

Epidemiological characteristics and risk factors of diabetic retinopathy in type 2 diabetes mellitus in Shandong Peninsula of China

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Abstract

• **AIM:** To determine the epidemiological characteristics and estimate the risk factors of diabetic retinopathy (DR) in patients with type 2 diabetes mellitus (T2DM) in Shandong Peninsula of China.

• **METHODS:** The cases of T2DM admitted to Affiliated Hospital of Medical College of Qingdao University, Shandong Province, China, from January 2006 to December 2010 were retrospectively reviewed. The epidemiological characteristics of DR were estimated. The cases were divided into two groups according to degrees of retinopathy: non-DR group and DR group. Logistic regression analysis was used to study the related risk factors of DR.

• **RESULTS:** The prevalence of DR in patients with T2DM was 25.08% (834/3326). There was significant difference between the average age for men (59.08 ± 15.43 years) and for women (62.92 ± 18.19 years, $P=0.0021$). The majority of DR occurred in women (female: male ratio=1.76:1, $P<0.0001$). The incidence rate of DR in urban (489/834) was higher than that in rural area (345/834, $P<0.0001$). In 834 DR patients, the mean duration of T2DM was 8.90 ± 4.15 years (range: 0-16 years); 440 people (52.76%) had received varying degrees of health education about prevention and primary care of DM; and 473 people (56.71%) suffered from other DM complications confirmed at the same time. In addition, the incidence rate of monocular (551/3326) and binocular retinopathy (283/3326) were statistically different ($P < 0.0001$). Factors associated ($P<0.05$) with the presence of DR included old age, lower health educational level, intraocular surgery history, longer duration of T2DM, accompanying with other DM complications, no standard treatment procedure,

lower body mass index (BMI) and higher fasting plasma glucose (FPG), glycated hemoglobin A_{1c} (HbA_{1c}), urine albumin (UA), total cholesterol (TC), low-density-lipoprotein cholesterol (LDL-C). The risk factors ($P<0.05$) independently associated with the presence of DR were: longer duration of T2DM, lower health educational level, higher FPG, higher UA, lower BMI and higher TC.

• **CONCLUSION:** DR is highly prevalent in the patients with T2DM in Shandong Peninsula of China. Besides blood glucose, many factors are associated with the present and development of DR.

• **KEYWORDS:** diabetic retinopathy; type 2 diabetes mellitus; risk factors

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INTRODUCTION

Globally, diabetes mellitus (DM) has become one of the most important chronic public health problems. Because of the rapid lifestyle change, the prevalence of DM is increasing in China. Yang *et al*^[1] estimate that currently 92.4 million adults in China have DM, and type 2 diabetes mellitus (T2DM) accounts for more than 90% above. China is considered one of the countries with the largest T2DM burden. Although T2DM is not among the top leading causes of death, such as cancer and cerebrovascular disease, it draws attention from the public due to its increasing trends and varying complications^[2]. Chronic complications are the major outcome of T2DM progress, which reduce the quality of life of patients, incur heavy burdens to the health care system, and increase diabetic mortality^[3]. The most common microvascular complication of T2DM is diabetic retinopathy (DR). DR is a leading cause of blindness both in developing and developed countries. Several countries have reported their incidence and progression of DR in T2DM^[4,5].

However, in recent years, there have been few reports about epidemiological characteristic of DR by use of large sample in China, especially in foreland of China, which is the representative region of rapid economic growth. After executing reforming and opening, foreland of China, such as Shandong Peninsula, becomes the bibcock of whole country economy. Following the growth of the economy, the income level of resident there has improvement by a large margin, and the people's lives are obviously better than that of inland areas. Under the circumstances, the incidence of DR may elevate obviously as well as T2DM, because of the changes of the traditional diet, such as over-taking of high-glucose, high-fat and high-calorie foods. So it's of great importance studying epidemiological characteristics in foreland of China.

Predictors of diabetic complications may be important in the prevention and the management of these complications. As a major complication, the prevention of DR is the most important method to decrease the cases of blindness due to DM. Considering the high prevalence and significant morbidity of DR in patients with T2DM, identification of risk factors is necessary to delay or prevent the onset of DR. Manaviat *et al*^[6] reported that urine albumin (UA), body mass index (BMI), age, fasting plasma glucose (FPG) and glycated hemoglobin A_{1c} (HbA_{1c}) were related to DR. Tapp *et al*^[7] concluded that duration of diabetes, HbA_{1c} and systolic blood pressure were risk factors of DR. However, there have been few studies on the factors associated with the onset and progression of DR in foreland population of China. Therefore, the aims of this study were to describe the prevalence and epidemiological characteristics of DR in a representative T2DM sample of Shandong Peninsula population; and to analyze the associations between some risk factors and the onset and progression of DR. It is hoped that the findings of this study will contribute to the current body of knowledge by elucidating to the epidemiological status of DR in foreland population of China, and assess the risk factors for DR to create more effective interventions.

MATERIALS AND METHODS

Subjects The area of investigation is Peninsula of Shandong Province, which is located in the northeast coast of China. It faces the Pacific on the east with more than 3000 kilometers coastline. Shandong Peninsula covers about almost 39,000km². The current population is just over 36,480,000. The economy includes agriculture (foodstuffs, vegetables and fruits), industries, marine and fisheries, commerce and trade, tourism, services. The main diet consists of meat, seafood, noodles, eggs, vegetables, etc.

The study included patients with T2DM at the Department of Ophthalmology and Endocrinology, Affiliated Hospital of

Medical College Qingdao University. This hospital is the major DM centre which serves as a major referral center for a large geographic area of the Shandong Peninsula's health district. Records from 3326 patients with T2DM were reviewed in a 5-year period from January 2006 till December 2010. All of the patients underwent thorough funduscopy in the Department of Ophthalmology. During the study period (2006 to 2010), the population was stable and there were not significant changes in age and sex structure of the population.

Methods Detailed information regarding the study procedures was provided to all subject investigated. Only patients who agreed to participate and signed the consent forms were included in this study. The subjects were interviewed face-to-face by trained interviewers using a questionnaire to capture information on demographics, T2DM and DR related characteristics. The results of physical examination and laboratory examination came from Regular Physical Examination Center and Laboratory Department of Affiliated Hospital of Medical College Qingdao University. A form was used to record identification data and the following variables for all T2DM patients: age, sexuality, health educational level, residence (urban or rural areas), personal history (drinking alcohol, smoking, etc.), family history, intraocular surgery history, diseased eye, time of explicit diagnosis, complications, treatment procedure, BMI, blood pressure, waist circumference (WC), and other laboratory examination, including FPG, HbA_{1c}, UA, total cholesterol (TC), triglyceride (TG), low-density-lipoprotein cholesterol (LDL-C), high-density-lipoprotein cholesterol (HDL-C) and C-reaction peptide (CRP), etc. The funduscopy findings were based on the direct and indirect ophthalmoscopy. All pupils were dilated before funduscopy. Detailed information on epidemiological characteristics of DR including the symptoms, physical signs, time of progression, grades of DR and treatment procedure was collected. DR was graded according to the International Clinical Diabetic Retinopathy Severity Scale^[8]. Our study was designed to provide accurate estimates of the prevalence of DR in patients with T2DM according to age, sexuality, health educational level, urban or rural residence, duration of T2DM, other DM complications, grades and treatment procedure in the general population in Shandong Peninsula. Through the analysis of above information, we can summarize epidemiology characteristics and rule of the morbidity. Then, the patients with DM were divided into non-DR group and DR group. Non-DR group had not retinopathy. Retinopathy in DR group included microaneurysms, hard exudates, cotton wool spots, retinal hemorrhages, new vessels, extensive

Table 1 Comparisons of clinical and biochemical data between two groups Mean±SD

Parameter	Non-DR(n=2492)	DR(n=834)	P values
Age (yr)	61.23±16.71	63.56±19.30	0.0008
Female: male ratio	1563/929	532/302	0.6089
With health education	1421	440	0.0351
Urban/rural residence	1428/1064	489/345	0.5273
Alcohol intake	516	185	0.3922
Ever smoker	705	247	0.4908
With family history	273	108	0.1329
With intraocular surgery history	179	93	0.0004
T2DM duration (yr)	5.92±3.28	8.90±4.15	<0.0001
Other DM complication(s)	562	514	<0.0001
With standard treatment	2069	725	0.0091
Body mass index (kg/m ²)	24.50±3.01	24.24±3.11	0.0323
Blood pressure (mmHg)			
Systolic blood pressure	133.54± 16.12	132.33± 15.48	0.0582
Diastolic blood pressure	77.78± 9.05	78.17± 8.82	0.2784
Waist circumference (cm)	85.46± 7.79	85.05± 8.01	0.1915
Fasting plasma glucose (mmol/L)	9.43±3.37	9.84±3.56	0.0027
Hemoglobin A _{1c} (%)	8.32±1.81	8.14±1.69	0.0116
Urine albumin (μmol /L)	0.25±0.08	0.29±0.06	<0.0001
Total cholesterol (mmol/L)	5.48±1.10	5.61±1.22	0.0041
Triglyceride (mmol/L)	2.19±0.63	2.21±0.58	0.4185
LDLC (mmol/L)	3.27±0.64	3.39±0.73	<0.0001
HDLC (mmol/L)	1.29±0.25	1.31±0.30	0.0578
C-reaction peptide (mg/L)	11.97±2.61	12.02±2.77	0.6373

neovascularization, vitreous hemorrhages, fibrovascular proliferation with or without retinal detachment. By comparison of the data in the two groups, the risk factors and preventive countermeasures would be estimated.

Statistical Analysis The categorical variables were expressed as rates or proportions and were compared using the chi-square test; one-way analysis of variance (ANOVA) was used to evaluate differences in parametric variables. We analyzed risk factors by the Logistic regression model. All probability values were two-tailed, and statistical significance was defined as $P < 0.05$. All the data were analyzed by SPSS version 14.0 statistical software package (SPSS, Inc., Chicago, IL, US).

RESULTS

DR Characteristics There were 834 DR (1 117 eyes) from 3326 patients with T2DM we investigated over a 5-year period. The average age was 61.23±16.71 years. There was significant difference between the average age for men (59.08±15.43 years) and for women (62.92±18.19 years, $P = 0.0021$; ANOVA test). The majority of DR occurred in women (63.79%; female:male ratio=1.76:1, $P < 0.0001$; Chi-square test). In 834 DR patients, 440 people (52.76%) had received varying degrees of health education about prevention and primary care of DM. The incidence rate of DR in urban (489/834) was higher than that in rural area (345/834, $P < 0.0001$; Chi-square test). The mean duration

of T2DM was 8.90 ±4.15 years (range: 0-16 years). Unfortunately, in 834 DR patients, 473 people (56.71%) suffered from other DM complications confirmed at the same time, such as kidney damage, stroke, nerve damage, heart disease and gangrene in the foot. In addition, the incidence rate of monocular (551/3326) and binocular retinopathy(283/3326) were statistically different($P < 0.0001$; Chi-square test). Graded according to the International Clinical Diabetic Retinopathy Severity Scale, 551 patients appeared to non-proliferative DR and 283 patients appeared to proliferative DR. Within them, 71 patients with severe lesion were present to proliferative DR in two eyes.

DR Risk Factors There were no significant differences between those patients with and those without retinopathy with respect to sexuality, urban or rural residence, alcohol drinking history, smoking history, family history, blood pressure, WC, TG, HDL-C and CRP. Factors associated ($P < 0.05$, Table 1) with the presence of DR included old age, lower health educational level, intraocular surgery history, longer duration of T2DM, accompanying with other DM complication(s), no standard treatment procedure, lower BMI and higher FPG, HbA_{1c}, UA, TC, LDL-C.

Regression Analyses All variables that were significant in the univariate analyses were entered in a multivariate model. In accordance with the degree of importance, the risk factors independently associated with the presence of DR were as

Table 2 Logistic regression analysis of DR independent contributing factors

Parameter	β	SE	Wald	P	OR (95% CI)
Age (yr, mean \pm SD)	0.078	0.163	1.744	0.0945	0.722-1.689
With health education	0.242	0.077	10.379	0.0011	1.107-1.502
With intraocular surgery	0.537	0.358	0.947	0.3753	0.782-2.267
T2DM duration	0.225	0.061	13.189	<0.0001	1.107-1.453
Other DM complication(s)	0.393	0.219	1.314	0.1360	0.948-2.335
With standard treatment	0.015	0.044	0.059	0.7322	0.933-1.242
Body mass index	-0.360	0.144	6.832	0.0095	0.538-0.948
Fasting plasma glucose	0.693	0.214	8.581	0.0025	1.267-3.049
Hemoglobin A ₁ C	0.128	0.323	0.158	0.6467	0.782-2.267
Urine albumin	1.667	0.535	6.744	0.0089	1.484 -21.410
Total cholesterol	0.792	0.398	4.029	0.0388	1.027- 4.231
LDLC	0.043	0.126	1.537	0.1142	0.760-1.532

follows: longer duration of T2DM, lower health educational level, higher FPG, higher UA, lower BMI and higher TC (Table 2).

DISCUSSION

Several previous national or regional studies have documented a rapid increase in the prevalence of DR in the world population [9-13]. The WHO estimates that DR is responsible for 4.8% of the 37 million cases of blindness throughout the world [14]. DR is increasingly becoming a major cause of blindness throughout the world. In addition, loss of productivity and quality of life for the patient with DR will lead to additional socioeconomic burdens on the community. So, it is essential to determine prevalence and estimate the risk factors of DR. With the sharp development of reform and opening-up, the improvement of the living standards, diet structure of the people in foreland of China gradually tends to irrational situation. In addition, the level of medical treatment and health service has not improved synchronously with economic development. The present study showed that the prevalence of DR in a representative sample of patients with T2DM in Shandong Peninsula of China in a 5-year period was 25.08%, which is similar to the findings of Zhang *et al* [13], in which a 28% prevalence of DR was reported in the United States, 2005-2008. However, our number was higher than the 12.75% reported in Enugu and 19% reported in the United Arab Emirates [15]. The higher prevalence of DR in this study could be due to the use of direct and indirect ophthalmoscope for funduscopy in this study, which may have made it possible to find some subtle retinal changes. However, the prevalence of DR in Shandong Peninsula was significantly lower than that in 10 medical centers of four central municipalities of China (Beijing, Shanghai, Tianjin, and Chongqing), which is 31.5% in 2002. This situation perhaps caused by two main reasons. First, the living standard of residents in those four central municipalities is higher than that in Shandong Peninsula. The food habits, such as over-taking of

high-glucose, high-fat and high-calorie foods, are more common. Second, because their better health care, the medical centers in central municipalities could attracted more seriously-ill patients from around the country and sometimes foreigners.

Moreover, it was remarkable that this study showed a higher prevalence of retinopathy among urban residents than among rural residents. It was also observed in other developing countries throughout the world [16]. Our analysis suggests that the level of economic development and associated lifestyle and diet may explain the differences. Urbanization is associated with changes in lifestyle that lead to physical inactivity, an unhealthful diet, and obesity, all of which have been implicated as contributing factors in the development of DM and DR [17]. The findings, which are based on the large population-based study, should provide an accurate estimate of the DR.

Logistic regression analysis revealed certain independent risk factors associated with the development of DR; they were longer duration of T2DM, lower health educational level, higher FPG, higher UA, and lower BMI and higher TC. This study has shown that the duration of T2DM significantly affects the development of DR. Our findings are consistent with those of other studies [18] and show that individuals who have suffered from DM for a long period of time are at risk of developing DR. This highlights the need for physicians to refer DM patients to ophthalmologists for evaluation. It also highlights the necessity of creating awareness among diabetics of the importance of routine eye evaluations, so as to detect early ocular complications that may arise from diabetes mellitus. Like previous studies [19], our study showed a significant inverse association between health educational level and the prevalence of DR. Health educational level is a good indicator of socioeconomic status, and a higher educational level has been associated with lower levels of cardiovascular risk factors, such as obesity, dyslipidemia, and hypertension [20].

FPG, UA and TC are also important independent risk factors of DR. Physicians should ensure the optimal control of blood glucose, blood lipid and UA among DM patients so as to prevent complications and enhance the quality of life of these patients. BMI was absolutely associated with elevated risks for retinopathy. We found that the BMI is negative correlation with the incidence of DR, and this is consistent with report from Lim *et al* [21]. They also found that BMI were associated with lower prevalence of DR. Persons with diabetes that had higher levels of BMI were less likely to have DR. Our study also has several limitations. For example, dietary intake and work-related physical activity were not assessed in our study. Therefore, we were not able to determine the association between these factors and the prevalence of DM more thoroughly. In summary, our results show that DR is highly prevalent in the patients with T2DM in Shandong Peninsula of China. Besides blood glucose, many factors are associated with the present and development of DR. The patients with T2DM should pay more attention to those risk factors and the public health measures should be undertaken to enhance health consciousness of people. DR has become an important public health challenge in China; it is crucial to underscore the need for national strategies aimed at the prevention, detection, and treatment in the general Chinese population.

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