Received: 19.9.2008 **Accepted: 10.3.2009**

Original Article

A risk score development for diabetic retinopathy screening in Isfahan-Iran

Sayed Mohsen Hosseini *[a], *Mohammad Reza Maracy* [b], *Masoud Amini* [c], *Hamid Reza Baradaran* [d]

Abstract

BACKGROUND: The purpose of this study was to develop a simple risk score as screening tool for retinopathy in type II diabetic patients.

METHODS: A cross-sectional study was carried out recruiting 3734 patients with type II diabetes in an outpatient clinic in Isfahan Endocrinology and Metabolism Research Center (IEMRC), Iran. The logistic regression was used as a model to predict diabetic retinopathy. The cut-off value for the risk score was determined using the Receiver Operating Characteristic (ROC) curve procedure.

RESULTS: According to final models, being male, having lower body mass index (BMI), being older, longer duration of diabetes and higher HbA1c were correlated with increased risk of diabetic retinopathy. Area under the Curve (ROC) was 0.704 (95% CI: 0.685-0.723). A value ≥ 52.5 had the optimum sensitivity (60%) and specificity (69%) for determining diabetic retinopathy.

CONCLUSIONS: The results indicated that risk factors for retinopathy were sex, BMI, age, duration of diabetes and HbA1c levels. In conclusion, applying developed retinopathy risk score is a practical way to identify patients who are at high risk for developing diabetic retinopathy for an early treatment.

KEYWORDS: Retinopathy risk score, sensitivity, specificity, receiver operating characteristic curve.

JRMS 2009; 14(2): 105-110

Type II diabetes is increasing in the world population. It is an important cause of death and complications, which can impose a burden on the patients, their relatives and the health care system. The most common complication of type II diabetes is diabetic retinopathy (DR), which is a leading cause of visual impairment among working age people. The prevalence of blindness among diabetics is estimated to be around 25 times more than non-diabetes population.[1-4]

Duration of diabetes, hyperglycemia, nutritional and genetic factors, high blood pressure, usage of insulin, pregnancy and hyperlipidemia are the risk factors for diabetic retinopathy.[5-14]

Important improvement has been achieved in diagnosis, medical care and risk factors that affect the prevalence of diabetes and retinopathy during the recent decades. Considering the increase of diabetes incidence, the patients who suffer from ophthalmologic complications should be properly managed to prevent permanent eye damage.[15-18]

Identifying individuals at risk of diabetes retinopathy is very important for health system. Recently, risk scores for diabetes retinopathy based on simple anthropometric and

[a] Department of Epidemiology & Biostatistics, School of Health, Isfahan University of Medical Sciences, Isfahan, Iran.
[b] Department of Community Medicine, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran.
[c] Endocrine and Metabolism Research Center, Isfahan University of Medical Sciences, Isfahan, Iran.
[d] Medical Education and Development Center, Iran University of Medical Sciences, Tehran, Iran.
* Corresponding Author
E-mail: hosseini@hlth.mui.ac.ir

demographic variables have been established to identify high risk individuals. It is also evident that a common risk score cannot be applied for all ethnic groups.

The final risk score form contains significant diabetic retinopathy risk factors. Each of the risk factors is weighted according to their contribution in the main model. The total risk score is sum of all risk factors varied from 0 to 100.

In this study, we have developed a simple and practical scoring system to screen Diabetic Retinopathy. Using such a risk score would be great help in the developing countries where there is a huge undiagnosed DR.

Method

This was a cross-sectional study on patients with type II diabetes mellitus using routinely collected data at outpatient clinics of the Isfahan Endocrinology and Metabolism Research Center (IEMRC), Iran. A total of 12,644 type II diabetes patients were registered in the IEMRC. Diabetes was defined according to the report of the expert committee on the diagnosis and classification of diabetes mellitus. Only type II diabetes was included in this study. We excluded the patients with missing data for diabetic retinopathy. Data of 3734 patients were included. These patients were initially screened by an endocrinologist and then referred to an ophthalmologist to undergo ophthalmologic examination.

The data source for these analyses was collected from all *patients* who *attended* for the *first time* and completed forms in the clinic. Data were collected through physical examinations including a retinal examination, blood pressure, fasting plasma glucose (FPS), glycosylated haemoglobin (HbA1c), urinary albumin, triglyceride, cholesterol and serum creatinine. Demographic information, family history and history of smoking were also obtained.

All ophthalmologic examination records were used in the study and *were* entered into a database.

The lowest score for each category was defined as zero. The total score for each subject was calculated by summing all weighted risk factors with variation from 0 to 100.

Because of complicated interpretation, interaction terms between various variables were not considered. ROC curves were constructed to identify the optimum value (> 60%) of diabetic patients for determining DR. Sensitivity and specificity for predicting DR were calculated for different cuts of score.

The cut-off value for the risk score was determined using the Receiver Operating Characteristic (ROC) curve procedure.

The DR risk score was developed using the β-coefficient of the model as follows: $\beta < 0.25$, the score is 5; $\beta = 0.25$-0.40, the score is 10; $\beta = 0.41$-0.55, the score is 15; $\beta = 0.56$-0.70, the score is 20, $\beta = 0.71$-0.85, the score is 25, $\beta = 0.86$-1.00, the score is 30, $\beta = 1.01$-1.25, the score is 35; $\beta = 1.25$-1.50, the score is 40; $\beta = 1.51$-1.75, the score is 45, $\beta = 1.75$-2.00, the score is 50.

Statistical Analysis

The following risk factors were analyzed: sex, age, duration of diabetic, body mass index (BMI), the presence or absence of high blood pressure (BP) with definition in an adult as BP ≥ 130 mmHg systolic pressure or ≥ 80 mm Hg diastolic pressure, the levels of glycated hemoglobin (HbA1c), fasting plasma glucose (FPS), cholesterol, triglyceride.

Age was categorized and changed at each subject's at 10-year interval starting at age 30 years, the earliest possible entry in the study. Diabetes duration was categorized as follow: first year as newly diagnosed diabetics and after that by 2, 5 and 10-year. Overweight and obesity was defined as body mass index (BMI) of more than 25 kg/m^2. HA1c level was defined as 9% or less, 9.01%-11% and more than 11% respectively.

Variables were included in the multiple logistic regressions using stepwise backward elimination, with DR as the dependent variable. The independent variables were categorized. P values less than 0.05 were considered statistically significant.

A risk score was developed from above factors. The variables of interest were treated in two ways. First, their distribution within each area was separately calculated and results were presented as the odds of DR in each

group and 95% confidence interval (CIs) for these relative odds were estimated from the logistic regression analysis. Second, the results were presented as logistic regression coefficients as well as significance levels. Coefficients of each significant variable in the model were used to assign a score value.

Optimal cut-point for the risk score (the point with the highest sensitivity and lowest false-positive rate) was depicted by the ROC analysis. Statistical analyses were done using the software package STATA version 9.0.

Results

Out of total patients included in this study 64% were female. Fifty four percent (54%) of patients were diagnosed having retinopathy. Basal characteristics of patients with and without DR are presented in table 1.

More than 70% of patients with diabetes for more than 10 years had diabetic retinopathy. Approximately 61% of patients had BMI below 25 kg/m^2.

Table 2 demonstrates the results of using logistic regression models with DR as dependent variable. Area under the curve for the ROC was 0.704 (95% CI: 0.685-0.723) as shown in Figure 1. Table 3 shows the sensitivity and specificity of different cut-off points for diabetic retinopathy in our patients. A diabetic retinopathy clinical outpatients' value ≥ 52.5 had the optimum sensitivity (60%) and specificity (69%) for determining DR.

Discussion

In this study the risk score of retinopathy for type II diabetic patients in Isfahan, Iran was investigated. It was shown that higher HbA1c, longer diabetes duration, being older and male increase the risk for development of retinopathy whereas body mass index > 25 kg/m^2 decreases it (Table 1).

Studies on diabetic patients conducted in other countries have similar results. The prevalence of retinopathy varies widely depending on the diabetes duration. Accordingly, the prevalence of diabetic retinopathy is reported to be 50%, 31.3%, 50% and around 50% in Mexico, Sri Lanka, UK and Spain, respectively. Some other studies also reported prevalence rate to be around 60.5%.[10,11] A low prevalence rate (26%) was reported in a study in Pakistan.[12]

Table 1. Type II diabetic patients' clinical characteristic by diabetic retinopathy.

	Diabetic retinopathy				
	Negative		Positive		
	Mean	S.D	Mean	S.D	P value
Age	50.1	10.51	53.9	10.1	0.01
BMI	27.9	4.7	26.7	4.2	0.01
Duration of diabetes	4.9	4.7	8.8	6.4	0.01
FPG	169.3	42.7	181.1	46.5	0.01
Diastolic	126.6	15.5	131.9	16.1	0.01
Systolic	80.24	7.6	80.7	7.5	0.05
Cholesterol	218.6	7.6	218.5	38.8	0.94
Triglyceride	213.6	112.1	212.4	104.8	0.73
HbA1c	8.7	1.9	9.1	1.97	0.01

Table 2. Logistic regression models with DR as dependent variable.

HbA1c (%)	B	SD	OR (95.0% C.I)	Score
7.01-9	0.187	0.119	1.21 (0.96-0.1.52)	5
9.01-11	0.237	0.091	1.27 (1.06,1.51)	5
> 11	0.348	0.128	1.42 (1.10,182)	10
Age (year)				
40-49	0.471	0.129	1.60 (1.24,2.06)	15
50-59	0.739	0.130	2.09 (1.62,2.69)	25
≥ 60	0.763	0.143	2.14 (1.62,2.84)	25
Duration (year)				
2-4	0.638	0.121	1.89 (1.49,2.40)	20
5-9	1.017	0.121	2.77 (2.18,3.51)	35
≥ 10	1.781	0.128	5.94 (4.61,7.63)	50
BMI (> 25kg/m^2)	0.347	0.091	1.41 (1.18,1.69)	10
Sex (Female)	0.216	0.089	1.24 (1.04,1.48)	5
Constant	-1.7	0.168	0.171	
Maximum score				100

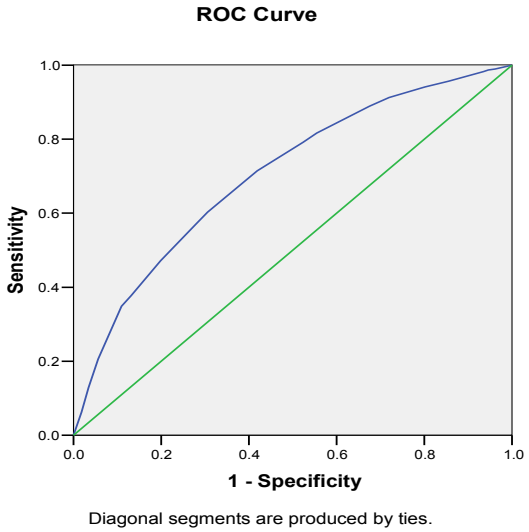

Figure 1. ROC curve of risk score for diabetic retinopathy in type II diabetic patients. The area under the curve was 0.704 (95% CI 0.685-0.723). The cut of point DR risk score ≥ 52.5, sensitivity was 60% and specificity 69%.

Table 3. Sensitivity, specificity, PPV and NPV of cut of points for diabetic retinopathy in type II diabetic patients.

Cut of points	Sensitivity	Specificity	PPV	NPV
≥ 37.5	0.816	0.445	0.623	0.682
≥ 42.5	0.791	0.476	0.630	0.670
≥ 47.5	0.714	0.418	0.657	0.644
≥ 52.5	0.603	0.694	0.689	0.608
≥ 57.5	0.569	0.722	0.697	0.598
≥ 62.5	0.472	0.801	0.728	0.574
≥ 67.5	0.377	0.869	0.764	0.553

A study comparing diabetics with and without DR in Kuwait found that high HbA1c, obesity (BMI > 30kg/m^2) and longer duration of diabetes mellitus were the risk factors for DR.[13] Furthermore, another study showed that HbA1c, BMI and length of illness are a contributing factor in the degree of retinopathy. The interesting finding of our study is that BMI as a risk factor has an inverse correlation with developing DR. Similarly, some previously done studies, including the Wisconsin Epidemiological Study of Diabetic Retinopathy,

demonstrated an inverse relationship between BMI and severity of diabetic retinopathy. To explore if poor glycemic control which may reflect in lower BMI can explain this reverse correlation, we examined the relation between BMI and other risk factors such as HbA1c, FPG and even diabetes duration, blood pressure, cholesterol and triglyceride. We found just a significant negative association between BMI and duration of diabetes. Therefore, our hypothesis was not supported by this analysis. However, further studies are needed to investigate this controversial issue.

This study indicates that diabetic retinopathy is much higher in patients with a relatively longer duration of diabetes. A few reports have shown age at diagnosis, total cholesterol, triglycerides, high HbA1c as risk factors. Also, we found a significant relation between age, BMI, sex, duration of diabetes and HbA1c, but we did not find any association between DR and blood pressure, triglyceride, cholesterol and FPG.

We also did not find any relationship between blood pressure, cholesterol, triglyceride and DR. However, several studies supported the positive relationship between blood pressure and DR. In conclusion, our study demonstrated that diabetic retinopathy was associated with HbA1c, age, diabetes duration, BMI and sex, but was not associated with FPG, blood pressure, cholesterol and triglyceride. Applying developed retinopathy risk score is a practical way to identify diabetics who are at high risk for developing DR for early treatment.

Conflict of Interest

Authors have no conflicts of interest.

Authors' Contributions

SMH carried out the design and coordinated the study, carried out all data analysis and prepared the manuscript.
MRM provides assistance in the design of the study, coordinated and participated in data analysis and participated in manuscript preparation.
MA provides assistance for the design and coordinated the study.
HRB participated in manuscript preparation.
All authors have read and approved the content of the manuscript.

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