not receiving ACEi/ARBs, see table 3. These drugs are important for patients with DR for several reasons. Studies have found beneficial effects of these drugs on DR regression in both types of diabetes regardless of blood pressure control[25-27]. Presence of advanced DR is closely associated with chronic kidney disease in the form of albuminuria and decreased GFR[28,29,30]. Patients with DR are at higher risk for cardiovascular mortality[4,5,31].

Unlike glycated hemoglobin and diabetes duration, several studies had found inconsistent role of lipids as a risk factor for DR[21,22]. We found a significant association with increased total cholesterol and LDL which is similar to the findings of one study[16].

The study shows that although more than 60% of patients with DR did not meet triglycerides target, only around 7% were on fibrates. The role of fenofibrate has emerged as a medical treatment of DR due to ACCORD eye study and FIELD study[10,32,33]. Both studies were done in patients with type 2 diabetes. It was found that fenofibrate reduces

DR progression and reduces the need for laser treatment in patients with proliferative DR and macular edema despite normal lipid concentration and glycemic control[10,32,33]. On the other hand, despite the suboptimal control of LDL in the total cohort of our study, we found improved rate of statins usage which is more than double which was seen in a previous study[14]. This may indicate increased awareness of health care providers about the importance of these drugs in the management of high risk patients.

Patients with DR were found to be significantly more likely to be on aspirin compared to those without DR. Aspirin is definitely indicated for secondary prevention (i.e. those with known cardiovascular diseases). However, its role in primary prevention is currently unclear and management should be individualized[13,34].

In this study, all modifiable risk factors are poorly controlled and there is suboptimal use of guardian drugs in patients with DR. This highlights the need for multifactorial intervention to decrease the burden of diabetes complications[8].

CONCLUSION

Control of the identified modifiable risk factors is suboptimal. The burden of DR can be reduced by more intensive control of these factors through effective use of the currently available guardian drugs.

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