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Severity of diabetic retinopathy at the first ophthalmological examination in the Lebanese population

Walid Harb, Georges Harb, Nabil Chamoun, Anthony Kanbar, Marc Harb and Wassef Chanbour

Abstract

Aim: To determine the percentage and stage of diabetic retinopathy at the first ophthalmological examination after the patient's diagnosis with type 2 diabetes mellitus.

Methods: A retrospective descriptive study was conducted at 'Clinique du Levant' hospital between 2006 and 2016. A total of 484 randomly selected patients were included. Data were collected and analyzed for selected variables (sex, age, sources of referral, and duration of diabetes).

Results: In total, 119 (24.6%) patients had diabetic retinopathy. Among them, 43 had proliferative diabetic retinopathy (8.9%). About 16.7% of the included patients had macular edema, which was severe in 6.2%. The average age of patients was 62.1 years with an average of 8.3 years of diabetes. About 55% were men, while 45% were women. The patients with no referral source presented 8.9 years after the onset of diabetes, whereas patients referred by general practitioners and secondary medical professionals presented after 5.8 and 5 years, respectively ($p < 0.05$), but they represented only 23.2% of diabetics. Women presented earlier than men (7.3 *versus* 9.1 years; $p = 0.012$). About 82.6% were symptomatic, 44.1% had a visual impairment on Snellen charts that was severe in 11.2%. Also, 37.8% of the patients had a visually significant cataract. The duration of diabetes was the only dependent variable, $p < 0.0001$. The average age, sources of referral, and sex were not related to the severity of retinopathy.

Conclusion: Diabetics with a more severe diabetic retinopathy are presenting late to the ophthalmology clinics. There is a need to promote outreach programs for people with diabetes for early detection of diabetic retinopathy in Lebanon.

Keywords: diabetes, Lebanon, macular edema, retinopathy

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Correspondence to:
Wassef Chanbour
Beirut Eye & ENT Specialist Hospital, Beirut 1100, Lebanon.
Wassef_c@hotmail.com

Walid Harb
Ophthalmology Department, Clinique du Levant, Beirut, Lebanon
Ophthalmology Department, Notre Dame du Liban Hospital, Jounie, Lebanon

Georges Harb
Ophthalmology Department, Notre Dame du Liban Hospital, Jounie, Lebanon

Nabil Chamoun
Ophthalmology Department, Clinique du Levant, Beirut, Lebanon

Anthony Kanbar
Ophthalmology Department, Notre Dame du Liban Hospital, Jounie, Lebanon

Marc Harb
Ophthalmology Department, Notre Dame du Liban Hospital, Jounie, Lebanon

Wassef Chanbour
Ophthalmology Department, Clinique du Levant, Beirut, Lebanon
Beirut Eye & ENT Specialist Hospital, Beirut, Lebanon

Introduction

Diabetic retinopathy (DR), an ocular complication of diabetes mellitus, is one of the major causes of avoidable blindness in both developing and developed countries.[1] DR remains one of the main causes of moderate to severe visual impairment among the global population in 2015.[2] Moreover, blindness and vision impairment attributable to DR increased between 1990 and 2015.[2]

Patients with diabetes and an undiagnosed retinopathy may remain asymptomatic until late stages are reached. Therefore, it is important for people with diabetes to undergo regular eye examination for early detection of DR. Importantly, once symptoms start to appear, the progression can be fast. However, treatment has proved to be beneficial in ameliorating symptoms and slowing down the rate of retinopathy progression.[3]

A pooled individual participant meta-analysis involving 35 studies conducted worldwide from 1980 to 2008 estimated the global prevalence of any DR and proliferative DR (PDR) among

patients with diabetes to be 35.4% and 7.5%, respectively. Prevalence of any DR and PDR was higher in those with type 1 diabetes, compared with those with type 2 diabetes (77.3% *versus* 25.2% for any DR, 32.4% *versus* 3.0% for PDR).[4]

In the Lebanese population, the prevalence of diabetes reported in 2017 by the International Diabetes Federation was 14.6% in adults.[5] DR was reported in 16.96% of patients with diabetes in 2000.[5] In 2009, a higher prevalence was described in patients with type 2 diabetes mellitus (T2DM), and DR was found in 35% of them. Moreover, 26% of the patients had non-PDR (NPDR), while 9% of them had PDR.[6]

The duration of diabetes, poor glycemic control, diabetic nephropathy, hypercholesterolemia, anemia, puberty, and pregnancy are proven risk factors behind the increase in frequency and progression of retinopathy in patients suffering from diabetes. Also, the prevalence and severity of DR increase with age in type 1 diabetes but not in type 2.[7–13]

Although effective treatment is available, fewer patients than expected are being referred by their primary care physicians for screening, a matter which is contrary to the guidelines stated by the American Diabetes Association and the American Academy of Ophthalmology.[14] In two community-based studies in the United States, 43% to 65% of participants had not received a dilated eye examination at the time of enrollment.[15,16]

In a survey done in 2014 among 2195 Lebanese adults aged over 25 years, the prevalence of T2DM was around 8.5%, 52.4% of them did not obtain the recommended yearly eye exam and retinopathy was one of the most common complications with a rate of 16.6%.[17]

For patients with T2DM, initial retinopathy screening should be done shortly after the diagnosis of diabetes is made,[18,19] and earlier than 5 years in type 1 diabetes (under age 30).[20] The United Kingdom has adopted 'the English national screening program for sight threatening diabetic retinopathy.'[21] After the wide adoption of this program, and for the first time in at least five decades, DR/maculopathy is no longer the leading cause of certifiable blindness among working age adults in England and Wales. It has in fact have been overtaken by inherited retinal disorders.[22]

In Lebanon, there is no official screening program for diabetes. Many patients present to the ophthalmology clinics with established retinopathy identified during their first funduscopic examination, years after their diagnosis with diabetes. All the studies done among the Lebanese population targeted the prevalence of DR in previously diagnosed patients, but none focused on their initial presentation.[6,23]

Hence, it is important to investigate the details of the first ophthalmological examination of patients diagnosed with diabetes.

This study aimed to determine their source of referral in order to, first of all, draw awareness of the medical professionals to the importance of early detection of retinopathy, and second, to highlight its significance.

Materials and methods

This is a retrospective and descriptive study of patients diagnosed with T2DM who attended the ophthalmology clinic at 'Clinique du Levant' hospital, Beirut, Lebanon, between 2006 and 2016. The 'Clinique du Levant' hospital board granted approval of the study in December 2016 (study number 75-2016) and ensured adherence to the guidelines of the Declaration of Helsinki.

Inclusion criteria were as follows: any patient undergoing the ophthalmological examination for the first time after being diagnosed with T2DM.

Exclusion criteria were as follows: patients with type 1 diabetes or diagnosed with diabetes at an age younger than 40, patients not undergoing a retinal examination, patients with previous congenital ocular disease, patients with any previous complicated ocular surgery, and non-Lebanese patients.

Note that non-Lebanese were excluded because they did not have health care access in Lebanon which may affect the results of the study by falsely increasing the percentage of DR.

The information collected from the patient's medical files included the following: age, sex, past medical history, the purpose of the visit (asymptomatic screening *versus* symptomatic if they complain of a decrease in the visual acuity whether far or near vision, an inflammatory or an infectious etiology) and the sources of referral: (1) endocrinologist and primary health care

professionals (HCPs) (general practitioners), (2) other HCPs (remaining medical specialists), and (3) patients with no identifiable referral source. Also, the best-corrected visual acuities were recorded and classified according to the revision of visual impairment definitions in the International Statistical Classification of Diseases.[24] The patients included in the categories numbered 3, 4, 5, and 6 of visual impairment were joined under the name of legal blindness in order to highlight the number of blind patients presenting for their first ocular examination. In addition, the manifest and cycloplegic refractions, the intraocular pressure, and the anterior and posterior segment evaluations with dilated fundus examination (using noncontact 90D Volk slit lamp lens by trained physicians) were assembled. In cases of dense cataract, funduscopy was done during the first week post op. Refined refraction was achieved using trial lenses. Angiography and optical coherence tomography (OCT) were performed in selected cases following insufficient clinical examination or for further classification of the severity of retinopathy and macular edema or to guide treatment.

The patients diagnosed with DR were then classified into NPDR (mild, moderate, and severe) and PDR. Macular edema was also divided to mild, moderate, and severe according to the International Clinical Diabetic Retinopathy and Diabetic Macular Edema Disease Severity scales.[25]

We hypothesized that the percentage of retinopathy would be high and the patient's presentation would be delayed compared with the international recommendations. The sources of referral, sex, duration of diabetes and age may be independent variables affecting this result.

Statistical analysis

The minimum sample size required to determine whether a correlation existed is 194 (α: 0.05, β: 0.2, correlation coefficient: 0.2). For descriptive statistics, continuous variable (age) was presented as mean and standard deviation, and categorical variables (purpose of the visit, retinopathy scale, visual impairment) were presented as proportions. To explore the relationships between different variables, chi-square test was used for categorical variables (sources of referral, sex); independent *t*-test and analysis of variance (ANOVA) were used for continuous variables (diabetes duration, age). The p value was considered significant if less than 0.05 and no adjustment for multiple comparisons was made. All data were analyzed using SPSS version 23.0 (SPSS, Inc., Chicago, IL, USA). Finally, multivariable analysis was done to show the adjusted association of variables with DR.

Results

A total of 484 patients, 55% men and 45% women, were included in the study. The average age at the first ophthalmological visit after diagnosis with diabetes was 62.1 years with no difference between sex ($p = 0.23$, confidence interval (CI): [−3.97; −0.09]) (Table 1).

About 82.6% of the patients were symptomatic at presentation. Among them, 59.6% were complaining of decrease in their far vision, 14% were complaining of a decrease in their near vision, and 9% had other complaints (red eye, vertigo, diplopia, phosphene). Only 17.4% were asymptomatic at presentation and presented for screening after they were diagnosed with diabetes (Table 2).

About 23.2% of the patients were referred by an HCP (5% by endocrinologists and general practitioners *versus* 18.2% by other HCP).

Patients presented for ophthalmological exam with an average of 8.3 years after their diagnosis with diabetes. The patients referred by HCP presented after 5 years of diagnosis of diabetes, while those with no identifiable referral source presented 8.9 years after diagnosis of diabetes ($p = 0.013$). Mann–Whitney test showed that the difference in diabetes duration at presentation between the subcategories is significant ($p = 0.02$ comparing the patients referred by 'other HCP' and those with 'no identifiable source') ($p = 0.04$ comparing the patients referred by endocrinologists and those with no identifiable source of referral). The average time before the first examination of a female patient was 7.3 years, while it was 9.1 years in a male patient ($p = 0.012$) (Table 3).

Visual acuity decreased in 44.1% of the patients, and 11.2% had a visual acuity less than 20/200 (0.1) (Table 4). Of the 484 patients, 183 (37.8%) had a cataract (grade higher than 1); 11 (2.2%) had corneal, conjunctival, or eyelid disease (keratitis, conjunctivitis, blepharitis, etc.); and 1

Table 1. Demographic data (age, sex, purpose of the visit).

	Diabetic patients		Age	
	N	%	Mean	SD
Gender				
Male	266	55	61.1	11.2
Female	218	45	63.2	10.2
Total	484	100	62.1	10.8
Purpose of the visit				
Symptomatic	400	82.6		
Screening	84	17.4		

N, number of patients; SD, standard deviation.

Table 2. Classification of the patients according to the purpose of the visit.

Purpose of the visit	N	%
Decrease in visual acuity	288	59.6
Screening	84	17.4
Presbiopia	69	14
Others	43	9

N, number of patients.

patient had lens subluxation. Further investigations were performed on 91 patients. Among them, 39 had angiography, 14 had OCT, and 38 had angiography and OCT.

About 24.6% of the patients (119 patients) met the criteria for DR during their first funduscopic examination and proliferative retinopathy was the most common at presentation (n = 43, 8.9%). On the other hand, 16.7% of these patients had macular edema which was severe (>500 μm) in 6.2%. In 18 patients, edema could not be assessed mostly due to intravitreous hemorrhage (Table 5).

Data analysis revealed no positive correlation comparing the sources of referral and sex with the retinopathy severity using chi-square test. In addition, no statistically significant difference was found between the mean age at presentation and the retinopathy severity ($p = 0.505$) and macular edema status ($p = 0.449$) using ANOVA test (Table 6).

On the other hand, the severity of the retinopathy had a positive correlation with the diabetes duration ($p = 0.0001$ using ANOVA test); multiple comparisons using Bonferroni test showed that the difference in average diabetes duration was significantly higher in the subcategory of patients with mild NPDR, moderate NPDR, and PDR, as compared with the patients with no apparent retinopathy. This difference was 6.7 years in the nonretinopathy group *versus* 16.2 years in mild NPDR ($p = 0.0001$, CI [−12.9; −5.91]), *versus* 11.6 years in moderate NPDR ($p = 0.001$, CI [−8.3; −1.4]), *versus* 13.2 years in PDR ($p = 0.0001$, CI [−9.4; −3.4]).

The macular edema status was also dependent on the duration of diabetes ($p = 0.0001$ using ANOVA test); multiple comparisons using Bonferroni test showed that the difference was high when comparing the duration of diabetes in patients with absence of macular edema (7.3 years) with the duration in patients with mild/moderate macular edema (12.3 years) ($p = 0.0001$, CI [−7.4; −2.5]), and severe macular edema (12.7 years) ($p = 0.0001$, CI [−8.5; −2.2]). But, no statistically significant difference in duration was found while comparing mild/moderate *versus* severe macular edema ($p = 1$).

Discussion

To the best of our knowledge, the abovementioned results would be the first of its kind to reflect the Lebanese population concerning the percentage of DR and its severity at the first ophthalmological examination in patients diagnosed to have T2DM.

Table 3. Influence of the sources of referral and sex on the duration of diabetes before presentation to the funduscopic exam.

		Patients		Diabetes duration			Group differences	
		N	%	Mean	Median	SD	Group variable	*p* value
Sources of referral	Endocrinologist/ PHCP	24	5	5.8	3.5	5.5	*versus* Other HCP[a]	0.395
	Other HCP	88	18.2	5	5.7	8.9	*versus* No identifiable sources of referral[a]	0.02
	No identifiable sources of referral	372	76.9	8.9	7	7.5	*versus* Endocrinologist/ PHCP[a]	0.04
	Total	484	100	8.3	6	7.1	Chi-square[b]	0.013
Gender	Male	266	55	9.1	8	11.24	*versus* Diabetes duration[a]	0.012
	Female	218	45	7.3	5	10.23		

HCP, health care professional; N, number of patients; PHCP, primary health care professional; SD, standard deviation.
[a]Mann–Whitney test.
[b]Kruskal–Wallis test, chi-square value: 8.7.

Table 4. Visual acuity classification.

Visual impairment	Visual acuity	N	%
No visual impairment	20/20→20/40	271	55.9
Mild visual impairment (c.1)	<20/40→20/60	71	14.7
Moderate visual impairment (c.2)	<20/60→20/200	88	18.2
Legal blindness (c.3, 4, 5, 6)	<20/20→0LP	54	11.2
Total		484	100.0

C, categories of severity of visual impairment in the International Statistical Classification of Diseases; LP, light perception; N, number of patients.

According to the latest T2DM retinopathy screening recommendations, patients should be screened for retinopathy directly after diagnosis with diabetes.[18,19] Even though the patients referred by the endocrinologist and HCPs presented earlier, they represent only the quarter of the total patients recruited. The delay in examination of the majority of the patents may be explained by noncompliance to the physicians' recommendations, the absence of a medical advisor, or the lack of knowledge concerning the screening and complications of DR. As a consequence, the mean age of presentation for examination was 8 years late. An interesting finding is that women tend to present 1.8 years earlier than men.

According to the obtained results, the number of newly diagnosed cases of DR was elevated. Even though these numbers do not represent the overall prevalence of DR because we eliminated the previously known diabetics, and they are indeed high compared with the findings reported in 2014, stating that the prevalence of DR was 16.6% in the Lebanese population.[17] But our results were lower than those reported in 2009 revealing a DR prevalence of 35%, 9% of the diabetic patients had PDR, and 8% a clinically significant macular edema.[6] In a meta-analysis, the global prevalence of retinopathy in newly diagnosed T2DM patients was 10.5% (6–16%).[26] Hence, the delay in the presentation for examination may be an associating factor leading to the

Table 5. Retinopathy and macular edema severity.

		N	%
Diabetic retinopathy severity scale	No apparent retinopathy	365	75.4
	Mild NPDR	30	6.2
	Moderate NPDR	32	6.6
	Severe NPDR	14	2.9
	PDR	43	8.9
	Total	484	100
Macular edema status	Absent	385	79.5
	Mild	18	3.7
	Moderate	33	6.8
	Severe	30	6.2
	Not available	18	3.7
	Total	484	100

N, number of patients; NPDR, nonproliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy.

Table 6. Comparison between retinopathy severity and dependent variables (age, sources of referral, sex, duration).

Severity scale	Mean age	Sources of referral			Gender		Duration
		Endocrinologist/ PHCP	Other health care professionals	No identifiable referral source	Male	Female	
No apparent Retinopathy	61.91	21	68	276	192	173	6.7
Mild NPDR	64.53	0	6	24	18	12	16.2
Moderate NPDR	63.91	1	6	25	18	14	11.6
Severe NPDR	62.29	0	4	10	8	6	11
PDR	60.1	2	4	37	30	13	13.2
p value	**0.505**[a]	**0.612**[b]			**0.289**[b]		**0.0001**[a]
Absence of macular edema	62.03	21	72	292	203	182	7.3
Mild or moderate macular edema	63.75	1	8	42	33	18	12.3
Severe macular edema	60.8	1	4	25	20	10	12.7
p value	**0.449**[a]	**0.679**[b]			**0.111**[b]		**0.0001**[a]

NPDR, nonproliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy; PHCP, primary health care professionals.
p value significant <0.05.
[a]ANOVA test.
[b]Chi-square tests. The bold numbers represent the p-value of the statistical tests performed on the variables cited above them.

development of higher rates of retinopathy in the Lebanese population at their first examination compared with the worldwide prevalence.

The majority of the patients were symptomatic at presentation and their most common complaint was a decrease in the far vision. These low acuities were explained partially by the high number of cataracts reported during the slit lamp examination.

The age, the sources of referral, and the sex differences were not related to the various degrees of retinopathy and macular edema. The duration of diabetes was the only dependent factor. Only mild, moderate NPDR, and PDR had this duration significantly higher than the patients without retinopathy. Duration was also higher in patients with any degree of macular edema compared with patients without edema. These observations were expected because of the natural progression of the complications in diabetics.

This study proves that patients are not receiving the appropriate funduscopic examination at the time of their diagnosis with T2DM and they are presenting late to the ophthalmologists with a decrease in their visual acuity due to cataract and to the more advanced stages of retinopathy and macular edema.

We can assume that the real numbers of retinopathy could be even higher due to two limitations of this study. First, this study was conducted in one hospital in Beirut and it may not include the subpopulation of patients living in rural areas with lower socio-economic status, with no access to medical systems and who will probably have a higher degree of retinopathy. Second, even though indirect ophthalmoscopy is a sensitive and specific screening tool, most experienced ophthalmologists may miss mild degrees of retinopathy and mild macular edema that may only be revealed on angiography and OCT. But, until now, these are not recommended as screening tools due to their high cost.

Two possible interventions may promote earlier presentation of patients and reduce complications from DR: first, increasing the awareness of physicians, from different medical specialties to the importance of an ophthalmological consultation in patients with diabetes, and second, adopting a national program for diabetes awareness to prevent and control the complications of diabetes. More studies are necessary to determine the applicability of the DR screening guidelines and its effect in preventing the complications of retinopathy with minimal cost among the Lebanese population.

In conclusion, patients diagnosed with T2DM in Lebanon have a delay in their first ophthalmological examination. This delay was found to be reason for the high number of diagnosed retinopathy. There is a need to promote outreach programs for people with diabetes for early detection of retinopathy.

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