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Original Article

Comparison of Associated Factors for Diabetic Retinopathy between Elderly and Younger Adult Patients with Type 2 Diabetes Mellitus in Northern Taiwan: Experience from One Medical Center

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SUMMARY

Background: The prevalence of diabetic retinopathy (DR) is higher in elderly patients with type 2 diabetes mellitus (T2DM) than the younger adult population, and the associated factors involved may be different between these two groups. This study aimed to investigate the prevalence and associated factors of DR in the elderly and younger adult population with T2DM.
Methods: The study recruited 428 patients with T2DM, including 220 elderly subjects and 208 younger adult subjects. All subjects were examined for DR using fundus photography by an experienced ophthalmologist. Data including age, anthropometric measurements, blood pressure, glycemic profiles, lipid profiles, liver enzymes, renal function and microalbuminuria were collected. Simple logistic regression analysis and multiple logistic regression analysis were then performed to analyze the associated factors of DR in the elderly and younger adult groups.
Results: The prevalence of DR was 26% and 16% in elderly and younger adult patients, respectively. In multiple logistic regression analysis, independent factors associated with DR in elderly patients were the presence of albuminuria (OR: 3.47, 95% CI: 1.79–6.71, $p < 0.001$) and longer DM duration (OR: 2.56, 95% CI: 1.20–5.46, $p = 0.015$). For younger adult patients, higher HbA1c level (OR: 3.26, 95% CI: 1.33–7.99, $p = 0.010$) was found to be associated with DR.
Conclusion: Microalbuminuria showed a stronger association with DR in elderly patients with T2DM, while high glucose level showed stronger association with DR in the younger adult population. In order to prevent development of retinopathy, these independent factors should be recognized early in T2DM patients according to different age groups.

1. Introduction

Diabetic retinopathy (DR) is a major cause of visual impairment and blindness in patients with type 2 diabetes mellitus (T2DM).[1] More than 75% diabetes patients develop DR within 20 years after the diagnosis of diabetes.[2] Since the prevalence of diabetes increases with age, the prevalence of DR in elderly is also higher than in younger patients.[3] Futhermore, as average life expectancy increases, more and more elderly patients have diabetic retinopathy. Therefore, it is important to understand the factors associated with DR in elderly patients with diabetes, which may serve as important indicators for diabetic microvascular complications. Previous studies had shown that the duration of diabetes, glycemic control, hypertension (HTN) and albuminuria are the main independent risk factors for DR,[4–6] however these researches about risk factors of DR mostly focused on adults in general or the general population.[7,8] The development of DR may be attributed to age, genetic background, lifestyle and food composition, therefore, data from these previous studies may not very well represent the condition for the elderly population or adults from a different region.[9] Few papers had reported factors related to DR in the elderly population. In addition, there is limited data on comparing the prevalence and factors of DR between elderly and younger adult patients with T2DM. Therefore, we conducted this study to compare the prevalence and factors associated with DR between elderly and younger adult patients with T2DM in Taiwan.

2. Materials and methods

This was a retrospective cross-sectional study comprising of 512 subjects with T2DM, ranging from 40 to 91 years of age, who received diabetes management in the Endocrine outpatient department at the Taipei branch of Mackay Memorial Hospital from September 2016 to February 2017. All 512 subjects underwent detailed examinations at the ophthalmologic clinic in MacKay Memorial Hospital. We excluded patients who did not have report for the fundoscopic examination, mainly because they were unable to undergo or cooperate with the examination. We were left with

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428 patients with T2DM, including 220 elderly (≥ 65 years of age) subjects and 208 younger adult subjects (< 65 years of age).

Participants received mydriatic fundoscopic examination from an experienced ophthalmologist. A 45° photograph of the central fundus was taken from all eyes using a digital retina camera (Nonmyd 7, Kowa Corp., Tokyo, Japan). Diagnosis of DR was based on the modified Early Treatment Diabetic Retinopathy Study classification system, and the patient was considered to have DR if any of the characteristic lesions was present: microaneurysm, hemorrhage, hard or soft exudates, beaded veins, retinal microvascular abnormalities, cotton woollen spots, preretinal new vessels, fibroplasia and/or photocoagulation scar.[10] We included both nonproliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR) in our study. All subjects were categorized into the DR group (N = 90) and non-DR group (N = 338) accordingly.

Data including age, waist circumference, body mass index (BMI), fasting plasma glucose (FPG), post-prandial plasma glucose (PPG), glycosylated hemoglobin (HbA1c), total cholesterol, triglycerides, low-density-lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), liver enzymes, serum creatinine, estimated glomerular filtration rate (eGFR) and urinary albumin-creatinine ratio (ACR) were collected. In addition, personal history (smoking and drinking) and diabetes duration were also recorded. All patients enrolled in this study received intensive treatment for T2DM and HTN, and received guidance from diabetes educators on lifestyle control.

This study was approved by the Institutional Ethics Committee, Mackay Memorial Hospital.

2.1. Statistical analyses

Statistical analysis was performed using IBM SPSS release 21.0 (IBM, Armonk, New York). The continuous variables of the baseline characteristics of the study participants were expressed as mean ± standard deviation (SD). Student's t-test was used to analyze the differences in baseline characteristics between the elderly and younger adult groups. The noncontinuous data were presented as percentages and analyzed by Pearson's Chi-square test. A simple logistic regression analysis was performed to determine the odds ratios (ORs) of DR-related factors and 95% confidence intervals (CI). Multiple logistic regression analyses were then performed using stepwise method, with p-value less than 0.05 (two-sided) consider statistically significant in this study.

3. Results

The elderly group was comprised of 220 subjects ranging from 65 to 91 years of age (73.1 ± 5.58 years). The younger adult group was comprised of 208 patients between 40 and 64 years of age (57.90 ± 5.04 years). The distribution of patients based on the presence of retinopathy is shown in (Fig. 1). The prevalence of DR was 26% and 16% in elderly and younger adult group, respectively (Table 1). Comparison of baseline and biochemical characteristics between DR patients and non-DR patients in both the elderly and the younger adult group was shown in Table 2. Elderly patients with DR had significantly higher PPG and higher SBP than those without DR. On the other hand, younger adult patients with DR had significantly longer DM duration, higher FPG, PPG, HbA1c and SBP than those without DR.

Table 3 showed clinical factors associated with DR for both age groups. The elderly group (26% vs. 16% for younger adult group; OR 1.85; p = 0.015) was significantly associated with DR in the simple logistic regression analysis. In addition, those with longer DM duration (> 10 years), higher SBP level (SBP > 140 mmHg), higher HbA1c level (HbA1c > 7%), presence of CKD (eGFR < 60 mL/min/1.73 m^2) and microalbuminuria (ACR > 30 mg/g) also had a higher chance of having DR among all subjects. In the elderly group, longer DM duration (OR 2.62; 95% CI: 1.33–5.15), higher HbA1c level (OR 1.83; 95% CI: 1.01–3.29), presence of CKD (OR 2.62; 95% CI: 1.43–4.77) and microalbuminuria (OR 3.94; 95% CI: 2.14–7.22) were significantly associated with DR, while, in the younger adult group, higher HbA1c level (OR 2.90; 95% CI: 1.30–6.46), higher SBP level

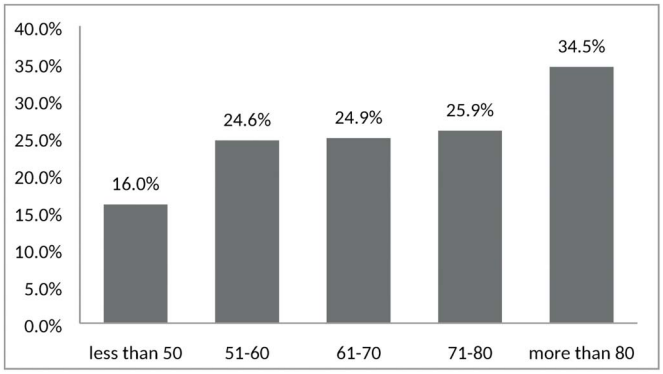

Fig. 1. Prevalence of DR according to age distribution (%). The prevalence of DR is higher in elderly patients with T2DM than the younger adult population.

Table 1
Demographic data and clinical and laboratory findings among elderly and younger adult patients with T2DM.

	Elderly (N = 220)	Younger adult (N = 208)	p
Age (years)	73.10 ± 5.58	57.90 ± 5.04	< 0.001
Gender (male, %)	39.4	39.5	0.978
BMI (kg/m^2)	25.25 ± 3.84	25.59 ± 4.718	0.433
DM duration (years)	13.18 ± 7.85	10.30 ± 5.748	< 0.001
FPG (mg/dL)	157.95 ± 40.61	161.04 ± 53.00	0.232
PPG (mg/dL)	201.31 ± 59.71	211.50 ± 73.69	0.182
HbA1c (%)	7.84 ± 7.18	7.65 ± 1.61	0.726
TC (mg/dL)	170.72 ± 33.03	173.96 ± 35.00	0.358
TG (mg/dL)	120.81 ± 65.20	128.98 ± 78.85	0.306
LDL-C (mg/dL)	93.83 ± 24.98	98.53 ± 26.25	0.075
HDL-C (mg/dL)	49.85 ± 14.96	49.94 ± 15.80	0.953
GPT (mg/dL)	24.93 ± 13.40	29.47 ± 29.14	0.075
Cr (mg/dL)	1.05 ± 0.64	0.83 ± 0.37	< 0.001
EGFR (mL/min/1.73 m^2)	70.16 ± 25.41	92.16 ± 31.56	< 0.001
ACR (mg/g)	231.90 ± 839.61	128.43 ± 481.23	0.139
SBP (mmHg)	142.58 ± 18.06	139.14 ± 18.48	0.065
DBP (mmHg)	76.49 ± 9.79	78.266 ± 10.09	0.079
Smoking (%)	6.6	8.0	0.379
Alcohol (%)	2.9	3.8	0.265
DR (%)	26	16	0.015
Medication			
Oral antidiabetic drug (%)	97.0	96.8	0.983
Insulin (%)	12.6	18.2	0.071
Antihypertensive agent (%)	58.5	41.5	< 0.001
Stain or fibrate (%)	51.9	48.1	0.413

Data are presented as the mean value ± standard deviation or %.
BMI, body mass index; FPG, fasting plasma glucose; PPG, post-prandial plasma glucose; HbA1c, glycosylated hemoglobin; TC, total cholesterol; TG, triglyceride; LDL, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; GPT, glutamic-pyruvic transaminase ; Cr, creatinine; eGFR, estimated glomerular filtration rate; ACR, urine albumin-creatinine ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; DR, diabetic retinopathy.

Table 2
Demographic data and clinical and laboratory findings among elderly and younger patients with DR.

	Elderly			Younger adult		
	DR (N = 57)	NDR (N = 163)	p	DR (N = 33)	NDR (N = 175)	p
Age (years)	73.33 ± 5.74	73.01 ± 5.54	0.728	57.87 ± 4.63	57.91 ± 5.14	0.970
Gender (male)	30.80%	42.60%	0.134	43.30%	38.60%	0.627
BMI (kg/m^2)	25.08 ± 3.04	25.31 ± 4.09	0.668	25.64 ± 4.68	25.59 ± 4.74	0.962
DM duration (years)	14.21 ± 5.90	12.82 ± 8.42	0.196	12.59 ± 4.78	9.89 ± 5.82	**0.020**
FPG (mg/dL)	148.85 ± 47.48	139.53 ± 37.79	0.205	192.20 ± 55.62	155.13 ± 50.54	**< 0.001**
PPG (mg/dL)	226.51 ± 62.82	192.14 ± 56.04	**0.001**	258.05 ± 94.18	203.75 ± 67.08	**0.018**
HbA1c (%)	7.76 ± 1.32	7.87 ± 8.31	0.930	8.78 ± 2.19	7.44 ± 1.39	**< 0.001**
TC (mg/dL)	172.88 ± 31.74	169.99 ± 33.54	0.594	174.48 ± 40.10	173.86 ± 34.08	0.930
TG (mg/dL)	137.40 ± 80.10	114.23 ± 57.30	0.066	118.71 ± 58.75	131.20 ± 82.57	0.449
LDL-C (mg/dL)	93.25 ± 21.99	94.04 ± 26.00	0.847	97.31 ± 30.43	98.77 ± 25.48	0.785
HDL-C (mg/dL)	47.62 ± 11.61	50.62 ± 15.92	0.222	53.29 ± 16.05	49.32 ± 15.74	0.224
GPT (mg/dL)	24.16 ± 12.57	25.21 ± 13.73	0.662	24.41 ± 10.96	30.41 ± 31.32	0.377
Cr (mg/dL)	1.12 ± 0.57	1.03 ± 0.67	0.386	0.80 ± 0.33	0.84 ± 0.39	0.625
EGFR (mL/min/1.73 m^2)	65.89 ± 30.00	71.66 ± 23.54	0.221	96.73 ± 33.67	91.22 ± 31.16	0.393
ACR (mg/g)	428.17 ± 1050.14	166.04 ± 748.81	0.058	317.09 ± 779.95	92.16 ± 392.91	0.113
SBP (mmHg)	148.06 ± 20.98	140.66 ± 16.58	**0.024**	145.90 ± 18.12	137.87 ± 18.32	**0.029**
DBP (mmHg)	77.13 ± 11.07	76.26 ± 9.34	0.582	81.47 ± 10.06	77.66 ± 10.02	0.058

Data are presented as the mean value ± standard deviation or %.
BMI, body mass index; FPG, fasting plasma glucose; PPG, post-prandial plasma glucose; HbA1c, glycosylated hemoglobin; TC, total cholesterol; TG, triglyceride; LDL, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; GPT, glutamic-pyruvic transaminase; Cr, creatinine; eGFR, estimated glomerular filtration rate; ACR, urine albumin-creatinine ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Table 3
Associated factors for DR among different age groups using stepwise logistic regression analysis.

	Total		Elderly		Younger adult	
	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted
	OR 95% (CI)	OR 95% (CI)	OR 95% (CI)	OR 95% (CI)	OR 95% (CI)	OR 95% (CI)
Elderly (> 65 years)	1.85 (1.12–3.05)*					
DM duration (> 10 years)	2.34 (1.37–3.99)**	1.98 (1.17–3.34)*	2.62 (1.33–5.15)**	2.56 (1.20–5.46)*	1.93 (0.93–4.00)	
Higher HbA1c level (> 7)	2.00 (1.18–3.37)**	1.80 (1.07–3.04)*	1.83 (1.01–3.29)*		2.90 (1.30–6.46)**	3.26 (1.33–7.99)**
Hypertension (SBP > 140)	1.95 (1.19–3.21)**		1.77 (0.99–3.16)		2.21 (1.07–4.55)*	
TG (per mg/dL)	1.00 (0.99–1.00)		1.00 (1.00–1.01)*		1.00 (0.99–1.01)	
LDL (per mg/dL)	0.99 (0.98–1.00)		1.00 (0.99–1.02)		0.99 (0.98–1.01)	
CKD (eGFR < 60 mL/min/1.73 m^2)	2.29 (1.40–3.72)**		2.62 (1.43–4.77)**		1.20 (0.42–3.42)	
Microalbumin (ACR > 30 mg/g)	3.25 (1.94–5.43)$^{\#}$	2.90 (1.77–4.73)$^{\#}$	3.94 (2.14–7.22)$^{\#}$	3.47 (1.79–6.71)$^{\#}$	2.53 (1.23–5.22)*	

* p < 0.05, ** p < 0.01, $^{\#}$ p < 0.001.
HbA1c, glycosylated hemoglobin; SBP, systolic blood pressure; TG, triglyceride; LDL, low-density lipoprotein cholesterol; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; ACR, urine albumin-creatinine ratio.

(OR 2.21; 95% CI: 1.07–4.55) and presence of microalbuminuria (OR 2.53; 95% CI: 1.23–5.22) were associated with DR.

Using multiple logistic regression analysis, also shown in Table 3, longer DM duration (OR: 1.98, 95% CI: 1.17–3.34, p < 0.05), higher HbA1c level (OR: 1.80, 95% CI: 1.07–3.04, p < 0.05) and presence of microalbuminuria (OR: 2.90, 95% CI: 1.77–4.73, p = < 0.001) were found to be significantly associated with DR after adjusting for other factors. In the elderly group, those with presence of microalbuminuria (OR: 3.47, 95% CI: 1.79–6.71, p < 0.001) and longer DM duration (OR: 2.56, 95% CI: 1.20–45.46, p = < 0.05) had higher chance of having DR. In the younger adult group, only higher HbA1c level (OR: 3.26, 95% CI: 1.33–7.99, p < 0.01) was significantly associated with DR.

4. Discussion

The prevalence of diabetic retinopathy varies among different populations, ranging from 11.9% to 43.1% in Asia-Pacific countries,[11] and 28.5 to 39.1% in western countries.[4] According to the 2013–2015 National and Health Survey in Taiwan, the prevalence of diabetes mellitus was 11.8% (13.1% for males and 10.5% for females), and is increasing at a rate of 25000 persons per year. The percentage of those with diabetes seeking care for diabetic retinopathy was roughly around 31.1% in 2011.[12] In our study, we found the prevalence of diabetic retinopathy in the elderly group to be 26%, and 16% in the younger adult group.

Cardiovascular risk factors such as age, DM duration, hypertension, hyperglycemia, albuminuria had been found to be associated with significantly increase in prevalence of diabetic retinopathy.[13,14] In our study, older age was significantly associated with DR (OR, 1.85, 95% CI: 1.12–3.05, p = 0.016). Zhang et al. found that the prevalence of diabetic retinopathy in the United States was correlated with longer diabetes duration (OR, 1.06; 95% CI, 1.03–1.10).[4] Our study showed that the average duration of diabetes in older adults was longer than the average duration of younger adult patients (13.18 vs. 10.30 years, p = .001). In addition, older patients with DR had a longer duration of disease than younger adult patients with DR (14.21 vs. 12.58 years, p = 0.209). In agreement with previous researches, our study results further showed presence of diabetic retinopathy was significantly associated with longer DM duration (OR: 2.34, 95%: 1.37–3.99, p = 0.001), presence of HTN (OR: 1.95, 95%: 1.19–3.21, p = 0.007), microalbuminuria (OR: 3.25,

95%: 1.94–5.43, p = < 0.001), and higher HbA1c level (OR: 2.00, 95%: 1.18–3.37, p = 0.008). In the multiple regression analyses for all study subjects and in the elderly group, diabetes duration and albuminuria were both associated with the presence of DR after adjusting for other factors.

For younger adult patients with DR, hyperglycemia was the only variable associated with DR after adjusting for other confounding factors in our study. Diabetes duration is a very important risk factor for DR, but for young people who don't have as long of a disease duration, other risk factors such as blood glucose control are more important than the duration of illness.[15] In a study of young diabetic patients with an average of 10 years of illness, patients with DR had worse glycemic control than patients without DR (p < 0.001). Through Cox regression analysis, time to retinopathy was found to be related to high HbA1c (p < 0.001) and high BMI (p = 0.001) in young diabetes patients.[16] It can be implied that for young people with type 2 diabetes, blood glucose control is more relevant and important than the length of the disease for development of DR.

In our study, albuminuria was more associated with elderly than younger adults for risk of DR. The prevalence of microalbuminuria in patients with T2DM is high. Age is usually a risk factor because about one-quarter of patients with an average diabetes duration of more than 10 years are affected.[17] Albuminuria is not only associated with DR but also may predict the risk for DR development and progression in patients with T2DM.[18] For T2DM, microalbuminuria, when compared with decline in GFR, has a greater impact on predicting the development and progression of diabetic retinopathy.[19]

Results were inconsistent for association between lipids and the occurrence of DR in many population-based studies and clinical trials.[20,21] The presence of hyperlipidemia, as well as individual lipid measurements including TC, LDL-C, HDL-C, and TGs, were all not significantly associated with diabetic retinopathy in our investigation (Table 2). It is generally believed that blood lipids are associated with diabetic macular edema or retinal hard exudates.[22] No association was found between serum lipids and diabetic retinopathy on atherosclerosis in multiple-ethnic study.[23]

One major limitation of our study is that we cannot draw conclusions about casual relationship between the factors and development of DR due to the cross-sectional nature of our study. Another limitation of our study is that the study sample is only from one hospital located in Northern Taiwan. The results of our study cannot be generalized to the Taiwanese population. Nevertheless, conclusions regarding factors associated with DR were recognized. Our study was first to make comparison of factors for DR between elderly and younger adult population.

5. Conclusion

Our data showed that the presence of associated factors for DR were different between elderly and younger adult patients. The presence of microalbuminuria was associated with DR in elderly patient with T2DM, while hyperglycemia was associated with DR in younger adult patients. In order to prevent development of retinopathy, these factors should be recognized early in patients according to different age groups. Comprehensive studies are needed to clarify the roles of these factors and their relationship with DR.

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