Med. J. Cairo Univ., Vol. 92, No. 4, Accepted 22/7/2024
DOI: 10.22608/MJCU. 1145-1150, December 2024
www.medicaljournalofcairouniversity.net

Prevalence and Factors Associated with Diabetic Retinopathy among Patients with Type 2 Diabetes Mellitus

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Abstract

Background: Diabetic retinopathy (DR) is the most important cause of irreversible blindness in working-age adults. It is mainly caused by microvascular complications in the retina.

Aim of Study: This work aimed was to determine the prevalence of DR and its associated factors among type 2 diabetic patients.

Patients and Methods: This retrospective cohort study was carried out on 220 patients diagnosed with T2DM. All patients were subjected to direct ophthalmoscopy examination and funduscopic examination.

Results: Out of 220 T2DM patients, 48 (21.82%) patients had DR. BMI, increased duration of DM, smoking, HTN, HbA1c, and FPG were significantly higher in T2DM patients with DR than those without DR. In univariate regression analysis, BMI, duration of DM, smoking, HTN, and HbA1c had a significant influence on prevalence of DR in T2DM patients. In multivariate regression analysis, duration of DM and HbA1c had a significant influence on prevalence of DR in T2DM patients.

Conclusions: Tight control of blood glucose levels along with screening for diabetes complications like DR soon after diagnosis, especially in patients with longer disease duration may help reduce risk of visual morbidity in T2DM patients.

Key Words: *Diabetic Retinopathy – Type 2 Diabetes Mellitus – Prevalence – Associated Factors.*

Introduction

DIABETES mellitus (DM) is caused by higher levels of blood glucose due to the lack of production of insulin by the body, resistance to insulin, or both **[1]**. It predisposes to vascular, renal, ophthalmic, and neurological complications that impair patients' quality of life and it presents a high burden in terms of morbidity and economic costs. The development of microvascular complications such as diabetic retinopathy (DR) is expected to increase with the rising prevalence of DM. There are several risk factors associated with DR, the most notable of which is the duration of DM **[2]**.

DR is vision loss due to complications from DM. It is mainly caused by microvascular complications in the retina, which strongly correlate to both the duration of diabetes and the level of glycemic control **[3]**.

DR can have severe effects on the eye, including microaneurysms, hemorrhages, hard exudates, cotton woolspots, and venous loops. Based on the observed features, DR is broadly classified as non-proliferative DR (NPDR) or proliferative DR (PDR) **[4]**.

DR is the mostimportant cause of irreversible blindness inworking-age adults. Chronic hyperglycemia causes not only retinal vascular diseases butalso damage to retinal neurons, both of which are factors that lead to vision loss **[5]**.

The pathogenesis of DR is multifactorial, but increasing evidence points to the involvement of inflammation in DR pathophysiology. Specifically, it was shown that low-grade subclinical inflammation can damage retinal vasculature, leading to neovascularization or macular edema, and pro- and anti-inflammatory markers in the serum and ocular fluids have been shown to be related to DR **[6]**.

The aim of this work was to determine the prevalence of DR and its associated factors among type 2 diabetic patients.

Patients and Methods

This retrospective cohort study was carried out on 220 patients aged from 18 to 65 years old, both sexes, diagnosed with T2DM.

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An informed written consent was obtained from the patients. The study was done from 1st January 2023 to 1st January 2024 after approval from the Ethical Committeeat Tanta Ophthalmology Hospitals.

Exclusion criteria were DM other than T2DM, retinal artery occlusion, retinal vein occlusion, and sickle cell retinopathy.

Adirect ophthalmoscopy examination was performed by a single examiner after dilating the pupils of both eyes with 1% tropicamide eye drops. To diagnose DR in patients with diabetes, ophthalmologist judged whether the patient had DR according to the results of the funduscopic examination and guidelines. The results were reported as either DR or non-DR. Non-DR here included a normal fundus andother retinopathy that may be caused by other causes (non-diabetic) such as fundus arteriosclerosis. The clinical data for each patient were obtained from the recorded data sheets and included age, gender, hypertension, and body massindex (BMI). Baseline fasting blood glucose (FBG), hemoglobin A1c (HbA1c), and lipid profiles [cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides] were undertaken at the time of diagnosis of T2DM.

Statistical analysis:

Statistical analysis was done by SPSS v26 (IBM Inc., Armonk, NY, USA). The Shapiro-Wilks test and histograms were used to evaluate the normality of the distribution of data. Quantitative parametric data were presented as mean and standard deviation (SD) and were analyzed by unpaired student *t*-test. Qualitative data were presented as frequency and percentage (%) and were analyzed using the Chi-square test or Fisher's exact test when appropriate. A two tailed *p*-value ≤0.05 was considered statistically significant.

Results

Out of 220 T2DM patients, 48 (21.82%) patients had DR. The distribution of DR is illustrated in Fig. (1).

BMI, increased duration of DM, smoking, HTN, HbA1c, andFPG were significantly higher in T2DM patients with DR than those without DR (*p*-value <0.05). Age, gender, family history of DM, IHD, CKD, treatment modalities, WBCs, platelets, cholesterol, LDL, HDL, and triglycerides were insignificantly different between T2DM patients with DR and those without DR. Table (1).

Table (1): Demographic, clinical, and laboratory data of the studied T2DM patients.

	Total (n=220)	Diabetic retinopathy		*p*-value
		Yes (n=48)	No (n=172)	
Age (years)	48.19±10.4	49.73±10.51	47.76±10.35	0.247
Gender:				
Male	105 (47.73%)	20 (41.67%)	85 (49.42%)	0.342
Female	115 (52.27%)	28 (58.33%)	87 (50.58%)	
BMI (kg/m^2)	27±4.78	28.62±3.93	26.54±4.91	0.007*
Duration of DM (months)	20.45±8.71	23.1±7.59	19.7±8.88	0.016*
Family history of DM	29 (13.18%)	7 (14.58%)	22 (12.79%)	0.746
Smoking:	68 (30.91%)	23 (47.92%)	45 (26.16%)	0.004*
HTN	55 (25%)	19 (39.58%)	36 (20.93%)	0.009*
IHD	47 (21.36%)	11 (22.92%)	36 (20.93%)	0.767
CKD	23 (10.45%)	4 (8.33%)	19 (11.05%)	0.791
Treatment modalities:				
Insulin	54 (24.55%)	11 (22.92%)	43 (25%)	0.305
Oral	107 (48.64%)	20 (41.67%)	87 (50.58%)	
Both	59 (26.82%)	17 (35.42%)	42 (24.42%)	
WBCs (x10^9/L)	8.37±1.83	8.19±1.94	8.42±1.8	0.443
Platelets (x10^9/L)	306.86±90.72	295.56±90.64	310.02±90.76	0.330
HbA1c (%)	7.73±2.72	9.45±1.97	7.24±2.71	<0.001*
FPG (mg/dl)	172.41±53.95	215.29±44.44	160.44±50.25	<0.001*
Cholesterol (mg/dl)	219.94±46.21	226.88±41.1	218.01±47.47	0.241
LDL (mg/dl)	132.2±47.39	136.15±53.17	131.09±45.76	0.515
HDL (mg/dl)	40.8±12.29	43.56±14.52	40.03±11.53	0.079
Triglycerides (mg/dl)	172.3±50.6	173.54±48.9	171.95±51.2	0.847

Data are presented as mean ± SD or frequency (%).
T2DM: Type 2 diabetes mellitus.
BMI : Body mass index.
DM : Diabetes mellitus.
HTN : Hypertension.
IHD : Ischemic heart disease.
CKD : Chronic kidney disease.
WBCs : White blood cells.
HbA1c: Glycated hemoglobin.
FPG : Fasting plasma glucose.
LDL : Low-density lipoprotein.
HDL : High-density lipoprotein.
* : Significant as *p*-value ≤0.05.

In univariate regression analysis, BMI, duration of DM, smoking, HTN, and HbA1c had a significant influence on prevalence of DR in T2DM patients (*p*-value <0.05) while age, gender, family history of DM, IHD, CKD, FPG, cholesterol, LDL, HDL, and triglycerides had an insignificant influence on DR.

In multivariate regression analysis, duration of DM and HbA1c had a significant influence on prevalence of DR in T2DM patients (*p*-value <0.05) while age, gender, BMI, family history of DM, smoking, HTN, IHD, CKD, FPG, cholesterol, LDL, HDL, and triglycerides had an insignificant influence on DR. Table (2).

Table (2): Univariate and multivariate logistic regression analysis of factor related to diabetic retinopathy in T2DM.

	Univariate analysis			Multivariate analysis		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Age (>50 vs. ≤50 years)	1.458	0.767 – 2.772	0.250	1.926	0.886 – 4.186	0.098
Gender (male vs. female)	0.731	0.383 – 1.396	0.343	0.626	0.294 – 1.337	0.227
BMI (>25 vs. ≤25 kg/m2)	2.546	1.190 – 5.446	0.016*	2.267	0.945 – 5.434	0.067
Duration of DM (>15 vs. ≤15 months)	2.142	0.999 – 4.594	0.050*	2.708	1.110 – 6.606	0.029*
Family history of DM (yes vs. no)	1.164	0.465 – 2.915	0.746	1.100	0.354 – 3.422	0.869
Smoking (yes vs. no)	2.596	1.341 – 5.026	0.005*	1.837	0.840 – 4.016	0.128
HTN (yes vs. no)	2.475	1.247 – 4.911	0.010*	2.460	0.947 – 6.390	0.065
IHD (yes vs. no)	1.123	0.522 – 2.418	0.767	0.631	0.210 – 1.898	0.412
CKD (yes vs. no)	0.732	0.237 – 2.264	0.588	0.885	0.232 – 3.374	0.858
HbA1c (>7.5 vs. ≤7.5 %)	4.069	1.981 – 8.358	<0.001*	3.826	1.724 – 8.494	0.001*
FPG (>100 vs. ≤100 mg/dl)			0.998			0.998
Cholesterol (>200 vs. ≤200 mg/dl)	2.043	0.975 – 4.284	0.059	1.968	0.857 – 4.519	0.110
LDL (>100 vs. ≤100 mg/dl)	1.336	0.645 – 2.770	0.436	1.633	0.685 – 3.890	0.268
HDL (≤40 vs. >40 mg/dl)	1.038	0.547 – 1.968	0.910	1.001	0.473 – 2.121	0.997
Triglycerides (>150 vs. ≤150 mg/dl)	1.054	0.540 – 2.055	0.877	1.569	0.703 – 3.503	0.272

T2DM: Type 2 diabetes mellitus.
BMI : Body mass index.
DM : Diabetes mellitus.
HTN : Hypertension.
IHD : Ischemic heart disease.
CKD : Chronic kidney disease.
HbA1c: Glycated hemoglobin.
FPG : Fasting plasma glucose.
LDL : Low-density lipoprotein.
HDL : High-density lipoprotein.
OR : Odds ratio.
CI : Confidence interval,
* : Significant as *p*-value ≤0.05.

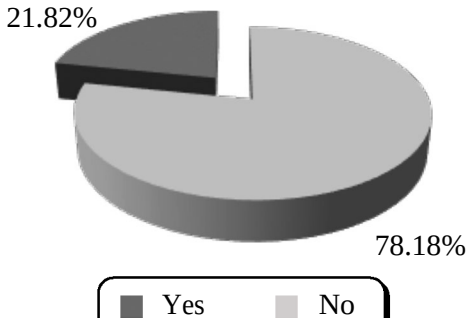

Fig. (1): Distribution of DR of the studied patients.

Discussion

DR will proceed from its minor anomalies to its severe forms if early identification and therapy are not provided. Tractional retinal detachment, macular oedema, and neovascular glaucoma worsen DR and finally cause seriously impaired vision **[7].**

The aim of this work was to determine the prevalence of DR and its associated factors among type 2 diabetic patients.

In our study, out of 220 T2DM patients, 48 (21.82%) patients had DR. This came in agreement with Hao et al. **[5]** who reported that there were 20.3% patients presented with DR among the newly diagnosed ones with T2DM. Our percentage is lower than what was reported in Srimaneekarn et al. **[8]** study asthey found that 34.01% of the 331 diabetic patients included had DR. This variance may result from racial diversity, gender disparities, and age-group presentations.

In our study, BMI, increased duration of DM, smoking, HTN, HbA1c, and FPG were significantly higher in T2DM patients with DR than those without DR (*p*-value <0.05). Age, gender, family history of DM, IHD, CKD, treatment modalities, WBCs, platelets, cholesterol, LDL, HDL, and triglycerides were insignificantly different between T2DM patients with DR and those without DR.

This slightly agrees with Tsegaw et al. **[9]** who reported that the prevalence of retinopathy increased with time from diagnosis of T2DM (*p*-value <0.001) and with increasing HbA1c level (*p*=0.03). Although half their case series had hypertension and

with no statistically significant association between retinopathy and hypertension.

The prevalence of retinopathy increased, as expected, with increasing levels of HbA1c, in agreement with many similar studies [10,11].

Stratton et al. [12] reported that hypertension was associated with the development of diabetic retinopathy in patients with T2DM. They also reported that no association was found between smoking and DR in patients with T2DM.

Others have shown that adequate control of blood pressure can reduce the effect of hypertension on the development of retinopathy [13].

Khan and Aslam [1] results strengthen the relationship between HbA1c and fasting glucose concentration in retinopathy patients.

Rema et al. [14] and Hayat et al. [15] reported that the degree of retinopathy was correlated with HbA1c levels and systolic blood pressure.

Hao et al. [5] reported that DR was negatively correlated to BMI. When BMI was >28 kg/m^2, they found that the incidence of DR was 12.4% in non-smokers, 12.1% in light and moderate smokers and 28.2% in heavy smokers (p-value=0.004).

Grey et al. [16] followed-up with 14657 patients with diabetes for an average of 6.68 years and found that increased risk of DR was associated with higher BMI.

Rooney et al. [17] also reported that BMI was not correlated or even negatively correlated with DR.

Hilawe et al. [18] demonstrated that smoking is associated with insulin resistance, inflammation, and dyslipidemia.

Garberg et al. [19] recorded a negative relationship between BMI and the development of retinopathy in T2DM while Zhou et al. [20] failed to demonstrate an association.

Jaimes et al. [21] showed that cigarette smoking impairs nitric oxide-mediated endothelial function via increased generation of superoxide anions, which may increase the risk of DR in patients with diabetes and could cause eye tissue ischemia, eye tissue hypoxia, retinal arteriosclerosis, and a decrease in choroidal blood flow, eventually leading to retinal ischemia.

Smoking may aggravate retinopathy damage by increasing arteriosclerosis. DR remains the leading cause of acquired blindness in working-age adults. Although Zhang et al. [22] identified many molecular, functional, and structural abnormalities. The exact molecular mechanism of this devastating disease remains obscure. A diabetic environment drives the dysfunction of the power generator of the cell and disturbs the homeostasis of the mitochondrial dynamic. Mitochondria seem to have a significant role in the development of DR, and unravelling the mechanism responsible for their damage as well as the role of epigenetic modifications in mitochondrial homeostasis should identify novel therapeutic targets [23].

In our study, in univariate regression analysis, BMI, duration of DM, smoking, HTN, and HbA1c had a significant influence on prevalence of DR in T2DM patients (p-value <0.05) while age, gender, family history of DM, IHD, CKD, FPG, cholesterol, LDL, HDL, and triglycerides had an insignificant influence on DR. In multivariate regression analysis, duration of DM and HbA1c had a significant influence on prevalence of DR in T2DM patients (p-value <0.05) while age, gender, BMI, family history of DM, smoking, HTN, IHD, CKD, FPG, cholesterol, LDL, HDL, and triglycerides had an insignificant influence on DR.

This partially agrees with Hasan et al. [4] who reported that the risk factors identified for DR were age, body mass index, systolic blood pressure, diastolic blood pressure, fasting blood glucose, 2h after breakfast sugar test, hemoglobin A1c, total cholesterol, triglycerides, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, serum creatinine, and duration of DM, as these risk factors were found to be significantly associated with DR (p-value <0.05).

On the other hand, Hao et al. [5] reported, after analyzing the related factors of DR, obese patients may have a lower incidence of DR (p-value $=0.004$). They showed that DR was related to BMI, smoking status, and age of DM diagnosis. They suggested that heavy smoking was associated with DR in obese (BMI >28 kg/m^2) patients with newly diagnosed T2DM (p-value=0.049), and there was a negative correlation between DR and the age of diagnosis of diabetes >60 years (p-value=0.009). Those correlations did not exist in non-obese (BMI <28 kg/m^2) patients.

Many researchers have shown that duration of DM, blood glucose, blood pressure and blood lipids are important risk factors for DR. The duration is the most important factor [24,25].

Tyrberg et al. [26] found that smoking history could increase the risk of DR during 9–17 years after diagnosis. Because smoking behavior occurred before the diagnosis of T2DM in this study, heavy smoking is very likely to be a risk factor for DR.

Limitations: The relatively small sample size. Also, this study considered only patients with T2DM, not those with type 1 DM and the study did not clarify the complex interplay between glycemic

control, disease duration and risk of microvascular complications.

Conclusions:

Tight control of blood glucose levels along with screening for diabetes complications like DR soon after diagnosis, especially in patients with longer disease duration may help reduce risk of visual morbidity in T2DM patients.

Financial support and sponsorship: Nil.

Conflict of Interest: Nil.

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مدى الانتشار والعوامل المرتبطة باعتلال الشبكية السكرى بين مرضى السكرى من النوع الثانى

الخلفية: اعتلال الشبكية السكرى هو السبب الأكثر أهمية للعمى الذى لا رجعة فيه لدى البالغين. يحدث هذا بشكل رئيسى بسبب مضاعفات الأوعية الدموية الدقيقة فى شبكية العين.

الهدف: كان الهدف من هذا العمل هو تحديد مدى انتشار اعتلال الشبكية السكرى والعوامل المرتبطة به بين مرضى السكرى من النوع الثانى.

الطريقة: تم إجراء هذه الدراسة الأترابية بأثر رجعى على ٢٢٠ مريضًا تم تشخيص إصابتهم بمرض السكرى من النوع الثانى. تعرض جميع المرضى لفحص تنظير العين المباشر وفحص قاع العين.

النتائج: من بين ٢٢٠ مريضًا من مرضى السكرى من النوع الثاني، كان ٤٨ (٢١,٨٢٪) مريضًا مصابين باعتلال الشبكية السكرى. كان مؤشر كتلة الجسم وزيادة مدة مرض السكرى والتدخين وارتفاع ضغط الدموالهيموجلوبين السكرى وسكر الدم بعد الصيام أعلى بكثير فى مرضى السكرى من النوع الثانى الذين يعانون من اعتلال الشبكية السكرى مقارنة بأولئك الذين لا يعانون من اعتلال الشبكية السكرى. فى تحليل الانحدار وحيد المتغير، كان لمؤشر كتلة الجسم، ومدة مرض السكرى، والتدخين، وارتفاع ضغط الدم، ونسبة الهيموجلوبين السكري تأثير كبير على انتشار اعتلال الشبكية السكرى فى مرضى السكرى من النوع الثانى. في تحليل الانحدار متعدد المتغيرات، كان لمدة مرض السكرى والهيموجلوبين السكرى تأثير كبير على انتشاراعتلال الشبكية السكرى فى مرضى السكرى من النوع الثانى.

الاستنتاجات: السيطرة الصارمة على مستويات الجلوكوز في الدم إلى جانب الكشف عن مضاعفات مرض السكرى مثل اعتلال الشبكية السكرى بعد وقت قصير من التشخيص، وخاصة فى المرضى الذين يعانون من مدة مرض أطول قد يساعد فى تقليل خطر الإصابة بالأمراض البصرية لدى مرضى السكرى من النوع الثانى.