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Prevalence and risk factors for diabetic retinopathy in rural southern China: Dongguan Eye Study

Short title: Diabetic retinopathy in rural southern China

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Abstract

***Objective*:** The current population-based study aims to investigate the prevalence of diabetic retinopathy (DR) and risk factors in residents 40 years and older conducted in Dongguan, rural southern China.

Design: The Dongguan Eye study (DES) (from September 2011 to February 2012) was a population-based study.

Setting: Dongguan, Southern China.

Participants: An adult rural population aged 40 years or older.

Intervention: Participants received hematological, physical, ophthalmic examinations and completed a questionnaire regarding life styles and systemic medical conditions.

Primary and secondary outcome measures: Frequency and risk factors of visual impairment and the major vision-threatening eye diseases.

Results: Of 8952 Han Chinese, 1,500 with an average age of 59.5±11.1 years were diagnosed as type 2 diabetes mellitus (DM) but 1310 participants with fundus photography results were analyzed. Standardized prevalence of DR was 18.2% for all patients with diabetes, 32.8% for the patients with previously diagnosed diabetes, and 12.6% for newly diagnosed DM patients. The prevalence of DR in males was significantly higher than that in females (23.0% vs. 14.1%, P<0.001). No significant difference was found in age-specific prevalence of DR between different age groups. The prevalence of VTDR, DME and CSME was 2.5%, 2.8%

and 0.9% respectively in diabetic patients. Male sex, higher education level, longer duration of DM, higher SBP, and higher HbA1c were the independent risk factors for the development of DR in patients with diabetes.

Conclusion: A relatively lower prevalence of DR was found among the participants with type 2 DM in residents 40 years and older from rural southern China. Ophthalmic examinations are recommended, especially in individuals who have risk factors for DM and DR.

Keywords: Diabetes mellitus; Diabetic Retinopathy; Epidemiology; Prevalence; risk factors

Strengths and limitations of this study

- Major strengths of this study are the large population-based sample, and the use of 2010 ADA diagnostic standards to decrease the possibility of misdiagnosis of DM.
- The study was conducted in an area that has undergone close to 30 years of economic development and urbanization
- A limitation of population-based cross-sectional investigations is that the long-term effects can not be found, and cause and effect relationships cannot be established.

Introduction

Diabetic retinopathy (DR) is one of the most common complications of diabetes mellitus (DM), and a leading cause of blindness and visual impairment among working-age populations in the developed world.[1] China, like many countries, has seen a marked increase in the prevalence of DM: the prevalence increased from 2.5% in 1994 to 9.7% in 2007, and it is estimated that over 60 million people in China will have DM by the year 2030.[2,3] Thus, the prevalence of DR will also increase significantly, which will seriously affect the visual function of diabetic patients.

Population based studies worldwide have revealed geographic and ethnic variability in the prevalence of DR.[4] A variety of risk factors including age, longer duration of DM, hyperglycemia, hypertension, hyperlipidemia, and obesity have been reported.[5-9] However, current estimates of prevalence and risk factors for DR are mostly from White populations, and the results may not fully represent other ethnic groups.[1] Although several population-based studies have examined the prevalence of DR in mainland China, certain limitations still exist such as regional and population differences and lack of uniformity in diagnosing type 2 DM.[7-10]

Urbanization is one of the factors that contribute to the rapid increase in the diabetes burden in the Chinese population.[4] A higher prevalence of diabetes among urban residents than among rural residents has been observed in developing countries throughout the world.[4]

However, a previous meta-analysis found that the prevalence rate of DR in the pooled rural population was higher than that in the urban population in China, and it was higher in the Northern region compared with the Southern region.[10] Therefore, we speculate that DR, as a complication of DM, its epidemiological characteristics is not exactly consistent with that of DM due to geographic and economic differences. Based on this, we performed a population-based study in one of the rural area in Southern China to examine the prevalence and risk factors of DR in adult population.

Methods

Study design and population

The Dongguan Eye study (DES) (from September 2011 to February 2012) was a population-based study on the frequency and risk factors of visual impairment and the major vision-threatening eye diseases in an adult rural population aged 40 years or older in Dongguan, Southern China. [11]. The study complied with the Declaration of Helsinki, and was approved by the Ethics Committee of Dongguan People's Hospital. The detailed design, survey, procedure, methods of examination and baseline characteristics of the DES were reported previously.[11]

Surveys of basic characteristics

The detail of community survey was shown in a previous report. [11] Briefly, a community survey was performed in the village courtyard or village center. Demographic data, socioeconomic risk status, and potential risk factors were recorded. Subsequently, participants received examinations that included venous blood collection, physical measurements and ophthalmic examinations as described below. In addition, participants completed a questionnaire regarding life styles and systemic medical conditions. When required, further ophthalmic examinations were performed at Hengli Hospital and Dongguan People's Hospital.

Ophthalmic examination

A basic ophthalmic examination included ocular history, visual acuity and autorefraction testing, intraocular pressure measurement, and anterior and posterior segment examinations by slit-lamp biomicroscopy. The best-corrected visual acuity (BCVA) was determined using the autorefraction results, and presenting visual acuity (PVA) with habitual refractive correction was tested.

Participants with DM and hypertension received non-mydriatic fundus photography. Fundus fluorescein angiography was performed in participants with severe non-proliferative DR (NPDR) or proliferative DR (PDR), and those suspected of having macular edema, retinal vascular lesions, posterior uveitis, or age-related maculopathy (ARM).

Definition and grading of DR and macular edema

Retinopathy was defined as the presence of any characteristic lesion as described by the International Clinical Diabetic Retinopathy Disease Severity Scales. Briefly, 5 categories define increasing severity of DR from "no apparent retinopathy" to PDR. Vision-threatening retinopathy was defined as the presence of severe NPDR, PDR, or clinically significant macular edema (CSME).[5] Diagnoses of diabetic macular edema (DME) and clinically significant macular edema (CSME) were based on standard diagnostic criteria.[8] In all cases, the diagnosis was based on the worse eye.

Assessment and definitions of risk factors

Demographic and medical and family history data collected, physical examinations conducted, and laboratory testing performed have been previously described.[11] History of myocardial infarction and stroke were ascertained from self-report, and cardiovascular disease was defined as history of myocardial infarction, angina, or stroke. Blood pressure (BP) was measured according to the protocol used in the Multi-Ethnic Study of Atherosclerosis.[12] Hypertension was defined as systolic BP (SBP) ≥ 140 mmHg, diastolic BP (DBP) ≥ 90 mmHg, or use of antihypertensive medication. Dyslipidemia was defined as in the Beijing eye study.[13] Hypercholesterolemia was defined as total cholesterol (TC) ≥ 5.72 mmol/l and triglyceride (TG) ≤ 1.70 mmol/l; hypertriglyceridemia as TG ≥ 1.70 mmol/l and TC ≤ 5.72

mmol/l; mixed hyperlipidemia as TC ≥ 5.72 mmol/l and TG ≥ 1.70 mmol/l; low high-density lipoprotein (HDL) hyperlipidemia as HDL-C ≤ 0.91 mmol/l.

Statistical analysis

The prevalence of DR was calculated as the ratio of the number of participants with DR in 1 or both eyes to the total number of diabetic participants. Known diabetes was assigned for the patients who had confirmed the diagnosis of diabetes previously. Newly diagnosed diabetes was assigned for the patients with 0 year of diabetes duration. The duration of diabetes was calculated as the difference between the year of diagnosis (as reported by the participant) and the year enrolled in DES. Age-adjusted prevalence was calculated using direct adjustment to the Chinese population from the 2010 China census.[14] Categorical data were described by number and percentage, and ranked data were compared with the rank sum test. Normally distributed data were expressed as mean ± standard deviation (SD). Two independent samples were compared using the *t* test, multiple groups were compared using analysis of variance, and two independent sample rates were compared using the χ^2 test. Unconditional logistic regression analyses (both univariate and stepwise) were conducted to examine the relation of the likelihood of ocular disease (dependent variable) to each of the demographic and medical variables studied. A value of $P < 0.05$ was considered to indicate statistical significance. Statistical analyses were performed in SPSS 16.0 (SPSS Inc., USA)

and SAS 9.1.3 (SAS Institute, USA) software.

Patient and public involvement

Patients and/or public were not involved in this study.

Results

Baseline characteristics of participants with type 2 diabetes

All eligible participants (8,952) were self-identified Han Chinese, and 59.9% were female. The average age was 54.0 years (range: 46.0–62.0 years), 87.2% of the individuals were 40 to 69 years old, 48.4% were farmers, and 77.2% had elementary or junior middle school levels of education. The average body mass index (BMI) was 24.6 ± 3.9 kg/m^2 and waist-hip ratio were 0.9 ± 0.1. Fifteen hundred participants were diagnosed as having type 2 DM, for a prevalence of 16.8%. Subject characteristics were summarized in Table 1. Of the 1,500 persons with type 2 DM, 1,310 had fundus photography results that were usable for DR grading.

Prevalence of diabetic retinopathy

The standardized prevalence of DR in participants with DM was 18.2%. The prevalence of different severity of DR and macular edema by gender were summarized in Table 2. The prevalence of DR in male was 23.0%, which was significantly higher than that in female with

14.1% (P<0.001). There was a significant difference in the prevalence of different grade of DR (mild NPDR, moderate NPDR, severe NPDR, PDR) (P<0.001). The prevalence of NPDR and PDR were 16.9% and 0.9%, respectively. NPDR was more common among the patients with DR, which accounted for 94.8%. The prevalence of vision-threatening DR (VTDR), DME and CSME was 2.5%, 2.8% and 0.9%, respectively, and they were not any significant differences between male and female.

The age-specific prevalence of DR and macular edema was summarized in Table 3. No significant difference was found in prevalence of DR between different age groups. Regarding the DR grade, there was a significant difference in prevalence between age groups (P=0.024). The prevalence of moderate NPDR increased with age, and rose from 1.9% in those 40-49 years old to 8.8% in those 70-79 years old. The prevalence of severe NPDR changed from 1.0% in those 40-49 years old to a peak of 4.8% in participants ≥80 years old (95% CI: 0.0%-11.3%). No significant difference was found in prevalence of macular edema (DME, CSME) between different age groups.

Among those diabetic patients, the standardized prevalence of DR was 32.8% for known diabetic patients, and 12.6% for newly diagnosed diabetic patients . Comparing with the newly diagnosed diabetic patients, the prevalence of DR at different grades in patients with known diabetes was markedly higher (P<0.001) (Table 4). Similarly, The prevalence of VTDR, DME and CSME in patients with known diabetes was higher than that in newly

diagnosed diabetic patients (P<0.001).

Risk factors for diabetic retinopathy

Univariable logistic regression showed that compared with participants without DR, those with DR were significantly associated with male, education level, duration of DM, SBP, waist-to-hip ratio, FBG and HbA1c (Table 5). Multivariable logistic regression showed that DR was significantly associated with male (odds ratio [OR] = 1.765, 95% CI: 1.267-2.459; P=0.001), higher education level (OR = 0.683, 95% CI: 0.471-0.988; P=0.043), longer duration of DM (> 10 years vs. ≤ 5 years; OR = 8.037, 95% CI: 3.467-18.631; P<0.001), higher SBP (OR = 1.113, 95% CI: 1.028-1.205; P=0.008), and higher HbA1c (OR = 1.237, 95% CI: 1.142-1.341; P<0.001) (Table 6). Those variables were the independent risk factors for the development of DR in patients with diabetes.

In participants with a new diagnosis of DM, the results of univariable logistic regression analysis indicated that those with DR were significantly associated with male, FBG, HbA1c, SBP, DBP, triglycerides and BMI compared with subjects without DR (Table 7). Multivariable logistic regression indicated that DR was significantly associated with male (OR = 2.750, 95% CI: 1.747-4.329; P<0.001), greater BMI (OR = 1.075, 95% CI: 1.014-1.139; P=0.015), higher SBP (OR = 1.147, 95% CI: 1.028- 1.279; P=0.014), and higher HbA1c (OR = 1.295, 95% CI: 1.166-1.439; P<0.001) which were the independent risk

factors for the development of DR (Table 8).

Longer duration of DM (OR = 1.192, 95% CI: 1.17-1.271; P<0.001) and higher HbA1c (OR = 1.278, 95% CI: 1.095-1.492; P=0.002) were significant independent risk factors for the occurrence of VTDR in diabetic patients (Table 9).

Questionnaire

The participants with DM completed a questionnaire for life-style and medical conditions, and the content and results of the questionnaire are summarized in supplementary Table. For the life style, 94.2% of participants with type 2 DM ate fresh fruits and vegetables daily, and 67.8% had exercise more than 30 minutes daily. For the clinical history, 21.2% of participants with a prior diagnosis of type 2 DM (known diabetes) had hypertension, while 32.0% of participants with a newly diagnosis of type 2 DM had hypertension. More than one-fourth of the participants (28.8%) had family history of hypertension. In terms of awareness of diabetes, only 28.1% of diabetic participants understood they had diabetes, and 63.3% did not know diabetes can lead to ocular complications. Furthermore, 41.8% of diabetic patients never received blood glucose monitoring, and 13.5% never had routine BP monitoring.

Discussion

The current study provides data on the prevalence of DR for an adult population in a rural

area of Southern China. The age-standardized DR prevalence was 18.2% for participants with diabetes, 32.8% for patients with previously diagnosed diabetes, and 12.6% for newly diagnosed diabetic patients. The prevalence of NPDR and PDR were 16.9% and 0.9%, respectively, and 2.5% for VTDR. The prevalence rates of DME and CSME were 2.8% and 0.9%, respectively. Significant independent risk factors of any DR were male sex, longer duration of DM, higher education level, and higher SBP and HbA1c.

Previous worldwide studies have reported a prevalence of DR ranging from 17.6% to 50%.[2-10] A systematic literature review including 35 population-based studies (1980-2008), largely from individuals of Caucasian background with limited data on other racial groups, showed the overall prevalence was 34.6% for any DR, 6.96% for PDR, 6.81% for DME, and 10.2% for VTDR.[1] Other reports have suggested the prevalence of DR, VTDR, and CSME were higher in African Americans and Latin Americans, and with the lowest rates in Asians.[1,4,15] A meta-analysis including 19 studies in China found that the prevalence of DR, NPDR and PDR in the diabetic group was 23%, 19.1%, and 2.8% respectively. The prevalence of DR was higher in the rural diabetic group compared with the urban diabetic group (29.1% vs. 18.1%), and was higher in the Northern region compared with the Southern region (26.5% vs. 15.7%).[10] The Handan Eye Study, a population-based cross-sectional study in Northern China rural region, even observed that the age-standardized prevalence of DR in Yongnian county, Handan city (Hebei province) was 45.6% in patients above 40 years old,[9] which was

markedly higher than our finding with 18.2%. The different prevalence rates of DR between previous study and our observation might result from the different life style and socioeconomic status as well as economic level between Northern *versus* Southern China. [3,10] Another possible reason for the differences may be related to the diagnosis criteria chosen. Only FBG was used for defining DM in the Handan Eye Study, while FBG, the oral glucose tolerance test (OGTT) and HbA1c were used according to American Diabetes Association (ADA) criteria in the DES, which may result in a lower prevalence of DR.

Risk factors for DR identified in the current study are similar to those reported in other studies of Caucasions.[5-9] Our study population from Southern China agrees with the Beijing Eye Study from Northern China on associations between incident DR and longer known duration of DM and the concentration of HbA1c[16]. The Wisconsin Epidemiologic Study of Diabetic Retinopathy, the first population-based study with the longest follow-up on DR, reported DR in 28.8% of participants with duration of DM of < 5 years, and a rate of 77.8% in those with a duration exceeding 15 years.[5] Although no follow-up study was conducted, the current study showed that the frequency of DR in participants with a duration of DM of > 10 years duration was approximately 8 times that of those with a duration of < 5 years (Table 6) , which further confirmed that the most consistent risk factor for DR was longer duration of DM.

After duration of diabetes, hyperglycemia has been the most consistently associated risk factor for retinopathy. HbA1c is a widely used as a marker for monitoring glycemic control. It is independent risk factors for the occurrence of DR in diabetic patients and newly-diagnosed diabetic patients in our study. Two landmark clinical trials, the United Kingdom Prospective Diabetes Study (UKPDS) and the Diabetes Control and Complications Trial (DCCT) provided strong evidence that tighter control of glycemia (HbA1c 7 %) reduces the risk of development and progression of DR in both type 1 and type 2 diabetes [17]. Although a small risk of early worsening in retinopathy in the first year of treatment exists, the overall long-term beneficial effects of intensive treatment outweigh this risk. Each percent reduction in HbA1c (e.g., from 9 % to 8 %) lowers the risk of retinopathy by 30–40 % and the effect is long-lasting ("metabolic memory")[18]. Recently published analysis of data from a large scale study showed that DR progressed in 5.8% of subjects receiving intensive glycemic control versus 12.7% receiving standard control (adjusted odds ratio [aOR] = 0.42, 95% CI 0.28-0.63, P<0.0001).[18] So it can be seen that it is very important to strict glucose control to reduce the occurrence and progression of DR.

Hypertension as an important modifiable risk factor for DR has been widely recognized [17]. Our results showed that SBP was the independent factor of DR in all diabetic patients (OR = 1.113, P=0.008) and newly-diagnosed diabetic patients (OR=1.147, P=0.014), which indicated that each 10 mmHg increase in SBP was associated with an approximately 10%

excess risk of DR. In the UKPDS, patients with hypertension with tight blood pressure control had a 37 % reduction in the risk of microvascular disease, a 34 % reduction in the rate of progression of retinopathy, and a 47 % reduction in the deterioration of visual acuity in people with type 2 diabetes[17]. It is believed that destruction of the automatic regulatory mechanism of the retinal capillaries by high blood glucose causes the capillary endothelial cells to be vulnerable to damage from hypertension, resulting in damage to the capillaries, reduced retinal blood supply, and eventually retinopathy.[21]

Although the influence of obesity on DR are inconclusive, most studies have been documented a relationship between higher BMI and increased risk of retinopathy.[23] We identified BMI (OR = 1.075, P=0.015) as one of the independent risk factors for the development of DR in newly diagnosed type 2 diabetic patients. However, conflicting data were generated in the WESDR in patients with type 1 diabetes [24, 25]. Although obesity (BMI>31.0 kg/m^2 for men and 32.1 kg/m^2 for women) was found to associate with progression and severity of retinopathy, these associations were not statistically significant and were limited to only individuals with older-onset insulin-independent diabetes. On the other hand, for those who were underweight (BMI<20 kg/m^2), a threefold increase in risk of developing retinopathy was demonstrated.[23, 24].

The current study found the prevalence of DR was higher in males than females, while other studies have provided different results. A study of rural residents of India also found a

higher frequency of DR in males.[26] On the contrary, female gender was an independent risk factor for the development of DR in Japanese patients with type 2 DM[27], and females have a higher frequency of moderate NPDR, severe NPDR, PDR, and VTDR in Malays from Singapore.[7] The Handan and Beijing eye disease studies performed in Northern China failed to find any correlation between sex and DR.[8,9] The higher HbA1c levels found in men in the current study may have an influence on the occurrence and development of DR since HbA1c is demonstrated to be an independent risk factor for DR. The exact role of sex as a possible determinant of DR remains to be determined.

Outcomes of questionnaire indicated the low level of awareness of DM and diabetic eye diseases among the rural participants of our study. Almost two-thirds of the participants did not know that DM could lead to serious ocular complications and vision loss. On the other hand, 71.5% (936/1310) of the DM patients were the, implying a lack of knowledge of diabetes in this population. The high proportion of persons with undiagnosed diabetes in this population may have contributed to their retinopathy going undetected. The extent of patient awareness and its relationship to DR care may be keys to further improvements to DR management and prevention. Therefore, improving the awareness, treatment, and control is urgently needed for the intervention of DM and diabetic eye diseases in the Chinese adult population. [28]

Major strengths of this study are the large population-based sample, and the use of 2010

ADA diagnostic standards to decrease the possibility of misdiagnosis of DM. Because the study was conducted in an area that has undergone close to 30 years of economic development and urbanization, the results may reflect how urbanization affects the development and prevalence of DR in a previous rural area to a certain extent. A limitation of population-based cross-sectional investigations is that the long-term effects can not be found, and cause and effect relationships cannot be established.

Conclusions

The current study provides new data on the epidemiological characteristics of DR in a population-based sample of Chinese adults in Southern China. The standardized prevalence of DR was 18.2%, which was lower than that reported in Northern China and Western Countries. There were 32.8% known diabetic patients and 12.6% newly diagnosed diabetic patients who were screened out DR. Male sex, higher education level, longer duration of DM, higher SBP, and higher HbA1c were the independent risk factors for the development of DR in patients with diabetes. Promotion of awareness and education of DM and DR, especially in subjects who have risk factors for DR, is needed to reduce the occurrence of DR and macular edema.

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Competing interest's statement

The authors declare that there is no competing interest.

Author's contribution

M. Q., G. H. and C. Y. designed the study and wrote the main manuscript text. M. Q., C. Y., Z. L., Z. M., Y. X., Z. LX. and L. Q. collected and managed data. M. Q., C. Y., Z. L., Z. G., and K. J. analyzed and interpreted data. All authors approved the manuscript.

Data sharing statement

There are no additional unpublished data from the study

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Table 1. Characteristics of the participants with or without type 2 diabetes in Dongguan Eye Study

	Without Type 2 Diabetes (n=7452)	With Type 2 Diabetes (n=1500)	P-value	Participants with Type 2 Diabetes		P-value
				Men (n=614)	Women (n=886)	
Age	54.5 (11.3)	59.5 (11.3)	<0.001	57.2 (11.1)	61.0 (11.2)	<0.001
Male	2997 (40.2)	614 (40.9)	20.516	—	—	
BMI (kg/m^2) §	24.3 (3.8)	26.2 (3.9)	<0.001	26.1 (3.9)	26.3 (3.9)	0.182
Waist-hip ratio§	0.88 (0.25)	0.91 (0.07)	<0.001	0.93 (0.07)	0.89 (0.07)	<0.001
SBP (mmHg)	131.7 (18.8)	141.8 (20.6)	<0.001	139.3 (19.9)	143.5 (20.9)	<0.001
DBP (mmHg)	75.7 (10.5)	78.5 (11.1)	<0.001	80.0 (11.4)	77.6 (10.8)	<0.001
FBG (mmol/L)	5.4 (0.6)	7.6 (2.9)	<0.001	7.8 (3.1)	7.4 (2.7)	0.005
HbA1c (%)	5.7 (0.4)	7.1 (1.7)	<0.001	7.2 (1.8)	7.0 (1.6)	0.011
TC (mmol/L)	5.2 (1.0)	5.5 (1.3)	<0.001	5.3 (1.2)	5.6 (1.3)	0.001
TG (mmol/L)	1.2 (0.9-1.7) †	1.6 (1.1-2.4) †	<0.001	1.7 (1.1-2.6) †	1.5 (1.1-2.3) †	0.024
HDL-C (mmol/L)	1.5 (0.5)	1.4 (0.4)	<0.001	1.3 (0.3)	1.5 (0.4)	<0.001
LDL-C (mmol/L)	3.0 (0.9)	3.2 (1.1)	<0.001	3.1 (1.1)	3.3 (1.1)	0.002
BUN (mmole/L)	5.8 (1.7)	5.9 (1.8)	0.305	5.9 (1.6)	5.8 (1.9)	0.582

Scr (μmole/L)	79.1 (36.6)	77.8 (38.6)	0.353	89.0 (43.6)	69.8 (32.5)	<0.001
UA (μmole/L)	379.5 (101.8)	391.8 (103.3)	0.002	417.5 (109.6)	373.8 (94.9)	<0.001
History myocardial infarction	—	—	—	3 (0.5)	3 (0.3)	0.693
History stroke	—	—	—	23 (3.8)	31 (3.5)	0.796
History of Cardiovascular disease	—	—	—	9 (1.5)	9 (1.0)	0.429
Current smoker	—	—	—	389 (63.4)	12 (1.4)	<0.001

Abbreviations: BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; FBG: fasting blood glucose; HbA1c: glycosylated hemoglobin; TC: serum total cholesterol; TG: triglycerides; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; BUN: blood urea nitrogen; Scr: serum creatinine; UA: uric acid.
Categorical data reported as number (percentage); continuous data as mean (standard deviation).
† Data were mean (range).
§ BMI = weight (kg) / height (m^2); Waist-hip ratio = waist circumference (cm) / hip circumference (cm).

Table 2. Prevalence of different severity of diabetic retinopathy and macular edema by gender

	Participants with diabetes‡ (n=1310)		Men with diabetes‡ (n=543)		Women with diabetes‡ (n=767) (%)		P-Value*
	Patient number	Prevalence (%) (95% CI)	Patient number	Prevalence (%) (95% CI)	Patient number	Prevalence (%) (95% CI)	
No DR	1075	82.1 (80.2-84.3)	418	77.0 (73.5-80.6)	659	85.9 (83.5-88.4)	_
diagnosed DR	233	17.8 (15.7-19.8)	125	23.0 (19.4-26.5)	108	14.1 (11.6-16.5)	<0.001
DR grade							<0.001
Mild NPDR	139	10.6 (9.0-12.3)	80	14.8 (11.8-17.8)	59	7.7 (5.8-9.6)	_
Moderate NPDR	65	5.0 (3.8-6.2)	31	5.7 (3.8-7.7)	34	4.4 (3.0-5.9)	_
Severe NPDR	17	1.3 (0.7-1.9)	9	1.7 (0.6-2.7)	8	1.0 (0.3-1.8)	_
PDR	12	0.9 (0.3-1.3)	5	0.9 (0-1.5)	7	0.9 (0.2-1.6)	_
VTDR	33	2.5 (1.7-3.4)	15	2.8 (1.4-4.2)	18	2.3 (1.3-3.4)	0.625
DME	37	2.8 (1.9-3.6)	18	3.3 (1.7-4.6)	19	2.5 (1.4-3.6)	0.466
CSME	12	0.9 (0.4-1.4)	6	1.1 (0.2-2.0)	6	0.8 (0.2-1.4)	0.539

Abbreviations: CI, confidence interval; DR, diabetic retinopathy; NPDR, non-proliferative DR; PDR, proliferative DR; VTDR: vision-threatening DR; DME, diabetic macular edema; CSME, clinically significant macular edema.

*P value for the difference of retinopathy by gender based on chi-square test.

‡ Of the 1,500 persons with type 2 DM, 1,310 had fundus photography results that were usable for DR grading.

Table 3. Age-specific prevalence of diabetic retinopathy and macular edema ¶

Type of DR or DME	40-49 years Prevalence (%) (95% CI)	50-59 years Prevalence (%) (95% CI)	60-69 years Prevalence (%) (95% CI)	70-79 years Prevalence (%) (95% CI)	≥ 80 years Prevalence (%) (95% CI)	P-Value†
Any DR	16.8 (12.6-21.0)	17.2 (13.4-20.9)	18.0 (14.2-21.7)	20.0 (13.8-26.2)	19.0 (7.0-31.1)	0.927
DR grade						0.024
Mild NPDR	13.3 (9.5-17.1)	10.0 (7.0-13.0)	9.6 (6.7-12.5)	9.4 (4.8-13.9)	11.9 (2.0-21.8)	
Moderate NPDR	1.9 (0.4-3.5)	4.9 (2.7-7.0)	6.2 (3.8-8.5)	8.8 (4.4-13.1)	2.4 (0-7.1)	
Severe NPDR	1.0 (0-2.1)	0.5 (0-1.2)	2.0 (0.6-3.3)	1.3 (0-3.0)	4.8 (0-11.3)	
PDR	0.6 (0-1.5)	1.8 (0.5-3.1)	0.2 (0-0.7)	0.6 (0-1.9)	—	
VTDR	1.6 (0.2-3.0)	2.6 (1.0-4.1)	3.2 (1.5-4.9)	1.9 (0-4.0)	4.8 (0-11.2)	0.571
DME	1.9 (0.4-3.5)	2.6 (1.0-4.1)	3.9 (2.0-5.8)	2.5 (0.1-4.9)	—	0.383
CSME	0.3 (0-1.0)	1.0 (0-2.0)	1.5 (0.3-2.7)	0.6 (0-1.9)	—	0.527

Abbreviations: CI, confidence interval; DR, diabetic retinopathy; NPDR, non-proliferative DR; VTDR: vision-threatening DR ;DME, diabetic macular edema; CSME, clinically significant macular edema;.
†P value for the difference of age groups based on chi-square test.

Table 4. Prevalence of different severity of diabetic retinopathy and macular edema by diabetes status¶

	Newly diagnosed diabetes‡ (n=936)		Known Diabetes‡ (n=374)		P- Value†
	Patient number	Prevalence (%) (95% CI)	Patient number	Prevalence (%) (95% CI)	
No DR	832	88.9 (86.8-90.9)	246	65.8 (61.0-70.6)	_
Any DR	104	11.1 (9.1-13.2)	129	34.5 (29.4-39.0)	<0.001
DR grade					<0.001
Mild NPDR	80	8.6 (6.8-10.4)	59	15.8 (12.1-19.5)	_
Moderate NPDR	17	1.8 (1.0-2.7)	48	12.8 (9.4-16.2)	_
Severe NPDR	6	0.6 (0.1-1.2)	11	2.9 (1.2-4.7)	_
PDR	1	0.1 (0-0.3)	11	2.9 (1.0-4.3)	_
VTDR	9	1.0 (0.3-1.6)	24	6.4 (3.9-8.9)	<0.001
DME	9	1.0 (0.3-1.6)	27	7.2 (4.6-9.8)	<0.001
CSME	3	0.3 (0-0.7)	9	2.4 (0.8-4.0)	<0.001

Abbreviations: CI, confidence interval; DR, diabetic retinopathy; NPDR, non-proliferative DR; PDR, proliferative DR; VTDR: vision-threatening DR; DME, diabetic macular edema;. CSME, clinically significant macular edema.

†P value for the difference of newly diagnosed vs. known diabetic patients based on chi-square test.

Table 5. Univariate logistic regression analysis of the occurrence of diabetic retinopathy among all diabetic patients

Variables	Non-DR (n=1077)	DR (n=233)	Statistics	P-value
Age (y)	58.5 (10.6)	59.1 (10.9)	-0.740	0.459
Male	417 (38.7)	126 (54.1)	17.467	<0.001
Education level (higher or equal to junior middle school)	456 (42.3)	121 (51.9)	6.438	0.011
DM duration (y)			-8.884	<0.001
≤ 5	1024 (95.1)	181 (77.7)		
≤ 10	44 (4.1)	34 (14.6)		
> 10	9 (0.8)	18 (7.7)		
BMI (kg/m^2)	26.2 (3.9)	26.7 (3.7)	-1.846	0.065
Waist-hip ratio	0.9 (0.1)	0.9 (0.1)	-2.917	0.004
SBP (mmHg)	140.7 (19.9)	143.5 (20.1)	-1.941	0.052
DBP (mmHg)	78.5 (11.2)	79.1 (10.6)	-0.702	0.483
FBG (mmol/L)	7.24 (2.53)	8.6 (3.5)	-5.641	<0.001
HbA1c (%)	6.88 (1.56)	7.7 (2.0)	-5.700	<0.001
TC (mmol/L)	5.4 (1.2)	5.5 (1.4)	-0.605	0.546
TG (mmol/L)	1.6 (1.1-2.4)	1.6 (1.1-2.3)	-0.037	0.971
HDL-C (mmol/L)	1.4 (0.3)	1.4 (0.3)	1.516	0.130
LDL-C (mmol/L)	3.2(1.1)	3.26 (1.16)	-1.095	0.274
BUN (μmol/L)	5.8 (1.7)	6.0 (1.8)	-1.937	0.053
Scr (μmol/L)	76.5 (30.3)	78.0 (23.5)	-0.678	0.498
UA (μmol/L)	395.0 (104.6)	385.1 (103.5)	1.238	0.216

Abbreviations: BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; FBG: fasting blood glucose; HbA1c: glycosylated hemoglobin; TC: serum total cholesterol; TG: triglycerides; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; BUN: blood urea nitrogen; Scr: serum creatinine; UA: uric acid.

Table 6. Multifactorial logistic regression analysis of the occurrence of diabetic retinopathy among all diabetic patients¶

Variables	B	S.E.	OR (95% CI)	P
Sex (male vs. female)	0.568	0.169	1.765 (1.267-2.459)	0.001
Age (per 10 y)	0.115	0.085	1.122 (0.950-1.326)	0.175
Education (below vs. higher or equal to junior middle school)	-0.382	0.189	0.683 (0.471-0.988)	0.043
Diabetes duration (y)				
≤ 5	Ref.		1.000	
≤ 10	1.561	0.268	4.762 (2.816-8.054)	<0.001
> 10	2.084	0.429	8.037 (3.467-18.631)	<0.001
SBP (per 10 mmHg)	0.107	0.040	1.113 (1.028-1.205)	0.008
HbA1c (%)	0.213	0.041	1.237 (1.142-1.341)	<0.001

Abbrevitions: OR, odds ratio; CI, confidence interval; SBP, systolic blood pressure ; HbA1c: glycosylated hemoglobin.

¶Multifactorial logistic regression analysis with backward selection procedure was performed by including significant factors identified in univariate analyses (i.e., P < 0.1).

Table 7. Univariate logistic regression analysis of the occurrence of diabetic retinopathy among new diagnosed diabetic patients

	Non-DR (n=832)	DR (n=104)	Statistics	P
Age (y)	58.1 (10.7)	57.7 (11.8)	0.279	0.781
Male	319 (38.3)	64 (61.5)	17.754	<0.001
Education level higher or equal to junior middle school	345 (41.5)	54 (51.9)	3.000	0.083
BMI (kg/m^2)	26.0 (3.8)	27.1 (3.7)	-2.549	0.011
Waist-hip ratio	0.9 (0.1)	0.9 (0.1)	-1.733	0.083
SBP (mmHg)	140.9 (20.1)	146.6 (21.3)	-2.645	0.008
DBP (mmHg)	79.1 (11.5)	82.4 (10.2)	-2.755	0.006
FBG (mmol/L)	7.1 (2.5)	8.6 (3.7)	-3.790	<0.001
HbA1c (%)	6.8 (1.6)	7.7 (2.1)	-3.926	<0.001
TC (mmol/L)	5.5 (1.2)	5.7 (1.2)	-1.204	0.231
TG (mmol/L)	1.6 (1.1-2.4)	1.8 (1.4-2.8)	-2.649	0.008
HDL-C (mmol/L)	1.4 (0.3)	1.4 (0.3)	1.087	0.277
LDL-C (mmol/L)	3.3 (1.1)	3.2 (1.1)	0.096	0.924
BUN (μmol/L)	5.7 (1.6)	5.7 (1.4)	-0.281	0.779
Scr (μmol/L)	76.2 (32.5)	76.2 (20.5)	0.002	0.998
UA (μmol/L)	393.2 (105.0)	390.2 (105.1)	0.261	0.794

Abbreviations: BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; FBG: fasting blood glucose; HbA1c: glycosylated hemoglobin ; TC: serum total cholesterol; TG: triglycerides; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; BUN: blood urea nitrogen; Scr: serum creatinine; UA: uric acid.

Table 8. Multifactorial logistic regression analysis of the occurrence of diabetic retinopathy among newly diagnosed diabetic patients

Variables	β	S.E.	OR (95% CI)	P
Sex (male vs. female)	1.011	0.232	2.750 (1.747-4.329)	<0.001
Age (per 10 y)	0.143	0.110	1.154 (0.930-1.432)	0.195
BMI (kg/m^2)	0.072	0.030	1.075 (1.014-1.139)	0.015
SBP (per 10 mmHg)	0.137	0.056	1.147 (1.028-1.279)	0.014
HbA1c (%)	0.259	0.054	1.295 (1.166-1.439)	<0.001

Abbreviations: OR, odds ratio; CI, confidence interval; BMI: body mass index; SBP, systolic blood pressure; HbA1c; glycosylated hemoglobin.

Table 9. Multifactorial logistic regression analysis of occurrence of vision-threatening diabetic retinopathy among all diabetic patients

Variables	β	S.E.	Wald	Df	P	OR (95% CI)
Sex (male vs. female)	0.298	0.386	0.596	1	0.440	1.348 (0.632-2.874)
Age (y)	0.023	0.018	1.631	1	0.202	1.024 (0.988-1.061)
Diabetes duration (y)	0.175	0.033	28.558	1	<0.001	1.192 (1.117-1.271)
HbA1c (%)	0.245	0.079	9.663	1	0.002	1.278 (1.095-1.492)

Abbreviations: OR, odds ratio; CI, confidence interval; HbA1c, glycosylated hemoglobin.

Supplementary Table Questionnaires regarding life styles and systemic medical conditions

Items	Patients with positive response (%)
Life styles	
Habit of eating fresh fruits and vegetables daily	**94.2%**
Exercise more than 30 minutes daily	67.8%
Smoke tobacco	22.6%
Drink alcohol	22.5%
Clinical history	
Family history of diabetes	14%
Family history of hypertension	28.8%
Family history of hyperlipidemia	1.7%
History of coronary heart disease (including myocardial infarction, angina, and heart failure)	4.4%
History of cerebrovascular disease (including cerebral infarction and cerebral hemorrhage)	3.6%
History of kidney disease	0.8%
Hypertension in participants with a history of diabetes	21.2%
Hypertension in newly diagnosed diabetic participants	32.0%
Hypertension in all diabetic participants	53.2%
Awareness of diabetes	
Diabetic participants understood they had diabetes	28.1%
Diabetic participants did not know ocular complications resulted from diabetes	63.3%
Diabetic participants who never received blood glucose monitoring	41.8%
Never had routine blood pressure monitoring	13.5%

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3-4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5-6
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	6
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, explain how loss to follow-up was addressed	
		(*e*) Describe any sensitivity analyses	
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	Report numbers of outcome events or summary measures over time	10-12
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	12-13
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	13-14
Limitations			18-19
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-18
Generalisability	21	Discuss the generalisability (external validity) of the study results	19
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19-20

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Prevalence and risk factors for diabetic retinopathyin rural southern China: Dongguan Eye Study

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Prevalence and risk factors for diabetic retinopathy in rural southern China: Dongguan Eye Study

Short title: Diabetic retinopathy in rural southern China

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Abstract

Research question: The current population-based study aims to investigate the prevalence of diabetic retinopathy (DR) and risk factors among residents over 40 years old in the rural area of Dongguan, southern China.

Study design: The Dongguan Eye study was a population-based study from September 2011 to February 2012.

Setting: The area was set in the rural area of Dongguan, Southern China.

Participants: Adult rural population aged 40 or older.

Intervention: Participants received hematological, physical, ophthalmic examinations and completed a questionnaire regarding life styles and systemic medical conditions.

Primary and secondary outcome measures: The frequency and risk factors of visual impairment and the major vision-threatening eye diseases.

Results: Of the 8,952 Han Chinese, 1,500 were diagnosed with type 2 diabetes mellitus (DM) with an average age of 59.5±11.1 years, and 1,310 participants with fundus photography results were analyzed. Standardized prevalence of DR was 18.2% for all patients with diabetes, 32.8% for the patients with previously diagnosed diabetes and 12.6% for newly diagnosed DM patients. The prevalence of male DR was significantly higher than that of female (23.0% vs. 14.1%, P<0.001). No significant difference was found in age-specific prevalence of DR. In diabetic patients, the prevalence of VTDR, DME and CSME was 2.5%,

2.8% and 0.9%, respectively. Male, higher education level, longer duration of DM, higher SBP and HbA1c were independent risk factors for the DR development in patients with diabetes.

Conclusion: A relatively lower prevalence of DR was found among the participants with type-2 DM in residents over 40 years in rural area of the southern China. Thus, an ophthalmic examination is recommended, especially for individuals with DM and DR risk factors. There is a need to increase awareness and education of DM and DR, especially in subjects with DR risk factors to reduce the incidence of DR and macular edema.

Keywords: Diabetes Mellitus; Diabetic Retinopathy; Epidemiology; Prevalence; Risk factors

Strengths and limitations of this study

- The large population-based study considers the importance and high prevalence of diabetic retinopathy
- This study conducts of 2010 ADA diagnostic standards to decrease the possibility of misdiagnosis of DM.
- The demographic characteristics of the participants were simple because this study focused on a rural area that have experience economic development and urbanization for nearly 30 years

- The limitation of the population-based cross-sectional study is that long-term effects cannot be found and causal relationships cannot be established.
- Time dimension is a limitation of this study because it may influence the risk of diabetes, causal relationship and recall bias.

Introduction

Diabetic retinopathy (DR) is one of the most common complications of diabetes mellitus (DM), and a leading cause of blindness and visual impairment among working-age populations in the developed world.[1 2] China, like many countries, has seen a marked increase in the prevalence of DM: the prevalence increased from 2.5% in 1994 to 9.7% in 2007, and it is estimated that over 60 million people in China will have DM by the year 2030.[3-6] Thus, the prevalence of DR will also increase significantly, which will seriously affect the visual function of diabetic patients.

Worldwide population-based studies revealed the geographic and ethnic variability in the prevalence of DR.[7-9] A variety of risk factors including age, longer duration of DM, hyperglycemia, hypertension, hyperlipidemia and obesity have been reported.[10-14] However, the current estimates of the prevalence and risk factors for DR were mostly from the White populations, and the results may not fully represent other ethnic groups.[2] Although several population-based studies have examined the prevalence of DR in mainland China[15] , certain limitations still exist such as regional and population differences and lack of uniformity in diagnosing type 2 DM.[11 12 14 16]

Urbanization is one of the factors that contribute to the rapid increase in the diabetes burden in the Chinese population. A higher prevalence of diabetes among urban residents than among rural residents has been observed in developing countries throughout the world.

However, a previous meta-analysis found that the prevalence rate of DR in the pooled rural population was higher than that in the urban population in China, and it was higher in the Northern region compared with the Southern region.[16] Therefore, we speculate that DR, as a complication of DM, its epidemiological characteristics is not exactly consistent with that of DM due to geographic and economic differences. Based on this, we performed a population-based study in one of the rural areas in Southern China to examine the prevalence and risk factors of DR in adult population.

Methods

Study design and population

The Dongguan Eye study (DES) (from September 2011 to February 2012) was a population-based study on the frequency and risk factors of visual impairment and the major vision-threatening eye diseases in an adult rural population aged 40 years or older in Dongguan, Southern China. [15] The study complied with the Declaration of Helsinki, and was approved by the Ethics Committee of Dongguan People's Hospital. The detailed design, survey, procedure, methods of examination and baseline characteristics of the DES were reported previously.[15]

Surveys of basic characteristics

The detail of community survey was shown in a previous report.[15] Briefly, a community survey was performed in the village courtyard or village center. Demographic data, socioeconomic risk status, and potential risk factors were recorded. Subsequently, participants received examinations that included venous blood collection, physical measurements and ophthalmic examinations as described below. In addition, participants completed a questionnaire (supplementary file 1) regarding life styles and systemic medical conditions. When required, further ophthalmic examinations were performed at Hengli Hospital and Dongguan People's Hospital.

Ophthalmic examination

A basic ophthalmic examination included ocular history, visual acuity and autorefraction testing, intraocular pressure measurement, and anterior and posterior segment examinations by slit-lamp biomicroscopy. The best-corrected visual acuity (BCVA) was determined using the autorefraction results, and presenting visual acuity (PVA) with habitual refractive correction was tested.

Participants with DM and hypertension received non-mydriatic fundus photography. Fundus fluorescein angiography was performed in participants with severe non-proliferative DR (NPDR) or proliferative DR (PDR), and those suspected of having macular edema, retinal vascular lesions, posterior uveitis, or age-related maculopathy (ARM).

Definition of DR, ME, CSME and VTDR

Retinopathy was defined as the presence of any characteristic lesion as described by the International Clinical Diabetic Retinopathy Disease Severity Scales. Briefly, 5 categories define increasing severity of DR from "no apparent retinopathy" to PDR. Macular edema (ME) is defined as the presence or absence of clinically significant macular edema (CSME). In other words, the ME is defined by the presence of a hard exudate in the presence of a microaneurysm and a spotted hemorrhage within one disk diameter from the center of the fovea or a focal photocoagulation scar in the macular area. CSME will be considered to exist when the ME is in the range of 500 μm of the center of the fovea, or if there is a focal photocoagulation scar in the macular area. Vision-threatening retinopathy (VTDR) was defined as the presence of severe NPDR, proliferative retinopathy or clinically significant macular edema (CSME).[10] Diagnoses of diabetic macular edema (DME) and clinically significant macular edema (CSME) were based on standard diagnostic criteria.[14] In all cases, the diagnosis was based on the worse eye.

Assessment and definitions of risk factors

Demographic and medical and family history data collected, physical examinations conducted, and laboratory testing performed have been previously described.[15] Known diabetes was assigned for the patients who had confirmed the diagnosis of diabetes

previously. Newly diagnosed diabetes was assigned for the patients with 0 year of diabetes duration. The duration of diabetes was calculated as the difference between the year of diagnosis (as reported by the participant) and the year enrolled in DES. History of myocardial infarction and stroke were ascertained from self-report, and cardiovascular disease was defined as history of myocardial infarction, angina, or stroke. Blood pressure (BP) was measured according to the protocol used in the Multi-Ethnic Study of Atherosclerosis.[17] Hypertension was defined as systolic BP (SBP) ≥ 140 mmHg, diastolic BP (DBP) ≥ 90 mmHg, or the use of antihypertensive medication. Dyslipidemia was defined as in the Beijing eye study.[18] Hypercholesterolemia was defined as total cholesterol (TC) ≥ 5.72 mmol/l and triglyceride (TG) ≤ 1.70 mmol/l; hypertriglyceridemia as TG ≥ 1.70 mmol/l and TC ≤ 5.72 mmol/l; mixed hyperlipidemia as TC ≥ 5.72 mmol/l and TG ≥ 1.70 mmol/l; low high-density lipoprotein (HDL) hyperlipidemia as HDL-C ≤ 0.91 mmol/l.

Statistical analysis

The prevalence of DR was calculated as the ratio of the number of participants with DR in 1 or both eyes to the total number of diabetic participants. Age-adjusted prevalence was calculated using direct adjustment to the Chinese population from the 2010 China census.[19] Categorical data was described by number and percentage, and ranked data was compared with the rank sum test. Normally distributed data was expressed as mean ± standard

deviation (SD). Two independent samples were compared using the *t* test, multiple groups were compared using analysis of variance, and two independent sample rates were compared using the χ^2 test. Unconditional logistic regression analyses (both univariate and stepwise) were conducted to examine the relation of the likelihood of ocular disease (dependent variable) to each of the demographic and medical variables studied. A value of $P < 0.05$ was considered to indicate statistical significance. Statistical analyses were performed in SPSS 16.0 (SPSS Inc., USA) and SAS 9.1.3 (SAS Institute, USA) software.

Patient and public involvement

Patients and/or public were not involved in this study.

Results

Baseline characteristics of participants with type 2 diabetes

All eligible participants (8,952) were self-identified Han Chinese, and 59.9% were female. The average age was 54.0 years (range: 46.0–62.0 years), 87.2% of the individuals were 40 to 69 years old, 48.4% were farmers, and 77.2% had elementary or junior middle school levels of education. The average body mass index (BMI) was 24.6 ± 3.9 kg/m^2, and the waist-hip ratio were 0.9 ± 0.1. Fifteen hundred participants were diagnosed with type 2 DM with a prevalence of 16.8%. Subject characteristics were summarized in Table 1. Of the 1,500 persons with type 2 DM, 1,310 have fundus photography results that were usable for DR

grading.

Prevalence of diabetic retinopathy

The standardized prevalence of DR in participants with DM was 18.2%. The prevalence of different severity of DR and macular edema by gender were summarized in Table 2. The prevalence of DR in male was 23.0%, which was significantly higher than that in female with 14.1% (P<0.001). There was a significant difference in the prevalence of different grade of DR (mild NPDR, moderate NPDR, severe NPDR, PDR) (P<0.001). The prevalence of NPDR and PDR was 16.9% and 0.9%, respectively. NPDR was more common among the patients with DR, which accounted for 94.8%. The prevalence of vision-threatening DR (VTDR), DME and CSME was 2.5%, 2.8% and 0.9%, respectively, and they were no any significant differences between male and female.

The age-specific prevalence of DR and macular edema was summarized in Table 3. No significant difference was found in prevalence of DR between different age groups. Regarding the DR grade, there was a significant difference in prevalence between age groups (P=0.024). The prevalence of moderate NPDR increased with age, and rose from 1.9% in those 40-49 years old to 8.8% in those 70-79 years old. The prevalence of severe NPDR changed from 1.0% in those 40-49 years old to a peak of 4.8% in participants ≥80 years old (95% CI: 0.0%-11.3%). No significant difference was found in prevalence of macular edema

(DME, CSME) between different age groups.

Among those diabetic patients, the standardized prevalence of DR was 32.8% for known diabetic patients, and 12.6% for newly diagnosed diabetic patients. Comparing with the newly diagnosed diabetic patients, the prevalence of DR at different grades in patients with known diabetes was markedly higher (P<0.001) (Table 4). Similarly, the prevalence of VTDR, DME and CSME in patients with known diabetes was higher than that in newly diagnosed diabetic patients (P<0.001).

Risk factors for diabetic retinopathy

Univariable logistic regression showed that compared with participants without DR, those with DR were significantly associated with male, education level, duration of DM, SBP, waist-to-hip ratio, FBG and HbA1c (Table 5). Multivariable logistic regression showed that DR was significantly associated with male (odds ratio [OR] = 1.765, 95% CI: 1.267-2.459; P=0.001), higher education level (OR = 0.683, 95% CI: 0.471-0.988; P=0.043), longer duration of DM (> 10 years vs. ≤ 5 years; OR = 8.037, 95% CI: 3.467-18.631; P<0.001), higher SBP (OR = 1.113, 95% CI: 1.028-1.205; P=0.008), and higher HbA1c (OR = 1.237, 95% CI: 1.142-1.341; P<0.001) (Table 6). Those variables were the independent risk factors for the development of DR in patients with diabetes.

In participants with a new diagnosis of DM, the results of univariable logistic regression

analysis indicated that those with DR were significantly associated with male, FBG, HbA1c, SBP, DBP, triglycerides and BMI compared with subjects without DR (Table 7). Multivariable logistic regression indicated that DR was significantly associated with male (OR = 2.750, 95% CI: 1.747-4.329; P<0.001), greater BMI (OR = 1.075, 95% CI: 1.014-1.139; P=0.015), higher SBP (OR = 1.147, 95% CI: 1.028- 1.279; P=0.014), and higher HbA1c (OR = 1.295, 95% CI: 1.166-1.439; P<0.001) which were the independent risk factors for the development of DR (Table 8).

Longer duration of DM (OR = 1.192, 95% CI: 1.17-1.271; P<0.001) and higher HbA1c (OR = 1.278, 95% CI: 1.095-1.492; P=0.002) were significant independent risk factors for the occurrence of VTDR in diabetic patients (Table 9).

Questionnaire

The participants with DM completed a questionnaire for life-style and medical conditions, and the content and results of the questionnaire are summarized in supplementary file 2. For the life style, 94.2% of participants with type 2 DM ate fresh fruits and vegetables daily, and 67.8% had exercise more than 30 minutes daily. For the clinical history, 21.2% of participants with a prior diagnosis of type 2 DM (known diabetes) has hypertension, while 32.0% of participants with a newly diagnosis of type 2 DM has hypertension. More than one-fourth of the participants (28.8%) have family history of hypertension. In terms of

awareness of diabetes, only 28.1% of diabetic participants know they have diabetes, and 63.3% of diabetic participants did not understand diabetes can lead to ocular complications. Furthermore, 41.8% of diabetic patients never received blood glucose monitoring, and 13.5% of diabetic patients never received routine BP monitoring.

Discussion

The current study provides data on the prevalence of DR for an adult population in a rural area of Southern China. The prevalence of age-standardized DR was 18.2% for participants with diabetes, 32.8% for patients with previously diagnosed diabetes and 12.6% for patients with newly diagnosed diabetes. The prevalence of NPDR, PDR and VTDR was 16.9%, 0.9% and 2.5%, respectively. The prevalence of DME and CSME was 2.8% and 0.9%, respectively. Significant independent risk factors of any DR were male, longer duration of DM, higher education level, and higher SBP and HbA1c.

Previous worldwide studies have reported a prevalence of DR ranging from 17.6% to 50%.[3 4 7 10-14 16] A systematic literature review including 35 population-based studies (1980-2008), largely from individuals of Caucasian background with limited data on other racial groups, showed that the overall prevalence was 34.6% for any DR, 6.96% for PDR, 6.81% for DME and 10.2% for VTDR.[1] Other reports suggested the prevalence of DR, VTDR and CSME was higher in African Americans and Latin Americans, while Asians have

the lowest prevalence.[1 20] The Singapore Epidemiology of Eye Disease (SEED) study[9] showed that the prevalence of any DR in Chinese (26.2%) is lower than that in Indians (30.7%) but comparable to that in Malays (25.5%).

A meta-analysis including 19 studies in China found that the prevalence of DR, NPDR and PDR in the diabetic group was 23%, 19.1% and 2.8%, respectively. The prevalence of DR was higher in the rural diabetic group compared with the urban diabetic group (29.1% vs. 18.1%). In addition, the prevalence was higher in the Northern region compared with that in the Southern region (26.5% vs. 15.7%).[16] Furthermore, the Handan Eye Study is a population-based cross-sectional study in Northern China rural region. The study observed that the age-standardized prevalence of DR in patients over 40 years in Handan city (Hebei province) was 45.6%,[11] markedly higher than our finding 18.2%. In addition, a Yangxi Eye study conducted in rural areas of Yangxi of Guangdong Province showed that the prevalence of DR over 50 years old was low (8.19%).[8] The different prevalence of DR between previous study and our observation may be due to different life style (dietary habits and exercise), socioeconomic status and economic level in North and South China. [2 4 16] Another possible reason of the differences may be related to selected the diagnosis criteria. FBG was only used to define DM in the Handan Eye Study, while FBG, oral glucose tolerance test (OGTT) and HbA1c were used further used in DES according to American Diabetes Association (ADA) criteria. These may be the reason for the lower prevalence of DR.

The risk factors for DR which identified in the current study were similar to those reported in other studies of Caucasions.[5-9] Another Beijing Eye Study from Northern China supports our finding in the associations between incident DR and longer known duration of DM and the concentration of HbA1c.[21] The Wisconsin Epidemiologic Study of Diabetic Retinopathy, the first population-based study with the longest follow-up on DR, reported that 28.8% of participants with duration of DM of < 5 years, and a rate of 77.8% in those with a duration exceeding 15 years.[10] Although no follow-up study was conducted, the current study showed that the DR frequency of participants with duration of DM > 10 years was approximately 8 times that of participants with duration < 5 years (Table 6) . The study further confirmed that the most consistent risk factor for DR is longer duration of DM.

After duration of diabetes, hyperglycemia has been the most consistently associated risk factor for retinopathy. HbA1c is a widely used as a marker for monitoring glycemic control. It is an independent risk factor for the occurrence of DR in diabetic patients and newly-diagnosed diabetic patients in our study. Two landmark clinical trials, the United Kingdom Prospective Diabetes Study (UKPDS) and the Diabetes Control and Complications Trial (DCCT) provided strong evidence that more stringent control of glycemia (HbA1c, 7 %) reduces the risk of developing and progressing DR in both type 1 and type 2 diabetes.[22] Although a small risk of early worsening in retinopathy in the first year of treatment exists, the overall long-term beneficial effects of intensive treatment outweigh this risk. Each

percent reduction in HbA1c (e.g., from 9 % to 8 %) lowers the risk of retinopathy by 30–40%, and the effect is long-lasting ("metabolic memory").[23] Recently a published analysis of data from a large scale study showed that DR progressed in 5.8% of subjects receiving intensive glycemic control versus 12.7% receiving standard control (adjusted odds ratio [aOR] = 0.42, 95%, CI: 0.28-0.63, P<0.0001).[23] Thus, it can be seen that stringent glucose control is very important to reduce the occurrence and progression of DR.

Hypertension is another important modifiable risk factor for DR.[22] Our results showed that SBP was the independent factor of DR in all diabetic patients (OR = 1.113, P=0.008) and newly-diagnosed diabetic patients (OR=1.147, P=0.014), which indicated that each 10 mmHg increase in SBP was associated with an approximately 10% excess risk of DR. In the UKPDS, patients with hypertension with tight blood pressure control had a 37 % reduction in the risk of microvascular disease, a 34 % reduction in the rate of progression of retinopathy, and a 47 % reduction in the deterioration of visual acuity in people with type 2 diabetes.[22] It is believed that destruction of the automatic regulatory mechanism of the retinal capillaries by high blood glucose causes the capillary endothelial cells to be vulnerable to damage from hypertension, resulting in damage to the capillaries, reduced retinal blood supply, and eventually retinopathy.[24]

Although the influence of obesity on DR are inconclusive, another study documented a relationship between higher BMI and increased risk of retinopathy.[25] We identified BMI (OR

= 1.075, P=0.015) as one of the independent risk factors for the development of DR in patients with newly diagnosed type 2 diabetes. However, conflicting data were generated in the WESDR in patients with type 1 diabetes. [26 27] Although obesity (BMI>31.0 kg/m^2 for men and 32.1 kg/m^2 for women) was found to be associated with the progression and severity of retinopathy, the association was not statistically significant and was limited to individuals with older-onset insulin-independent diabetes. On the other hand, for those who were underweight (BMI<20 kg/m^2), a threefold increase in risk of developing retinopathy was demonstrated.[25 26]

The current study found that the prevalence of DR was higher in male than female, while other studies have provided different results. A study of rural residents in India also found a higher frequency of DR in male.[28] On the contrary, female gender was an independent risk factor for the development of DR in Japanese patients with type 2 DM,[29] and females have a higher frequency of moderate NPDR, severe NPDR, PDR and VTDR in Malays from Singapore.[12] However, the Handan and Beijing eye disease studies performed in Northern China cannot find any correlation between gender and DR.[11 14] In the current study, higher HbA1c levels was found in male, suggesting that HbA1c may be an influence factor on the occurrence and development of DR. The exact role of the gender as a possible determinant of DR remains to be determined.

The analyzed results of questionnaire indicated that the rural participants in our study had

a low level of awareness of DM and diabetic eye disease. Almost two-thirds of participants did not know that DM can cause severe ocular complications and loss of vision. On the other hand, 71.5% of the DM patients in this population lack knowledge of diabetes. The proportion of undiagnosed diabetics in this population is high and may cause their retinopathy to be undetected. Thus, the degree of patient awareness and its relationship to DR care may be the key to further improving DR management and prevention. Therefore, intervention in DM and diabetic eye disease in the Chinese adult population is urgently needed to raise awareness, treatment and control. [30]

The strengths of this study are to conduct 2010 ADA diagnostic standards to decrease the possibility of misdiagnosis of DM and consider the importance and high prevalence of diabetic retinopathy. In addition, the sample size was big and the demographic characteristics of the participants were simple to reflect the actual results. This is because that this study focused on a rural area that have experience economic development and urbanization for nearly 30 years. However, the limitation of the population-based cross-sectional study is that long-term effects cannot be found and causal relationships cannot be established. Since there is no time dimension, it will reduce the supporting intensity in the conclusion and causal relationship of diabetes risk. It may also exhibit recall bias, because diabetes may influence subjects' response to questionnaires.

Conclusions

The current study provided new data on the epidemiological characteristics of DR in a population-based sample of Chinese adults in Southern China. The standardized prevalence of DR was 18.2%, which was lower than the reported prevalence in Northern China and Western Countries. There were 32.8% known diabetic patients and 12.6% newly diagnosed diabetic patients who were screened out DR. Male, higher education level, longer duration of DM, higher SBP, and HbA1c were the independent risk factors for the development of DR in patients with diabetes. In addition, a high proportion of previously undiagnosed subjects with diabetes and diabetic ocular complications and subjects lacking diabetes care were observed in this study. This indicates the need to improve awareness and health education for DM and DR in parts of rural China, especially for subjects with DR risk factors.

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Competing interest's statement

The authors declare that there is no competing interest.

Author's contribution

M. Q., G. H. and C. Y. designed the study and wrote the main manuscript text. M. Q., C. Y., Z. L., Z. M., Z. LX. and L. Q. collected and managed data. M. Q., C. Y., Z. L., Z. G., and K. J. analyzed and interpreted data. All authors approved the manuscript.

Data sharing statement

There are no additional unpublished data from the study

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Table 1. Characteristics of the participants with or without type 2 diabetes in Dongguan Eye Study

	Without Type 2 Diabetes (n=7452)	With Type 2 Diabetes (n=1500)	P-value	Participants with Type 2 Diabetes		P-value
				Men (n=614)	Women (n=886)	
Age	54.5 (11.3)	59.5 (11.3)	<0.001	57.2 (11.1)	61.0 (11.2)	<0.001
Male	2997 (40.2)	614 (40.9)	20.516	—	—	
BMI (kg/m^2) §	24.3 (3.8)	26.2 (3.9)	<0.001	26.1 (3.9)	26.3 (3.9)	0.182
Waist-hip ratio§	0.88 (0.25)	0.91 (0.07)	<0.001	0.93 (0.07)	0.89 (0.07)	<0.001
SBP (mmHg)	131.7 (18.8)	141.8 (20.6)	<0.001	139.3 (19.9)	143.5 (20.9)	<0.001
DBP (mmHg)	75.7 (10.5)	78.5 (11.1)	<0.001	80.0 (11.4)	77.6 (10.8)	<0.001
FBG (mmol/L)	5.4 (0.6)	7.6 (2.9)	<0.001	7.8 (3.1)	7.4 (2.7)	0.005
HbA1c (%)	5.7 (0.4)	7.1 (1.7)	<0.001	7.2 (1.8)	7.0 (1.6)	0.011
TC (mmol/L)	5.2 (1.0)	5.5 (1.3)	<0.001	5.3 (1.2)	5.6 (1.3)	0.001
TG (mmol/L)	1.2 (0.9-1.7) †	1.6 (1.1-2.4) †	<0.001	1.7 (1.1-2.6) †	1.5 (1.1-2.3) †	0.024
HDL-C (mmol/L)	1.5 (0.5)	1.4 (0.4)	<0.001	1.3 (0.3)	1.5 (0.4)	<0.001
LDL-C (mmol/L)	3.0 (0.9)	3.2 (1.1)	<0.001	3.1 (1.1)	3.3 (1.1)	0.002
BUN (mmole/L)	5.8 (1.7)	5.9 (1.8)	0.305	5.9 (1.6)	5.8 (1.9)	0.582

Scr (μmole/L)	79.1 (36.6)	77.8 (38.6)	0.353	89.0 (43.6)	69.8 (32.5)	<0.001
UA (μmole/L)	379.5 (101.8)	391.8 (103.3)	0.002	417.5 (109.6)	373.8 (94.9)	<0.001
History myocardial infarction	—	—	—	3 (0.5)	3 (0.3)	0.693
History stroke	—	—	—	23 (3.8)	31 (3.5)	0.796
History of Cardiovascular disease	—	—	—	9 (1.5)	9 (1.0)	0.429
Current smoker	—	—	—	389 (63.4)	12 (1.4)	<0.001

Abbreviations: BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; FBG: fasting blood glucose; HbA1c: glycosylated hemoglobin; TC: serum total cholesterol; TG: triglycerides; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; BUN: blood urea nitrogen; Scr: serum creatinine; UA: uric acid.

Categorical data reported as number (percentage); continuous data as mean (standard deviation).

† Data were mean (range).

§ BMI = weight (kg) / height (m^2); Waist-hip ratio = waist circumference (cm) / hip circumference (cm).

Table 2. Prevalence of different severity of diabetic retinopathy and macular edema by gender

	Participants with diabetes‡ (n=1310)		Men with diabetes‡ (n=543)		Women with diabetes‡ (n=767) (%)		P-Value*
	Patient number	Prevalence (%) (95% CI)	Patient number	Prevalence (%) (95% CI)	Patient number	Prevalence (%) (95% CI)	
No DR	1075	82.1 (80.2-84.3)	418	77.0 (73.5-80.6)	659	85.9 (83.5-88.4)	_
diagnosed DR	233	17.8 (15.7-19.8)	125	23.0 (19.4-26.5)	108	14.1 (11.6-16.5)	<0.001
DR grade							<0.001
Mild NPDR	139	10.6 (9.0-12.3)	80	14.8 (11.8-17.8)	59	7.7 (5.8-9.6)	_
Moderate NPDR	65	5.0 (3.8-6.2)	31	5.7 (3.8-7.7)	34	4.4 (3.0-5.9)	_
Severe NPDR	17	1.3 (0.7-1.9)	9	1.7 (0.6-2.7)	8	1.0 (0.3-1.8)	_
PDR	12	0.9 (0.3-1.3)	5	0.9 (0-1.5)	7	0.9 (0.2-1.6)	_
VTDR	33	2.5 (1.7-3.4)	15	2.8 (1.4-4.2)	18	2.3 (1.3-3.4)	0.625
DME	37	2.8 (1.9-3.6)	18	3.3 (1.7-4.6)	19	2.5 (1.4-3.6)	0.466
CSME	12	0.9 (0.4-1.4)	6	1.1 (0.2-2.0)	6	0.8 (0.2-1.4)	0.539

Abbreviations: CI, confidence interval; DR, diabetic retinopathy; NPDR, non-proliferative DR; PDR, proliferative DR; VTDR: vision-threatening DR; DME, diabetic macular edema; CSME, clinically significant macular edema.

*P value for the difference of retinopathy by gender based on chi-square test.

‡ Of the 1,500 persons with type 2 DM, 1,310 had fundus photography results that were usable for DR grading.

Table 3. Age-specific prevalence of diabetic retinopathy and macular edema ¶

Type of DR or DME	40-49 years Prevalence (%) (95% CI)	50-59 years Prevalence (%) (95% CI)	60-69 years Prevalence (%) (95% CI)	70-79 years Prevalence (%) (95% CI)	≥ 80 years Prevalence (%) (95% CI)	P-Value†
Any DR	16.8 (12.6-21.0)	17.2 (13.4-20.9)	18.0 (14.2-21.7)	20.0 (13.8-26.2)	19.0 (7.0-31.1)	0.927
DR grade						0.024
Mild NPDR	13.3 (9.5-17.1)	10.0 (7.0-13.0)	9.6 (6.7-12.5)	9.4 (4.8-13.9)	11.9 (2.0-21.8)	
Moderate NPDR	1.9 (0.4-3.5)	4.9 (2.7-7.0)	6.2 (3.8-8.5)	8.8 (4.4-13.1)	2.4 (0-7.1)	
Severe NPDR	1.0 (0-2.1)	0.5 (0-1.2)	2.0 (0.6-3.3)	1.3 (0-3.0)	4.8 (0-11.3)	
PDR	0.6 (0-1.5)	1.8 (0.5-3.1)	0.2 (0-0.7)	0.6 (0-1.9)	—	
VTDR	1.6 (0.2-3.0)	2.6 (1.0-4.1)	3.2 (1.5-4.9)	1.9 (0-4.0)	4.8 (0-11.2)	0.571
DME	1.9 (0.4-3.5)	2.6 (1.0-4.1)	3.9 (2.0-5.8)	2.5 (0.1-4.9)	—	0.383
CSME	0.3 (0-1.0)	1.0 (0-2.0)	1.5 (0.3-2.7)	0.6 (0-1.9)	—	0.527

Abbreviations: CI, confidence interval; DR, diabetic retinopathy; NPDR, non-proliferative DR; VTDR: vision-threatening DR ;DME, diabetic macular edema; CSME, clinically significant macular edema;.

†P value for the difference of age groups based on chi-square test.

Table 4. Prevalence of different severity of diabetic retinopathy and macular edema by diabetes status

	Newly diagnosed diabetes‡ (n=936)		Known Diabetes‡ (n=374)		P- Value†
	Patient number	Prevalence (%) (95% CI)	Patient number	Prevalence (%) (95% CI)	
No DR	832	88.9 (86.8-90.9)	246	65.8 (61.0-70.6)	_
Any DR	104	11.1 (9.1-13.2)	129	34.5 (29.4-39.0)	<0.001
DR grade					<0.001
Mild NPDR	80	8.6 (6.8-10.4)	59	15.8 (12.1-19.5)	_
Moderate NPDR	17	1.8 (1.0-2.7)	48	12.8 (9.4-16.2)	_
Severe NPDR	6	0.6 (0.1-1.2)	11	2.9 (1.2-4.7)	_
PDR	1	0.1 (0-0.3)	11	2.9 (1.0-4.3)	_
VTDR	9	1.0 (0.3-1.6)	24	6.4 (3.9-8.9)	<0.001
DME	9	1.0 (0.3-1.6)	27	7.2 (4.6-9.8)	<0.001
CSME	3	0.3 (0-0.7)	9	2.4 (0.8-4.0)	<0.001

Abbreviations: CI, confidence interval; DR, diabetic retinopathy; NPDR, non-proliferative DR; PDR, proliferative DR; VTDR: vision-threatening DR; DME, diabetic macular edema;. CSME, clinically significant macular edema.

†P value for the difference of newly diagnosed vs. known diabetic patients based on chi-square test.

Table 5. Univariate logistic regression analysis of the occurrence of diabetic retinopathy among all diabetic patients

Variables	Non-DR (n=1077)	DR (n=233)	Statistics	P-value
Age (y)	58.5 (10.6)	59.1 (10.9)	-0.740	0.459
Male	417 (38.7)	126 (54.1)	17.467	<0.001
Education level (higher or equal to junior middle school)	456 (42.3)	121 (51.9)	6.438	0.011
DM duration (y)			-8.884	<0.001
≤ 5	1024 (95.1)	181 (77.7)		
≤ 10	44 (4.1)	34 (14.6)		
> 10	9 (0.8)	18 (7.7)		
BMI (kg/m^2)	26.2 (3.9)	26.7 (3.7)	-1.846	0.065
Waist-hip ratio	0.9 (0.1)	0.9 (0.1)	-2.917	0.004
SBP (mmHg)	140.7 (19.9)	143.5 (20.1)	-1.941	0.052
DBP (mmHg)	78.5 (11.2)	79.1 (10.6)	-0.702	0.483
FBG (mmol/L)	7.24 (2.53)	8.6 (3.5)	-5.641	<0.001
HbA1c (%)	6.88 (1.56)	7.7 (2.0)	-5.700	<0.001
TC (mmol/L)	5.4 (1.2)	5.5 (1.4)	-0.605	0.546
TG (mmol/L)	1.6 (1.1-2.4)	1.6 (1.1-2.3)	-0.037	0.971
HDL-C (mmol/L)	1.4 (0.3)	1.4 (0.3)	1.516	0.130
LDL-C (mmol/L)	3.2(1.1)	3.26 (1.16)	-1.095	0.274
BUN (μmol/L)	5.8 (1.7)	6.0 (1.8)	-1.937	0.053
Scr (μmol/L)	76.5 (30.3)	78.0 (23.5)	-0.678	0.498
UA (μmol/L)	395.0 (104.6)	385.1 (103.5)	1.238	0.216

Abbreviations: BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; FBG: fasting blood glucose; HbA1c: glycosylated hemoglobin; TC: serum total cholesterol; TG: triglycerides; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; BUN: blood urea nitrogen; Scr: serum creatinine; UA: uric acid.

Table 6. Multifactorial logistic regression analysis of the occurrence of diabetic retinopathy among all diabetic patients¶

Variables	B	S.E.	OR (95% CI)	P
Sex (male vs. female)	0.568	0.169	1.765 (1.267-2.459)	0.001
Age (per 10 y)	0.115	0.085	1.122 (0.950-1.326)	0.175
Education (below vs. higher or equal to junior middle school)	-0.382	0.189	0.683 (0.471-0.988)	0.043
Diabetes duration (y)				
≤ 5	Ref.		1.000	
≤ 10	1.561	0.268	4.762 (2.816-8.054)	<0.001
> 10	2.084	0.429	8.037 (3.467-18.631)	<0.001
SBP (per 10 mmHg)	0.107	0.040	1.113 (1.028-1.205)	0.008
HbA1c (%)	0.213	0.041	1.237 (1.142-1.341)	<0.001

Abbrevitions: OR, odds ratio; CI, confidence interval; SBP, systolic blood pressure ; HbA1c: glycosylated hemoglobin.

¶ Multifactorial logistic regression analysis with backward selection procedure was performed by including significant factors identified in univariate analyses (i.e., P < 0.1).

Table 7. Univariate logistic regression analysis of the occurrence of diabetic retinopathy among new diagnosed diabetic patients

	Non-DR (n=832)	DR (n=104)	Statistics	P
Age (y)	58.1 (10.7)	57.7 (11.8)	0.279	0.781
Male	319 (38.3)	64 (61.5)	17.754	<0.001
Education level higher or equal to junior middle school	345 (41.5)	54 (51.9)	3.000	0.083
BMI (kg/m^2)	26.0 (3.8)	27.1 (3.7)	-2.549	0.011
Waist-hip ratio	0.9 (0.1)	0.9 (0.1)	-1.733	0.083
SBP (mmHg)	140.9 (20.1)	146.6 (21.3)	-2.645	0.008
DBP (mmHg)	79.1 (11.5)	82.4 (10.2)	-2.755	0.006
FBG (mmol/L)	7.1 (2.5)	8.6 (3.7)	-3.790	<0.001
HbA1c (%)	6.8 (1.6)	7.7 (2.1)	-3.926	<0.001
TC (mmol/L)	5.5 (1.2)	5.7 (1.2)	-1.204	0.231
TG (mmol/L)	1.6 (1.1-2.4)	1.8 (1.4-2.8)	-2.649	0.008
HDL-C (mmol/L)	1.4 (0.3)	1.4 (0.3)	1.087	0.277
LDL-C (mmol/L)	3.3 (1.1)	3.2 (1.1)	0.096	0.924
BUN (μmol/L)	5.7 (1.6)	5.7 (1.4)	-0.281	0.779
Scr (μmol/L)	76.2 (32.5)	76.2 (20.5)	0.002	0.998
UA (μmol/L)	393.2 (105.0)	390.2 (105.1)	0.261	0.794

Abbreviations: BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; FBG: fasting blood glucose; HbA1c: glycosylated hemoglobin ; TC: serum total cholesterol; TG: triglycerides; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; BUN: blood urea nitrogen; Scr: serum creatinine; UA: uric acid.

Table 8. Multifactorial logistic regression analysis of the occurrence of diabetic retinopathy among newly diagnosed diabetic patients

Variables	β	S.E.	OR (95% CI)	P
Sex (male vs. female)	1.011	0.232	2.750 (1.747-4.329)	<0.001
Age (per 10 y)	0.143	0.110	1.154 (0.930-1.432)	0.195
BMI (kg/m^2)	0.072	0.030	1.075 (1.014-1.139)	0.015
SBP (per 10 mmHg)	0.137	0.056	1.147 (1.028-1.279)	0.014
HbA1c (%)	0.259	0.054	1.295 (1.166-1.439)	<0.001

Abbreviations: OR, odds ratio; CI, confidence interval; BMI: body mass index; SBP, systolic blood pressure; HbA1c; glycosylated hemoglobin.

Table 9. Multifactorial logistic regression analysis of occurrence of vision-threatening diabetic retinopathy among all diabetic patients

Variables	β	S.E.	Wald	Df	P	OR (95% CI)
Sex (male vs. female)	0.298	0.386	0.596	1	0.440	1.348 (0.632-2.874)
Age (y)	0.023	0.018	1.631	1	0.202	1.024 (0.988-1.061)
Diabetes duration (y)	0.175	0.033	28.558	1	<0.001	1.192 (1.117-1.271)
HbA1c (%)	0.245	0.079	9.663	1	0.002	1.278 (1.095-1.492)

Abbreviations: OR, odds ratio; CI, confidence interval; HbA1c, glycosylated hemoglobin.

Table 1

高血压糖尿病危险因素调查问卷

编号：□□□□□ **受检者姓名：**

尊敬的先生/女士，您好！我们拟进行高血压糖尿病危险因素调查，请您如实回答以下调查问卷内容，您的信息会保存在社区健康档案中给予保密，谢谢您的合作！

n3、您是否每天都食用新鲜蔬菜或者水果？

①是 ②否

n7aa、您通常每次运动的时间大概是多少？

①<15 分钟 ②15-30 分钟 ③≧30 分钟

n10oeoe、您是否长时间使用过激素（强的松、地塞米松）？（口服或者静滴）

①是（激素使用持续的时间为_a1 ___个月）

②否 ③不清楚

n13ae、您开始有规律吸香烟的时候多少岁？ _____ 岁，吸烟__a2____年

n14ae、您平均每天吸烟量：（_____支/天）

① 小于 10 支 ②11-20 支 ③21-30 支 ④31-40 支 ⑤41 支以上

n18ae、您有饮酒吗？[选①、②者，__a5__年，每次_b3__什么酒（c1）]

①每天 ②1-3 次 / 周 ③每月 1 次或更少 ④从不

n20、您的家人中有高血压患者吗？

①有 ②没有 ③不知道

n21、您的家人中有糖尿病患者吗？与您的关系（a7）

①有 ②没有 ③不知道

N22、您的家人中有高脂血症患者吗？

①有 ②没有 ③不知道

n24、您是否有冠心病？

①是_a9___年 ②否

n25、您的体重最重时曾经达到过____kg？

28、您是否被医生诊断患过下列疾病？（可多选，在选中的答案打“√”）

A12（1）脑梗塞	①有	②没有	③不知道
B6（2）脑出血	①有	②没有	③不知道
C4（3）心肌梗死	①有	②没有	③不知道
D3（4）心绞痛	①有	②没有	③不知道
E2（5）心力衰竭	①有	②没有	③不知道

F3（6）肾功能衰竭 ①有 ②没有 ③不知道

G1（7）糖尿病肾病 ①有 ②没有 ③不知道

H1（8）视网膜出血性渗出、视乳头水肿 ①有 ②没有 ③不知道

n29、您测量过血压吗？

①没有 ②有，血压不高 ③有，血压高，a13 年

n31、您最后一次测量血压值是多少？① a15 / b7 mmHg ②不记得

n32ae、是否有医生告知您有高血压？①是 a16 年 ②否

n34、您检测过血糖吗？

①没有 ②有，血糖不高 ③有，血糖高，a18 年

n36、您最后一次检测血糖值是多少？① a20 mmol/L ②不记得

n37ae、是否有医生告知您有糖尿病？①是 a21 年 （1 型、2 型 b8）②否

n42ae、是否有医生告知您有高血脂？①是 a26 年 ②否

n45ae、 您知道糖尿病可以引起眼部病变吗？

①知道 ②不知道

n46oeae、您目前采用哪些方法来控制血压和/或血糖？

①非药物治疗 ②药物治疗

③两者都采用 ④没有治疗

b1049、请您列出当前使用的药物名称

降血糖药物名称（ b11 、不知道、不记得）

问卷结束，谢谢！

调查员：_____调查日期：_____

Table 2

眼科问卷 1　　眼病意识和治疗意识调查表

1. 你第 1 次知道你的眼睛有病，距今有多久（眼病存在的意识）？

□患有眼病，距今的时间：_____　□无眼病　□不清楚是否患有眼病

2. 何时知道你的眼病可以治疗（眼病治疗意识）？

□患有眼病，何时知道可以治疗：_____　□无眼病　□不清楚是否有眼病　□不知道可以治疗

3. 在检查之前，是否看过医生?　□是　□否

4. 如果看过医生但你最后未进行手术和药物治疗的原因是什么（眼病治疗障碍）？

①经济问题；②没有时间；③无人陪伴；④还能看到一点(白内障还没有成熟)；

⑤路太远；⑥年龄太大，觉得不需要；⑦害怕手术；⑧害怕丧失视力；

⑨一眼有足够的视力，觉得不需要；⑩有禁忌症。

5. 如果未看过医生或你不去看医生的原因是什么（眼病治疗障碍）？

①经济问题；②没有时间；③无人陪伴；④还能看到一点(白内障还没有成熟)；

⑤路太远；⑥年龄太大，觉得不需要；⑦害怕手术；⑧害怕丧失视力；

⑨一眼有足够的视力，觉得不需要；⑩有禁忌症。

6. 仅对已接受白内障手术者：白内障手术详情　（如未做白内障手术者，请在此处划"╳"　）

	右眼	左眼
手术时间		
手术地点		
防盲流动车		
公立医院		
私立医院		
手术费用		
完全免费		
部分免费		
完全自费		
是否使用眼镜	□是　□否	□是　□否
不用眼镜的原因		
从未配过		
丢失		
损坏		
不需戴镜（IOL 植入）		

	不需戴镜（另一眼视力好）			
手术类型				
	超声乳化			
	非超声乳化			
	是否联合 IOL 植入	□是 □否	□是	□否

受试者签名： **2011 年 月 日**

Table 3

眼科问卷 2：　　生存质量和视功能调查问卷

我要问您一些关于您视力的问题，每个问题我说出 4 种答案，请您挑选一个最适合您实际情况的回答。

1. 自理：由于视力原因，在无人帮助时，你觉得做下列事情有多大困难?

	一点也没有	稍有一点	有些困难	十分困难	是否有人帮你	
洗澡	1	2	3	4	无= 1	有= 2
自己吃饭	1	2	3	4	无= 1	有=2
穿衣服	1	2	3	4	无= 1	有= 2
上厕所	1	2	3	4	无= 1	有= 2

2. 活动：由于视力原因，在无人帮助您时，您自己做下列事情有多大困难？

	一点也没有	稍有一点	有些困难	十分困难	是否有人帮你	
走到邻居家	1	2	3	4	无= 1	有= 2
去买东西	1	2	3	4	无= 1	有=2
做家务	1	2	3	4	无= 1	有= 2

3. 社交：由于视力原因，对您参加下列活动的愿望影响有多大?

	一点也没有	稍有一点	有些困难	十分困难
参加婚礼或过节日	1	2	3	4
看朋友或亲戚	1	2	3	4

4. 心理：由于视力原因，您是否觉得

	一点也不	稍有一点	比较明显	十分明显
是别人的负担	1	2	3	4
情绪低落	1	2	3	4
做事无信心	1	2	3	4

	很好	好	一般	差
5. 一般来讲，你认为您的视(眼)力是： (如果您是戴眼镜的，告诉我您戴镜后的情况)	1	2	3	4

	一点也不	稍有一点	有些困难	十分困难
6. 您的视(眼)力对您的日常生活限制有多大？	1	2	3	4
7. 您看清路对面的人有多大困难？	1	2	3	4
8. 您看清站在您旁边的人脸有多大困难？	1	2	3	4
9. 您看清细小的东西(如您手上的谷粒或手纹) 有多大困难？	1	2	3	4
10.当您一个人向前走路时，发现路边的东西有多大困难？	1	2	3	4
11.您从亮处来到暗处时，适应暗的环境有多大困难？	1	2	3	4

12.您从暗处来到亮处时，适应亮的环境有多大困难？	1	2	3	4
13.当一种东西和其它许多东西混在一起时，您找出它有多大困难？(如从饭碗里找到某种您想吃的食物)	1	2	3	4
14.您辨认颜色有多大困难？	1	2	3	4
15.当您想拿某样东西(如玻璃杯)时，您要拿到它有多大困难？	1	2	3	4
16.当您和您要辨认的人都在强光时，您看清对方有多大困难？	1	2	3	4
17.当强光(如迎面开来汽车灯光)晃您眼时，您看清东西有多大困难？	1	2	3	4

医生/护士/工作人员： **2011年** 月 日

Supplementary Table Questionnaires regarding life styles and systemic medical conditions

Items	Patients with positive response (%)
Life styles	
Habit of eating fresh fruits and vegetables daily	**94.2%**
Exercise more than 30 minutes daily	67.8%
Smoke tobacco	22.6%
Drink alcohol	22.5%
Clinical history	
Family history of diabetes	14%
Family history of hypertension	28.8%
Family history of hyperlipidemia	1.7%
History of coronary heart disease (including myocardial infarction, angina, and heart failure)	4.4%
History of cerebrovascular disease (including cerebral infarction and cerebral hemorrhage)	3.6%
History of kidney disease	0.8%
Hypertension in participants with a history of diabetes	21.2%
Hypertension in newly diagnosed diabetic participants	32.0%
Hypertension in all diabetic participants	53.2%
Awareness of diabetes	
Diabetic participants understood they had diabetes	28.1%
Diabetic participants did not know ocular complications resulted from diabetes	63.3%
Diabetic participants who never received blood glucose monitoring	41.8%
Never had routine blood pressure monitoring	13.5%

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3-4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5-6
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	6
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, explain how loss to follow-up was addressed	
		(*e*) Describe any sensitivity analyses	
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	Report numbers of outcome events or summary measures over time	10-12
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	12-13
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	13-14
Limitations			18-19
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-18
Generalisability	21	Discuss the generalisability (external validity) of the study results	19
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19-20

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Prevalence and risk factors for diabetic retinopathy in a cross-sectional population-based study from rural southern China: Dongguan Eye Study

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Prevalence and risk factors for diabetic retinopathy in a cross-sectional population-based study from rural southern China: Dongguan Eye Study

Short title: Diabetic retinopathy in rural southern China

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Abstract

Research question: The current population-based study aims to investigate the prevalence of diabetic retinopathy (DR) and risk factors among residents over 40 years old in the rural area of Dongguan, southern China.

Study design: The Dongguan Eye study was a population-based study from September 2011 to February 2012.

Setting: The area was set in the rural area of Dongguan, Southern China.

Participants: Adult rural population aged 40 or older.

Intervention: Participants received hematological, physical, ophthalmic examinations and completed a questionnaire regarding life styles and systemic medical conditions.

Primary and secondary outcome measures: The frequency and risk factors of visual impairment and the major vision-threatening eye diseases.

Results: Of the 8,952 Han Chinese, 1,500 were diagnosed with type 2 diabetes mellitus (T2DM) with an average age of 59.5±11.1 years, and 1,310 participants with fundus photography results were analyzed. Standardized prevalence of DR was 18.2% for all patients with diabetes, 32.8% for the patients with previously diagnosed diabetes and 12.6% for newly diagnosed T2DM patients. The prevalence of male DR was significantly higher than that of female (23.0% vs. 14.1%, P<0.001). No significant difference was found in age-specific prevalence of DR. In diabetic patients, the prevalence of VTDR, DME and CSME was 2.5%,

2.8% and 0.9%, respectively. Male, higher education level, longer duration of DM, higher SBP and HbA1c were independent risk factors for the DR development in patients with diabetes.

Conclusion: A relatively lower prevalence of DR was found among the participants with T2DM in residents over 40 years in rural area of the southern China. Thus, an ophthalmic examination is recommended, especially for individuals with DM and DR risk factors. There is a need to increase awareness and education of DM and DR, especially in subjects with DR risk factors to reduce the incidence of DR and macular edema.

Keywords: Diabetes Mellitus; Diabetic Retinopathy; Epidemiology; Prevalence; Risk factors

Strengths and limitations of this study

- The large population-based study considers the importance and high prevalence of diabetic retinopathy
- This study conducts of 2010 ADA diagnostic standards to decrease the possibility of missed diagnosis of DM.
- The limitation of the population-based cross-sectional study is that long-term effectscannot be found and causal relationships cannot be established.
- Time dimension is another limitation of this study because it may influence the risk of

diabetes, causal relationship and recall bias.

Introduction

Diabetic retinopathy (DR) is one of the most common complications of diabetes mellitus (DM), and a leading cause of blindness and visual impairment among working-age populations in the developed world.[1 2] China, like many countries, has seen a marked increase in the prevalence of DM: the prevalence increased from 2.5% in 1994 to 9.7% in 2007, and it is estimated that over 60 million people in China will have DM by the year 2030.[3-6] Thus, the prevalence of DR will also increase significantly, which will seriously affect the visual function of diabetic patients.

Worldwide population-based studies revealed the geographic and ethnic variability in the prevalence of DR.[7-9] A variety of risk factors including age, longer duration of DM, hyperglycemia, hypertension, hyperlipidemia and obesity have been reported.[10-14] However, the current estimates of the prevalence and risk factors for DR were mostly from the White populations, and the results may not fully represent other ethnic groups.[2] Although several population-based studies have examined the prevalence of DR in mainland China[15] , certain limitations still exist such as regional and population differences and lack of uniformity in diagnosing type 2 DM.[11 12 14 16]

Urbanization is one of the factors that contribute to the rapid increase in the diabetes burden in the Chinese population. It has been found that the prevalence of diabetes among urban residents is higher than village residents in developing countries. However, a previous

meta-analysis found that the prevalence rate of DR in the pooled rural population was higher than that in the urban population in China, and it was higher in the Northern region compared with the Southern region.[16] Therefore, we speculate that DR, as a complication of DM, its epidemiological characteristics is not exactly consistent with that of DM due to geographic and economic differences. Based on this, we performed a population-based study in one of the rural areas in Southern China to examine the prevalence and risk factors of DR in adult population.

Methods

Study design and population

The Dongguan Eye study (DES) (from September 2011 to February 2012) was a population-based study on the frequency and risk factors of visual impairment and the major vision-threatening eye diseases in an adult rural population aged 40 years or older in Dongguan, Southern China. [15] The study complied with the Declaration of Helsinki, and was approved by the Ethics Committee of Dongguan People's Hospital. The detailed design, survey, procedure, methods of examination and baseline characteristics of the DES were reported previously.[15]

Patient and public involvement

The Patients and/or public were not involved in this study. In this study, the participants were fully informed , a written description was given to them and consents were obtained from the participants. If the participants could not know the consent statement because of vision loss or illiteracy, the consent was read by the interviewer[15]. .

Surveys of basic characteristics

The detail of community survey was shown in a previous report.[15] Briefly, a community survey was performed in the village courtyard or village center. Demographic data, socioeconomic risk status, and potential risk factors were recorded. Subsequently, participants received examinations that included venous blood collection, physical measurements and ophthalmic examinations as described below. In addition, participants completed a questionnaire (supplementary file 1) regarding life styles and systemic medical conditions. When required, further ophthalmic examinations were performed at Hengli Hospital and Dongguan People's Hospital.

Ophthalmic examination

A basic ophthalmic examination included ocular history, visual acuity and autorefraction testing, intraocular pressure measurement, and anterior and posterior segment examinations

by slit-lamp biomicroscopy. The best-corrected visual acuity (BCVA) was determined using the autorefraction results, and presenting visual acuity (PVA) with habitual refractive correction was tested.

Participants with DM and hypertension received non-mydriatic fundus photography. Fundus fluorescein angiography was performed in participants with severe non-proliferative DR (NPDR) or proliferative DR (PDR), and those suspected of having macular edema, retinal vascular lesions, posterior uveitis, or age-related maculopathy (ARM).

Definition of DR, DME, CSME and VTDR

Diabetic Retinopathy was defined as the presence of any characteristic lesion as described by the International Clinical Diabetic Retinopathy Disease Severity Scales which is a grading standard designed according to the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) and Early Treatment Diabetic Retinopathy Study (ETDRS)[17,18]. Briefly, 5 categories define increasing severity of DR from "no apparent retinopathy", mild NPDR (microaneruysms only), moderate NPDR (more than just microaneurysms but less than severe NPDR), severe NPDR (any of the following: more than 20 intraretinal hemorrhages in each of 4 quadrants; definite venous beading in 2+ quadrants; prominent intraretinal microvascular abnormalities in 1+quadrant And no signs of PDR) or PDR (one of more of the following: neovascularization, vitreous/preretinal hemorrhage).

Diabetic macular oedema (DME) was defined according to the International Diabetic

Macular Oedema Severity Scales proposed by Wilkinson,[17] with either apparent retinal thickening or hard exudates in the posterior pole. When edema involved the fovea or within 500 μm of the fovea, or a 1+disc area of edema appeared with at least a portion of it within the macular, clinically significant macular edema (CSME) was regarded to be existing. Vision-threatening retinopathy (VTDR) was defined as the presence of severe NPDR, PDR and/or CSME.[10] In all cases, the diagnosis was based on the worse eye. The graders were independent and masked from the patients' demographics, medical history, diabetic control and results of previous ophthalmic examination.

Assessment and definitions of risk factors

Demographic and medical and family history data collected, physical examinations conducted, and laboratory testing performed have been previously described.[15] Known diabetes was assigned for the patients who had confirmed the diagnosis of diabetes previously. Newly diagnosed diabetes was assigned for the patients with 0 year of diabetes duration. The difference between the year of diagnosis (as claimed by participants) and the year enrolled in DES was considered as the duration of DM. Cardiovascular disease was defined as the history of myocardial infarction, angina, or stroke. We confirmed the history of myocardial infarction and stroke by self-report. Hypertension was defined as systolic BP (SBP) ≥ 140 mmHg, diastolic BP (DBP) ≥ 90 mmHg, or the use of antihypertensive medication. Dyslipidemia was

defined as in the Beijing eye study.[19] Hypercholesterolemia was defined as total cholesterol (TC) ≥ 5.72 mmol/l and triglyceride (TG) ≤ 1.70 mmol/l; hypertriglyceridemia as TG ≥ 1.70 mmol/l and TC ≤ 5.72 mmol/l; mixed hyperlipidemia as TC ≥ 5.72 mmol/l and TG ≥ 1.70 mmol/l; low high-density lipoprotein (HDL) hyperlipidemia as HDL-C ≤ 0.91 mmol/l.

Statistical analysis

The prevalence of DR was calculated as the ratio of the number of participants with DR in 1 or both eyes to the total number of diabetic participants. Age-adjusted prevalence was calculated using direct adjustment to the Chinese population from the 2010 China census.[20] Categorical data was described by number and percentage, and ranked data was compared with the rank sum test. Normally distributed data was expressed as mean ± standard deviation (SD). Two independent samples were compared using the *t* test, multiple groups were compared using analysis of variance, and two independent sample rates were compared using the χ^2 test. Unconditional logistic regression analyses (both univariate and stepwise) were conducted to examine the relation of the likelihood of ocular disease (dependent variable) to each of the demographic and medical variables studied. A value of $P < 0.05$ was considered to indicate statistical significance. Statistical analyses were performed in SPSS 16.0 (SPSS Inc., USA) and SAS 9.1.3 (SAS Institute, USA) software.

Results

Baseline characteristics of participants with T2DM

All eligible participants (8,952) were self-identified Han Chinese, and 59.9% were female. The average age was 54.0 years (range: 46.0–62.0 years), 87.2% of the individuals were 40 to 69 years old, 48.4% were farmers, and 77.2% had elementary or junior middle school levels of education. The average body mass index (BMI) was 24.6 ± 3.9 kg/m^2, and the waist-hip ratio were 0.9 ± 0.1. Fifteen hundred participants were diagnosed with T2DM with a prevalence of 16.8%. Subject characteristics were summarized in Table 1. Of the 1,500 persons with type 2 DM, 1,310 have fundus photography results that were usable for DR grading.

Prevalence of diabetic retinopathy

The standardized prevalence of DR in participants with DM was 18.2%. The prevalence of different severity of DR and macular edema by gender were summarized in Table 2. The prevalence of DR in male was 23.0%, which was significantly higher than that in female with 14.1% (P<0.001). There was a significant difference in the prevalence of different grade of DR (mild NPDR, moderate NPDR, severe NPDR, PDR) (P<0.001). The prevalence of NPDR and PDR was 16.9% and 0.9%, respectively. NPDR was more common among the patients with DR, which accounted for 94.8%. The prevalence of vision-threatening DR (VTDR), DME and CSME was 2.5%, 2.8% and 0.9%, respectively, and they were no any significant differences

between male and female.

The age-specific prevalence of DR and macular edema was summarized in Table 3. No significant difference was found in prevalence of DR between different age groups. Regarding the DR grade, there was a significant difference in prevalence between age groups (P=0.024). The prevalence of moderate NPDR increased with age, and rose from 1.9% in those 40-49 years old to 8.8% in those 70-79 years old. The prevalence of severe NPDR changed from 1.0% in those 40-49 years old to a peak of 4.8% in participants ≥80 years old (95% CI: 0.0%-11.3%). No significant difference was found in prevalence of macular edema (DME, CSME) between different age groups.

Among those diabetic patients, the standardized prevalence of DR was 32.8% for known diabetic patients, and 12.6% for newly diagnosed diabetic patients. Comparing with the newly diagnosed diabetic patients, the prevalence of DR at different grades in patients with known diabetes was markedly higher (P<0.001) (Table 4). Similarly, the prevalence of VTDR, DME and CSME in patients with known diabetes was higher than that in newly diagnosed diabetic patients (P<0.001).

Risk factors for diabetic retinopathy

Univariable logistic regression showed that compared with participants without DR, those with DR were significantly associated with male, education level, duration of DM, SBP, waist-to-

hip ratio, FBG and HbA1c (Table 5). Multivariable logistic regression showed that DR was significantly associated with male (odds ratio [OR] = 1.765, 95% CI: 1.267-2.459; P=0.001), higher education level (OR = 0.683, 95% CI: 0.471-0.988; P=0.043), longer duration of DM (> 10 years vs. ≤ 5 years; OR = 8.037, 95% CI: 3.467-18.631; P<0.001), higher SBP (OR = 1.113, 95% CI: 1.028-1.205; P=0.008), and higher HbA1c (OR = 1.237, 95% CI: 1.142-1.341; P<0.001) (Table 6). Those variables were the independent risk factors for the development of DR in patients with diabetes.

In participants with a new diagnosis of DM, the results of univariable logistic regression analysis indicated that those with DR were significantly associated with male, FBG, HbA1c, SBP, DBP, triglycerides and BMI compared with subjects without DR (Table 7). Multivariable logistic regression indicated that DR was significantly associated with male (OR = 2.750, 95% CI: 1.747-4.329; P<0.001), greater BMI (OR = 1.075, 95% CI: 1.014-1.139; P=0.015), higher SBP (OR = 1.147, 95% CI: 1.028- 1.279; P=0.014), and higher HbA1c (OR = 1.295, 95% CI: 1.166-1.439; P<0.001) which were the independent risk factors for the development of DR (Table 8).

Longer duration of DM (OR = 1.192, 95% CI: 1.17-1.271; P<0.001) and higher HbA1c (OR = 1.278, 95% CI: 1.095-1.492; P=0.002) were significant independent risk factors for the occurrence of VTDR in diabetic patients (Table 9).

Questionnaire

The participants with DM completed a questionnaire for life-style and medical conditions, and the content and results of the questionnaire are summarized in supplementary file 2. For the life style, 94.2% of participants with T2DM ate fresh fruits and vegetables daily, and 67.8% had exercise more than 30 minutes daily. For the clinical history, 21.2% of participants with a prior diagnosis of T2DM (known diabetes) has hypertension, while 32.0% of participants with a newly diagnosis of T2DM has hypertension. More than one-fourth of the participants (28.8%) have family history of hypertension. In terms of awareness of diabetes, only 28.1% of diabetic participants know they have diabetes, and 63.3% of diabetic participants did not understand diabetes can lead to ocular complications. Furthermore, 41.8% of diabetic patients never received blood glucose monitoring, and 13.5% of diabetic patients never received routine BP monitoring.

Discussion

The current study provides data on the prevalence of DR for an adult population in a rural area of Southern China. The prevalence of age-standardized DR was 18.2% for participants with diabetes, 32.8% for patients with previously diagnosed diabetes and 12.6% for patients with newly diagnosed diabetes. The prevalence of NPDR, PDR and VTDR was 16.9%, 0.9% and 2.5%, respectively. The prevalence of DME and CSME was 2.8% and 0.9%, respectively.

Significant independent risk factors of any DR were male, longer duration of DM, higher education level, and higher SBP and HbA1c.

Previous worldwide studies have reported a prevalence of DR ranging from 17.6% to 50%.[3 4 7 10-14 16] A systematic literature review including 35 population-based studies (1980-2008), largely from individuals of Caucasian background with limited data on other racial groups, showed that the overall prevalence was 34.6% for any DR, 6.96% for PDR, 6.81% for DME and 10.2% for VTDR.[1] Other reports suggested the prevalence of DR, VTDR and CSME was higher in African Americans and Latin Americans, while Asians have the lowest prevalence.[1 17 21] The Singapore Epidemiology of Eye Disease (SEED) study[9] showed that the prevalence of any DR in Chinese (26.2%) is lower than that in Indians (30.7%) but comparable to that in Malays (25.5%).

A meta-analysis including 19 studies in China found that the prevalence of DR, NPDR and PDR in the diabetic group was 23%, 19.1% and 2.8%, respectively. The prevalence of DR was higher in the rural diabetic group compared with the urban diabetic group (29.1% vs. 18.1%). In addition, the prevalence was higher in the Northern region compared with that in the Southern region (26.5% vs. 15.7%).[16] Furthermore, the Handan Eye Study is a population-based cross-sectional study in Northern China rural region. The study observed that the age-standardized prevalence of DR in patients over 40 years in Handan city (Hebei province) was 45.6%,[11] markedly higher than our finding 18.2%. In addition, a Yangxi Eye study conducted

in rural areas of Yangxi of Guangdong Province showed that the prevalence of DR over 50 years old was low (8.19%).[8] The different prevalence of DR between previous study and our observation may be due to different life style (dietary habits and exercise), socioeconomic status and economic level in North and South China. [2 4 16] Another possible reason of the differences may be related to selected the diagnosis criteria. FBG was only used to define DM in the Handan Eye Study, while FBG, oral glucose tolerance test (OGTT) and HbA1c were used further used in DES according to American Diabetes Association (ADA) criteria. These may be the reason for the lower prevalence of DR.

The risk factors for DR which identified in the current study were similar to those reported in other studies of Caucasions.[5-9] Another Beijing Eye Study from Northern China supports our finding in the associations between incident DR and longer known duration of DM and the concentration of HbA1c.[22] The Wisconsin Epidemiologic Study of Diabetic Retinopathy, the first population-based study with the longest follow-up on DR, reported that 28.8% of participants with duration of DM of < 5 years, and a rate of 77.8% in those with a duration exceeding 15 years.[10] Although no follow-up study was conducted, the current study showed that the DR frequency of participants with duration of DM > 10 years was approximately 8 times that of participants with duration < 5 years (Table 6). The study further confirmed that the most consistent risk factor for DR is longer duration of DM. The results of this study reinforce these links or findings about DR. We recommend the patients with risk factors should

be tracked clinically.

In addition to duration of diabetes, hyperglycemia is considered one of the most important risk factors for retinopathy. The present study showed that HbA1c was an independent risk factor for the occurrence of DR in diabetic patients and newly-diagnosed diabetic patients in our study. In two clinical trials, the United Kingdom Prospective Diabetes Study (UKPDS) and the Diabetes Control and Complications Trial (DCCT) reported that the strict control of glycemia (HbA1c, 7 %) decreases the incidence rate of DR in type 1 and 2 DM.[23,24] The long-term advantages of intensive therapy are more than the related disadvantages, though the early worsening risks in retinopathy probably appears in the first year treatment[24].The risk of retinopathy will be reduced by 30–40% when every percent of HbA1c is lowered (e.g., from 8% to 7 %), and the effect is considered as metabolic memory.[24, 25] Recently a published analysis of data from a large scale study showed that DR progressed in 5.8% of subjects receiving intensive glycemic control versus 12.7% receiving standard control (adjusted odds ratio [aOR] = 0.42, 95%, CI: 0.28-0.63, P<0.0001).[25] Thus, it can be seen that stringent glucose control is very important to reduce the occurrence and progression of DR.

Hypertension is another important modifiable risk factor for DR.[23] Our results showed that SBP was the independent factor of DR in all diabetic patients (OR = 1.113, P=0.008) and newly-diagnosed diabetic patients (OR=1.147, P=0.014), which indicated that each 10 mmHg increase in SBP was associated with an approximately 10% excess risk of DR. In the UKPDS,

if the patients with hypertension had blood pressure control, their risk of microvascular disease would reduce by a 37 %; additionally, the patients'risk of progression of retinopathy would reduce by 34 %, and the deterioration of visual acuity in people with T2DM would reduce by 47 % .[23, 24] It is believed that destruction of the automatic regulatory mechanism of the retinal capillaries by high blood glucose causes the capillary endothelial cells to be vulnerable to damage from hypertension, resulting in damage to the capillaries, reduced retinal blood supply, and eventually retinopathy. [26]

Although the influence of obesity on DR are inconclusive, another study demonstrated a relationship between higher BMI and increased risk of retinopathy.[27] We identified BMI (OR = 1.075, P=0.015) as one of the independent risk factors for the development of DR in patients with newly diagnosed T2DM. However, the WESDR showed contradictory results in patients with type 1 DM.[28, 29]The obesity (BMI>31.0 kg/m^2 for men and 32.1 kg/m^2 for women) was related to the progression and severity of retinopathy in patients with T2DM; however, their association was not statistically significant[24,30] Furthermore, the risk of developing retinopathy was shown to increase by three folds for those whose BMI is low (<20 kg/m^2). [24,27, 28]

The current study found that the higher prevalence of DR in male, while other studies had the opposite results. A study of rural residents in India also found a higher frequency of DR in male.[31] On the contrary, female gender was an independent risk factor for the development of DR in Japanese patients with T2DM,[32] and females have a higher frequency of moderate NPDR,

severe NPDR, PDR and VTDR in Malays from Singapore.[12] However, the Handan and Beijing eye disease studies performed in Northern China cannot find any correlation between gender and DR.[11 14] In the current study, higher HbA1c levels was found in male, suggesting that HbA1c may be an influence factor on the occurrence and development of DR. The exact role of the gender as a possible determinant of DR remains to be determined.

The analyzed results of questionnaire indicated that the rural participants in our study had a low level of awareness of DM and diabetic eye disease. Almost two-thirds of participants did not know that DM can cause severe ocular complications and loss of vision. On the other hand, 71.5% of the DM patients in this population lack knowledge of diabetes. The proportion of undiagnosed diabetics in this population is high and may cause their retinopathy to be undetected. Thus, the degree of patient awareness and its relationship to DR care may be the key to further improving DR management and prevention. Therefore, intervention in DM and diabetic eye disease in the Chinese adult population is urgently needed to raise awareness, treatment and control. [33]

The strengths of this study are to conduct 2010 ADA diagnostic standards to decrease the possibility of misdiagnosis of DM and consider the importance and high prevalence of diabetic retinopathy. In addition, the sample size was big and the demographic characteristics of the participants were simple to reflect the actual results. This is because that this study focused on a rural area that have experience economic development and urbanization for nearly 30 years.

However, the limitation of the population-based cross-sectional study is that long-term effects cannot be found and causal relationships cannot be established. Since there is no time dimension, it will reduce the supporting intensity in the conclusion and causal relationship of diabetes risk. It may also exhibit recall bias, because diabetes may influence subjects' response to questionnaires.

Conclusions

The current study provided new data on the epidemiological characteristics of DR in a population-based sample of Chinese adults in Southern China. The standardized prevalence of DR was 18.2%, which was lower than the reported prevalence in Northern China and Western Countries. There were 32.8% known diabetic patients and 12.6% newly diagnosed diabetic patients who were screened out DR. Male, higher education level, longer duration of DM, higher SBP, and HbA1c were the independent risk factors for the development of DR in patients with diabetes. In addition, a high proportion of previously undiagnosed subjects with diabetes and diabetic ocular complications and subjects lacking diabetes care were observed in this study. This indicates the need to improve awareness and health education for DM and DR in parts of rural China, especially for subjects with DR risk factors.

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Competing interest's statement

The authors declare that there is no competing interest.

Author's contribution

M. Q., G. H. and C. Y. designed the study and wrote the main manuscript text. M. Q., C. Y., Z. L., Z. M., Y. X., Z. LX. and L. Q. collected and managed data. M. Q., C. Y., Z. L., Z. G., and K. J. analyzed and interpreted data. All authors approved the manuscript.

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Data sharing statement

No additional data

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Table 1. Characteristics of the participants with or without type 2 diabetes in Dongguan Eye Study

	Without Type 2 Diabetes (n=7452)	With Type 2 Diabetes (n=1500)	P-value	Participants with Type 2 Diabetes		P-value
				Men (n=614)	Women (n=886)	
Age	54.5 (11.3)	59.5 (11.3)	<0.001	57.2 (11.1)	61.0 (11.2)	<0.001
Male	2997 (40.2)	614 (40.9)	0.606	—	—	
BMI (kg/m^2) §	24.3 (3.8)	26.2 (3.9)	<0.001	26.1 (3.9)	26.3 (3.9)	0.182
Waist-hip ratio§	0.88 (0.25)	0.91 (0.07)	<0.001	0.93 (0.07)	0.89 (0.07)	<0.001
SBP (mmHg)	131.7 (18.8)	141.8 (20.6)	<0.001	139.3 (19.9)	143.5 (20.9)	<0.001
DBP (mmHg)	75.7 (10.5)	78.5 (11.1)	<0.001	80.0 (11.4)	77.6 (10.8)	<0.001
FBG (mmol/L)	5.4 (0.6)	7.6 (2.9)	<0.001	7.8 (3.1)	7.4 (2.7)	0.005
HbA1c (%)	5.7 (0.4)	7.1 (1.7)	<0.001	7.2 (1.8)	7.0 (1.6)	0.011
TC (mmol/L)	5.2 (1.0)	5.5 (1.3)	<0.001	5.3 (1.2)	5.6 (1.3)	0.001
TG (mmol/L)	1.2 (0.9-1.7) †	1.6 (1.1-2.4) †	<0.001	1.7 (1.1-2.6) †	1.5 (1.1-2.3) †	0.024
HDL-C (mmol/L)	1.5 (0.5)	1.4 (0.4)	<0.001	1.3 (0.3)	1.5 (0.4)	<0.001
LDL-C (mmol/L)	3.0 (0.9)	3.2 (1.1)	<0.001	3.1 (1.1)	3.3 (1.1)	0.002
BUN (mmole/L)	5.8 (1.7)	5.9 (1.8)	0.305	5.9 (1.6)	5.8 (1.9)	0.582

Scr (μmole/L)	79.1 (36.6)	77.8 (38.6)	0.353	89.0 (43.6)	69.8 (22.5)	<0.001
UA (μmole/L)	379.5 (101.8)	391.8 (103.3)	0.002	417.5 (109.6)	373.8 (94.9)	<0.001
History myocardial infarction	—	—	—	3 (0.5)	3 (0.3)	0.693
History stroke	—	—	—	23 (3.8)	31 (3.3)	0.796
History of Cardiovascular disease	—	—	—	9 (1.5)	9 (1.0)	0.429
Current smoker	—	—	—	389 (63.4)	12 (1.4)	<0.001

Abbreviations: BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; FBG: fasting blood glucose; HbA1c: glycosylated hemoglobin; TC: serum total cholesterol; TG: triglycerides; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; BUN: blood urea nitrogen; Scr: serum creatinine; UA: uric acid.

Categorical data reported as number (percentage); continuous data as mean (standard deviation).

† Data were mean (range).

§ BMI = weight (kg) / height (m^2); Waist-hip ratio = waist circumference (cm) / hip circumference (cm).

Table 2. Prevalence of different severity of diabetic retinopathy and macular edema by gender

	Participants with diabetes‡ (n=1310)		Men with diabetes‡ (n=543)		Women with diabetes‡ (n=767) (%)		P-Value*
	Patient number	Prevalence (%) (95% CI)	Patient number	Prevalence (%) (95% CI)	Patient number	Prevalence (%) (95% CI)	
No DR	1075	82.1 (80.2-84.3)	418	77.0 (73.5-80.6)	659	85.9 (83.5-88.4)	<0.001
diagnosed DR	233	17.8 (15.7-19.8)	125	23.0 (19.4-26.5)	108	14.1 (11.6-16.5)	-
DR grade							<0.001
Mild NPDR	139	10.6 (9.0-12.3)	80	14.8 (11.8-17.8)	59	7.7 (5.8-9.6)	_
Moderate NPDR	65	5.0 (3.8-6.2)	31	5.7 (3.8-7.7)	34	4.4 (3.0-5.9)	_
Severe NPDR	17	1.3 (0.7-1.9)	9	1.7 (0.6-2.7)	8	1.0 (0.3-1.8)	_
PDR	12	0.9 (0.3-1.3)	5	0.9 (0-1.5)	7	0.9 (0.2-1.6)	_
VTDR	33	2.5 (1.7-3.4)	15	2.8 (1.4-4.2)	18	2.3 (1.3-3.4)	0.625
DME	37	2.8 (1.9-3.6)	18	3.3 (1.7-4.6)	19	2.5 (1.4-3.6)	0.466
CSME	12	0.9 (0.4-1.4)	6	1.1 (0.2-2.0)	6	0.8 (0.2-1.4)	0.539

Abbreviations: CI, confidence interval; DR, diabetic retinopathy; NPDR, non-proliferative DR; PDR, proliferative DR; VTDR: vision-threatening DR; DME, diabetic macular edema; CSME, clinically significant macular edema.

*P value for the difference of retinopathy by gender based on chi-square test.

‡ Of the 1,500 persons with type 2 DM, 1,310 had fundus photography results that were usable for DR grading.

Table 3. Age-specific prevalence of diabetic retinopathy and macular edema ¶

Type of DR or DME	40-49 years Prevalence (%) (95% CI)	50-59 years Prevalence (%) (95% CI)	60-69 years Prevalence (%) (95% CI)	70-79 years Prevalence (%) (95% CI)	≥ 80 years Prevalence (%) (95% CI)	P-Value†
Any DR	16.8 (12.6-21.0)	17.2 (13.4-20.9)	18.0 (14.2-21.7)	20.0 (13.8-26.2)	19.0 (7.0-31.1)	0.927
DR grade						0.024
Mild NPDR	13.3 (9.5-17.1)	10.0 (7.0-13.0)	9.6 (6.7-12.5)	9.4 (4.8-13.9)	11.9 (2.0-21.8)	
Moderate NPDR	1.9 (0.4-3.5)	4.9 (2.7-7.0)	6.2 (3.8-8.5)	8.8 (4.4-13.1)	2.4 (0-7.1)	
Severe NPDR	1.0 (0-2.1)	0.5 (0-1.2)	2.0 (0.6-3.3)	1.3 (0-3.0)	4.8 (0-11.3)	
PDR	0.6 (0-1.5)	1.8 (0.5-3.1)	0.2 (0-0.7)	0.6 (0-1.9)	—	
VTDR	1.6 (0.2-3.0)	2.6 (1.0-4.1)	3.2 (1.5-4.9)	1.9 (0-4.0)	4.8 (0-11.2)	0.571
DME	1.9 (0.4-3.5)	2.6 (1.0-4.1)	3.9 (2.0-5.8)	2.5 (0.1-4.9)	—	0.383
CSME	0.3 (0-1.0)	1.0 (0-2.0)	1.5 (0.3-2.7)	0.6 (0-1.9)	—	0.527

Abbreviations: CI, confidence interval; DR, diabetic retinopathy; NPDR, non-proliferative DR; VTDR: vision-threatening DR ;DME, diabetic macular edema; CSME, clinically significant macular edema;.

†P value for the difference of age groups based on chi-square test.

Table 4. Prevalence of different severity of diabetic retinopathy and macular edema by diabetes status

	Newly diagnosed diabetes‡ (n=936)		Known Diabetes‡ (n=374)		P- Value†
	Patient number	Prevalence (%) (95% CI)	Patient number	Prevalence (%) (95% CI)	
No DR	832	88.9 (86.8-90.9)	246	65.8 (61.0-70.6)	_
Any DR	104	11.1 (9.1-13.2)	129	34.5 (29.4-39.0)	<0.001
DR grade					<0.001
Mild NPDR	80	8.6 (6.8-10.4)	59	15.8 (12.1-19.5)	_
Moderate NPDR	17	1.8 (1.0-2.7)	48	12.8 (9.4-16.2)	_
Severe NPDR	6	0.6 (0.1-1.2)	11	2.9 (1.2-4.7)	_
PDR	1	0.1 (0-0.3)	11	2.9 (1.0-4.3)	_
VTDR	9	1.0 (0.3-1.6)	24	6.4 (3.9-8.9)	<0.001
DME	9	1.0 (0.3-1.6)	27	7.2 (4.6-9.8)	<0.001
CSME	3	0.3 (0-0.7)	9	2.4 (0.8-4.0)	<0.001

Abbreviations: CI, confidence interval; DR, diabetic retinopathy; NPDR, non-proliferative DR; PDR, proliferative DR; VTDR: vision-threatening DR; DME, diabetic macular edema;. CSME, clinically significant macular edema.

†P value for the difference of newly diagnosed vs. known diabetic patients based on chi-square test.

Table 5. Univariate logistic regression analysis of the occurrence of diabetic retinopathy among all diabetic patients

Variables	Non-DR (n=1077)	DR (n=233)	Statistics	P-value
Age (y)	58.5 (10.6)	59.1 (10.9)	-0.740	0.459
Male	417 (38.7)	126 (54.1)	17.467	<0.001
Education level (higher or equal to junior middle school)	456 (42.3)	121 (51.9)	6.438	0.011
DM duration (y)			-8.884	<0.001
≤ 5	1024 (95.1)	181 (77.7)		
≤ 10	44 (4.1)	34 (14.6)		
> 10	9 (0.8)	18 (7.7)		
BMI (kg/m^2)	26.2 (3.9)	26.7 (3.7)	-1.846	0.065
Waist-hip ratio	0.9 (0.1)	0.9 (0.1)	-2.917	0.004
SBP (mmHg)	140.7 (19.9)	143.5 (20.1)	-1.941	0.052
DBP (mmHg)	78.5 (11.2)	79.1 (10.6)	-0.702	0.483
FBG (mmol/L)	7.24 (2.53)	8.6 (3.5)	-5.641	<0.001
HbA1c (%)	6.88 (1.56)	7.7 (2.0)	-5.700	<0.001
TC (mmol/L)	5.4 (1.2)	5.5 (1.4)	-0.605	0.546
TG (mmol/L)	1.6 (1.1-2.4)	1.6 (1.1-2.3)	-0.037	0.971
HDL-C (mmol/L)	1.4 (0.3)	1.4 (0.3)	1.516	0.130
LDL-C (mmol/L)	3.2(1.1)	3.26 (1.16)	-1.095	0.274
BUN (μmol/L)	5.8 (1.7)	6.0 (1.8)	-1.937	0.053
Scr (μmol/L)	76.5 (30.3)	78.0 (23.5)	-0.678	0.498
UA (μmol/L)	395.0 (104.6)	385.1 (103.5)	1.238	0.216

Abbreviations: BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; FBG: fasting blood glucose; HbA1c: glycosylated hemoglobin; TC: serum total cholesterol; TG: triglycerides; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; BUN: blood urea nitrogen; Scr: serum creatinine; UA: uric acid.

Table 6. Multifactorial logistic regression analysis of the occurrence of diabetic retinopathy among all diabetic patients¶

Variables	B	S.E.	OR (95% CI)	P
Sex (male vs. female)	0.568	0.169	1.765 (1.267-2.459)	0.001
Age (per 10 y)	0.115	0.085	1.122 (0.950-1.326)	0.175
Education (below vs. higher or equal to junior middle school)	-0.382	0.189	0.683 (0.471-0.988)	0.043
Diabetes duration (y)				
≤ 5	Ref.		1.000	
≤ 10	1.561	0.268	4.762 (2.816-8.054)	<0.001
> 10	2.084	0.429	8.037 (3.467-18.631)	<0.001
SBP (per 10 mmHg)	0.107	0.040	1.113 (1.028-1.205)	0.008
HbA1c (%)	0.213	0.041	1.237 (1.142-1.341)	<0.001

Abbrevitions: OR, odds ratio; CI, confidence interval; SBP, systolic blood pressure ; HbA1c: glycosylated hemoglobin.

¶ Multifactorial logistic regression analysis with backward selection procedure was performed by including significant factors identified in univariate analyses (i.e., P < 0.1).

Table 7. Univariate logistic regression analysis of the occurrence of diabetic retinopathy among new diagnosed diabetic patients

	Non-DR (n=832)	DR (n=104)	Statistics	P
Age (y)	58.1 (10.7)	57.7 (11.8)	0.279	0.781
Male	319 (38.3)	64 (61.5)	17.754	<0.001
Education level higher or equal to junior middle school	345 (41.5)	54 (51.9)	3.000	0.083
BMI (kg/m^2)	26.0 (3.8)	27.1 (3.7)	-2.549	0.011
Waist-hip ratio	0.9 (0.1)	0.9 (0.1)	-1.733	0.083
SBP (mmHg)	140.9 (20.1)	146.6 (21.3)	-2.645	0.008
DBP (mmHg)	79.1 (11.5)	82.4 (10.2)	-2.755	0.006
FBG (mmol/L)	7.1 (2.5)	8.6 (3.7)	-3.790	<0.001
HbA1c (%)	6.8 (1.6)	7.7 (2.1)	-3.926	<0.001
TC (mmol/L)	5.5 (1.2)	5.7 (1.2)	-1.204	0.231
TG (mmol/L)	1.6 (1.1-2.4)	1.8 (1.4-2.8)	-2.649	0.008
HDL-C (mmol/L)	1.4 (0.3)	1.4 (0.3)	1.087	0.277
LDL-C (mmol/L)	3.3 (1.1)	3.2 (1.1)	0.096	0.924
BUN (μmol/L)	5.7 (1.6)	5.7 (1.4)	-0.281	0.779
Scr (μmol/L)	76.2 (32.5)	76.2 (20.5)	0.002	0.998
UA (μmol/L)	393.2 (105.0)	390.2 (105.1)	0.261	0.794

Abbreviations: BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; FBG: fasting blood glucose; HbA1c: glycosylated hemoglobin ; TC: serum total cholesterol; TG: triglycerides; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; BUN: blood urea nitrogen; Scr: serum creatinine; UA: uric acid.

Table 8. Multifactorial logistic regression analysis of the occurrence of diabetic retinopathy among newly diagnosed diabetic patients

Variables	β	S.E.	OR (95% CI)	P
Sex (male vs. female)	1.011	0.232	2.750 (1.747-4.329)	<0.001
Age (per 10 y)	0.143	0.110	1.154 (0.930-1.432)	0.195
BMI (kg/m^2)	0.072	0.030	1.075 (1.014-1.139)	0.015
SBP (per 10 mmHg)	0.137	0.056	1.147 (1.028-1.279)	0.014
HbA1c (%)	0.259	0.054	1.295 (1.166-1.439)	<0.001

Abbreviations: OR, odds ratio; CI, confidence interval; BMI: body mass index; SBP, systolic blood pressure; HbA1c; glycosylated hemoglobin.

Table 9. Multifactorial logistic regression analysis of occurrence of vision-threatening diabetic retinopathy among all diabetic patients

Variables	β	S.E.	Wald	Df	P	OR (95% CI)
Sex (male vs. female)	0.298	0.386	0.596	1	0.440	1.348 (0.632-2.874)
Age (y)	0.023	0.018	1.631	1	0.202	1.024 (0.988-1.061)
Diabetes duration (y)	0.175	0.033	28.558	1	<0.001	1.192 (1.117-1.271)
HbA1c (%)	0.245	0.079	9.663	1	0.002	1.278 (1.095-1.492)

Abbreviations: OR, odds ratio; CI, confidence interval; HbA1c, glycosylated hemoglobin.

Table 1

高血压糖尿病危险因素调查问卷

编号：□□□□□ **受检者姓名：**

尊敬的先生/女士，您好！我们拟进行高血压糖尿病危险因素调查，请您如实回答以下调查问卷内容，您的信息会保存在社区健康档案中给予保密，谢谢您的合作！

n3、您是否每天都食用新鲜蔬菜或者水果？

①是 ②否

n7aa、您通常每次运动的时间大概是多少？

①<15 分钟 ②15-30 分钟 ③≧30 分钟

n10oeoe、您是否长时间使用过激素（强的松、地塞米松）？（口服或者静滴）

①是（激素使用持续的时间为_a1 ___个月）

②否 ③不清楚

n13ae、您开始有规律吸香烟的时候多少岁？ _____ 岁，吸烟__a2____年

n14ae、您平均每天吸烟量：（_____支/天）

① 小于 10 支 ②11-20 支 ③21-30 支 ④31-40 支 ⑤41 支以上

n18ae、您有饮酒吗？[选①、②者，__a5__年，每次_b3__什么酒（c1）]

①每天 ②1-3 次 / 周 ③每月 1 次或更少 ④从不

n20、您的家人中有高血压患者吗？

①有 ②没有 ③不知道

n21、您的家人中有糖尿病患者吗？与您的关系（a7）

①有 ②没有 ③不知道

N22、您的家人中有高脂血症患者吗？

①有 ②没有 ③不知道

n24、您是否有冠心病？

①是_a9___年 ②否

n25、您的体重最重时曾经达到过____kg？

28、您是否被医生诊断患过下列疾病？（可多选，在选中的答案打“√”）

A12（1）脑梗塞	①有	②没有	③不知道
B6（2）脑出血	①有	②没有	③不知道
C4（3）心肌梗死	①有	②没有	③不知道
D3（4）心绞痛	①有	②没有	③不知道
E2（5）心力衰竭	①有	②没有	③不知道

F3（6）肾功能衰竭　①有　②没有　③不知道

G1（7）糖尿病肾病　①有　②没有　③不知道

H1（8）视网膜出血性渗出、视乳头水肿　①有　②没有　③不知道

n29、您测量过血压吗？

①没有　②有，血压不高　③有，血压高，a13 年

n31、您最后一次测量血压值是多少？① a15 / b7 mmHg　②不记得

n32ae、是否有医生告知您有高血压？①是 a16 年　②否

n34、您检测过血糖吗？

①没有　②有，血糖不高　③有，血糖高，a18 年

n36、您最后一次检测血糖值是多少？① a20 mmol/L　②不记得

n37ae、是否有医生告知您有糖尿病？①是 a21 年 （1 型、2 型 b8）②否

n42ae、是否有医生告知您有高血脂？①是 a26 年　②否

n45ae、 您知道糖尿病可以引起眼部病变吗？

①知道　②不知道

n46oeae、您目前采用哪些方法来控制血压和/或血糖？

①非药物治疗　②药物治疗

③两者都采用　④没有治疗

b1049、请您列出当前使用的药物名称

降血糖药物名称（ b11 、不知道、不记得）

问卷结束，谢谢！

调查员：_____调查日期：_____

Table 2

眼科问卷 1　　眼病意识和治疗意识调查表

1. 你第 1 次知道你的眼睛有病，距今有多久（眼病存在的意识）？

□患有眼病，距今的时间：_____　□无眼病　□不清楚是否患有眼病

2. 何时知道你的眼病可以治疗（眼病治疗意识）？

□患有眼病，何时知道可以治疗：_____　□无眼病　□不清楚是否有眼病　□不知道可以治疗

3. 在检查之前，是否看过医生?　□是　□否

4. 如果看过医生但你最后未进行手术和药物治疗的原因是什么（眼病治疗障碍）？

①经济问题；②没有时间；③无人陪伴；④还能看到一点(白内障还没有成熟)；

⑤路太远；⑥年龄太大，觉得不需要；⑦害怕手术；⑧害怕丧失视力；

⑨一眼有足够的视力，觉得不需要；⑩有禁忌症。

5. 如果未看过医生或你不去看医生的原因是什么（眼病治疗障碍）？

①经济问题；②没有时间；③无人陪伴；④还能看到一点(白内障还没有成熟)；

⑤路太远；⑥年龄太大，觉得不需要；⑦害怕手术；⑧害怕丧失视力；

⑨一眼有足够的视力，觉得不需要；⑩有禁忌症。

6. 仅对已接受白内障手术者：白内障手术详情　（如未做白内障手术者，请在此处划"╳"　　）

	右眼	左眼
手术时间		
手术地点		
防盲流动车		
公立医院		
私立医院		
手术费用		
完全免费		
部分免费		
完全自费		
是否使用眼镜	□是　□否	□是　□否
不用眼镜的原因		
从未配过		
丢失		
损坏		
不需戴镜（IOL 植入）		

不需戴镜（另一眼视力好）				
手术类型				
超声乳化				
非超声乳化				
是否联合 IOL 植入	□是	□否	□是	□否

受试者签名： **2011 年 月 日**

Table 3

眼科问卷 2：　　生存质量和视功能调查问卷

我要问您一些关于您视力的问题，每个问题我说出 4 种答案，请您挑选一个最适合您实际情况的回答。

1. 自理：由于视力原因，在无人帮助时，你觉得做下列事情有多大困难?

	一点也没有	稍有一点	有些困难	十分困难	是否有人帮你	
洗澡	1	2	3	4	无= 1	有= 2
自己吃饭	1	2	3	4	无= 1	有=2
穿衣服	1	2	3	4	无= 1	有= 2
上厕所	1	2	3	4	无= 1	有= 2

2. 活动：由于视力原因，在无人帮助您时，您自己做下列事情有多大困难？

	一点也没有	稍有一点	有些困难	十分困难	是否有人帮你	
走到邻居家	1	2	3	4	无= 1	有= 2
去买东西	1	2	3	4	无= 1	有=2
做家务	1	2	3	4	无= 1	有= 2

3. 社交：由于视力原因，对您参加下列活动的愿望影响有多大?

	一点也没有	稍有一点	有些困难	十分困难
参加婚礼或过节日	1	2	3	4
看朋友或亲戚	1	2	3	4

4. 心理：由于视力原因，您是否觉得

	一点也不	稍有一点	比较明显	十分明显
是别人的负担	1	2	3	4
情绪低落	1	2	3	4
做事无信心	1	2	3	4

	很好	好	一般	差
5. 一般来讲，你认为您的视(眼)力是：(如果您是戴眼镜的，告诉我您戴镜后的情况)	1	2	3	4

	一点也不	**稍有一点**	**有些困难**	**十分困难**
6. 您的视(眼)力对您的日常生活限制有多大？	1	2	3	4
7. 您看清路对面的人有多大困难？	1	2	3	4
8. 您看清站在您旁边的人脸有多大困难？	1	2	3	4
9. 您看清细小的东西(如您手上的谷粒或手纹) 有多大困难？	1	2	3	4
10.当您一个人向前走路时，发现路边的东西有多大困难？	1	2	3	4
11.您从亮处来到暗处时，适应暗的环境有多大困难？	1	2	3	4

12.您从暗处来到亮处时，适应亮的环境有多大困难？	1	2	3	4
13.当一种东西和其它许多东西混在一起时，您找出它有多大困难？(如从饭碗里找到某种您想吃的食物)	1	2	3	4
14.您辨认颜色有多大困难？	1	2	3	4
15.当您想拿某样东西(如玻璃杯)时，您要拿到它有多大困难？	1	2	3	4
16.当您和您要辨认的人都在强光时，您看清对方有多大困难？	1	2	3	4
17.当强光(如迎面开来汽车灯光)晃您眼时，您看清东西有多大困难？	1	2	3	4

医生/护士/工作人员： **2011年 月 日**

Supplementary Table Questionnaires regarding life styles and systemic medical conditions

Items	Patients with positive response (%)
Life styles	
Habit of eating fresh fruits and vegetables daily	**94.2%**
Exercise more than 30 minutes daily	67.8%
Smoke tobacco	22.6%
Drink alcohol	22.5%
Clinical history	
Family history of diabetes	14%
Family history of hypertension	28.8%
Family history of hyperlipidemia	1.7%
History of coronary heart disease (including myocardial infarction, angina, and heart failure)	4.4%
History of cerebrovascular disease (including cerebral infarction and cerebral hemorrhage)	3.6%
History of kidney disease	0.8%
Hypertension in participants with a history of diabetes	21.2%
Hypertension in newly diagnosed diabetic participants	32.0%
Hypertension in all diabetic participants	53.2%
Awareness of diabetes	
Diabetic participants understood they had diabetes	28.1%
Diabetic participants did not know ocular complications resulted from diabetes	63.3%
Diabetic participants who never received blood glucose monitoring	41.8%
Never had routine blood pressure monitoring	13.5%

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3-4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5-6
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	6
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, explain how loss to follow-up was addressed	
		(*e*) Describe any sensitivity analyses	
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	Report numbers of outcome events or summary measures over time	10-12
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	12-13
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	13-14
Limitations			18-19
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-18
Generalisability	21	Discuss the generalisability (external validity) of the study results	19
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19-20

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.