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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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ABSTRACT

Research question The current population-based study aimed 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 underwent haematological, physical, ophthalmic examinations and completed a questionnaire regarding lifestyles 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 8952 Han Chinese, 1500 were diagnosed with type 2 diabetes mellitus (T2DM) with an average age of 59.5±11.1 years, and 1310 participants with fundus photography results were analysed. Standardised prevalence rate 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 patients with T2DM. The prevalence rate of male DR was significantly higher than that of female DR (23.0% vs 14.1%, p<0.001). No significant difference was found in age-specific prevalence of DR. In diabetic patients, the prevalence rates of vision-threatening diabetic retinopathy, diabetic macular oedema and clinically significant macular oedema were 2.5%, 2.8% and 0.9%, respectively. Male gender, higher education level, longer duration of diabetes mellitus (DM), higher systolic blood pressure and glycosylated haemoglobin were independent risk factors for 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 the rural area of 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 on DM and DR, especially in subjects with DR risk factors to reduce the incidence of DR and macular oedema.

Strengths and limitations of this study

- ► The large population-based study considers the importance and the high prevalence of diabetic retinopathy.
- ► This study uses 2010 American Diabetes Association diagnostic standards to decrease the possibility of missed diagnosis of diabetes mellitus.
- ► 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 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 high-income countries.[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 geographical and ethnic variability in the prevalence of DR.[7–9] A variety of risk factors including age, longer duration of DM, hyperglycaemia, hypertension, hyperlipidaemia 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 diabetes mellitus (T2DM).[11 12 14 16]

Urbanisation 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 that among village residents in low-income 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, has epidemiological characteristics that are not exactly consistent with those of DM due to geographical 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 the 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 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 the 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 details of the community survey were shown in a previous report.[15] Briefly, a community survey was performed in the village courtyard or village centre. Demographic data, socioeconomic risk status and potential risk factors were recorded. Subsequently, participants underwent examinations that included venous blood collection, physical measurements and ophthalmic examinations as described below. In addition, participants completed a questionnaire (online supplementary file 1) regarding lifestyles 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 was determined using autorefraction results, and presenting visual acuity with habitual refractive correction was tested.

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

Definition of DR, diabetic macular oedema (DME), clinically significant macular oedema (CSME) and vision-threatening diabetic retinopathy (VTDR)

DR was defined as the presence of any characteristic lesion as described by the International Clinical Diabetic Retinopathy Disease Severity Scale, which is a grading standard designed according to the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) and Early Treatment Diabetic Retinopathy Study.[17 18] Briefly, five 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 haemorrhages in each of four quadrants, definite venous beading in 2+ quadrants and prominent intraretinal microvascular abnormalities in 1+ quadrant and no signs of PDR) or PDR (one or more of the following: neovascularisation and vitreous/preretinal haemorrhage).

DME was defined according to the International Diabetic Macular Oedema Severity Scales proposed by Wilkinson *et al*,[17] with either apparent retinal thickening or hard exudates in the posterior pole. When oedema involved the fovea or within 500 µm of the fovea, or a 1+ disc area of oedema appeared with at least a portion of it within the macular, CSME was regarded to be existing. 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 the 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 a systolic blood pressure (SBP) of ≥140 mm Hg, a diastolic blood pressure (DBP) of ≥90 mm Hg or the use of antihypertensive medication. Dyslipidaemia was defined as in the Beijing Eye Study.[19] Hypercholesterolaemia was defined as a total cholesterol (TC) of ≥5.72 mmol/L and a triglyceride (TG) of ≤1.70 mmol/L, hypertriglyceridaemia as TG≥1.70 mmol/L and TC≤5.72 mmol/L, mixed hyperlipidaemia as TC≥5.72 mmol/L and TG≥1.70 mmol/L, and low high-density lipoprotein hyperlipidaemia 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 one 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 were described by number and percentage, and ranked data were compared with the rank-sum test. Normally distributed data were expressed as mean±SD. Two independent samples were compared using 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 V.16.0 and SAS V.9.1.3 software.

RESULTS

Baseline characteristics of participants with T2DM

All eligible participants (8952) were self-identified Han Chinese, and 59.9% were female. The average age was 54.0 years (range: 46–62 years), 87.2% of the individuals were 40–69 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 was 0.9±0.1. Fifteen hundred participants were diagnosed with T2DM with a prevalence of 16.8%. Subject characteristics are summarised in

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

	Without type 2 diabetes (n=7452)	With type 2 diabetes (n=1500)	P value	Participants with type 2 diabetes		
				Men (n=614)	Women (n=886)	P value
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 (mm Hg)	131.7 (18.8)	141.8 (20.6)	<0.001	139.3 (19.9)	143.5 (20.9)	<0.001
DBP (mm Hg)	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 (μmol/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 of myocardial infarction	–	–	–	3 (0.5)	3 (0.3)	0.693
History of 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

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

Table 2 Prevalence of different severity levels of DR and macular oedema by gender

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

*Of the 1500 persons with type 2 diabetes mellitus, 1310 had fundus photography results that were usable for DR grading.
†P value for the difference of retinopathy by gender based on χ^2 test.
CSME, clinically significant macular oedema; DME, diabetic macular oedema; DR, diabetic retinopathy; NPDR, non-proliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy; VTDR, vision-threatening diabetic retinopathy.

table 1. Of the 1500 persons with T2DM, 1310 have fundus photography results that were usable for DR grading.

Prevalence of DR

The standardised prevalence of DR in participants with DM was 18.2%. The prevalence rates of different severity levels of DR and macular oedema by gender are summarised in table 2. The prevalence rate of DR in men was 23.0%, which was significantly higher than that in women at 14.1% (p<0.001). There was a significant difference in the prevalence of different grades of DR (mild Exeter@123

NPDR, moderate NPDR, severe NPDR and PDR) (p<0.001). The prevalence rates 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 rates of VTDR, DME and CSME were 2.5%, 2.8% and 0.9%, respectively, and there were no any significant differences between men and women.

The age-specific prevalence of DR and macular oedema is summarised in table 3. No significant difference was found in the 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 aged 40–49 years to 8.8% in those aged 70–79 years. The prevalence of severe NPDR

Table 3 Age-specific prevalence of DR and macular oedema

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 to 21.0)	17.2 (13.4 to 20.9)	18.0 (14.2 to 21.7)	20.0 (13.8 to 26.2)	19.0 (7.0 to 31.1)	0.927
DR grade						0.024
Mild NPDR	13.3 (9.5 to 17.1)	10.0 (7.0 to 13.0)	9.6 (6.7 to 12.5)	9.4 (4.8 to 13.9)	11.9 (2.0 to 21.8)	
Moderate NPDR	1.9 (0.4 to 3.5)	4.9 (2.7 to 7.0)	6.2 (3.8 to 8.5)	8.8 (4.4 to 13.1)	2.4 (0 to 7.1)	
Severe NPDR	1.0 (0 to 2.1)	0.5 (0 to 1.2)	2.0 (0.6 to 3.3)	1.3 (0 to 3.0)	4.8 (0 to 11.3)	
PDR	0.6 (0 to 1.5)	1.8 (0.5 to 3.1)	0.2 (0 to 0.7)	0.6 (0 to 1.9)	–	
VTDR	1.6 (0.2 to 3.0)	2.6 (1.0 to 4.1)	3.2 (1.5 to 4.9)	1.9 (0 to 4.0)	4.8 (0 to 11.2)	0.571
DME	1.9 (0.4 to 3.5)	2.6 (1.0 to 4.1)	3.9 (2.0 to 5.8)	2.5 (0.1 to 4.9)	–	0.383
CSME	0.3 (0 to 1.0)	1.0 (0 to 2.0)	1.5 (0.3 to 2.7)	0.6 (0 to 1.9)	–	0.527

†P value for the difference in age groups based on χ^2 test.
CSME, clinically significant macular oedema;DME, diabetic macular oedema; DR, diabetic retinopathy; NPDR, non-proliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy; VTDR, vision-threatening diabetic retinopathy.

Table 4 Prevalence of different severity levels of DR and macular oedema by diabetes status

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

*Of the 1,500 persons with type 2 DM, 1,310 had fundus photography results that were usable for DR grading.
†P value for the difference between newly diagnosed and known diabetic patients based on χ^2 test.
CSME, clinically significant macular oedema; DME, diabetic macular oedema; DR, diabetic retinopathy; NPDR, non-proliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy; VTDR, vision-threatening diabetic retinopathy.

changed from 1.0% in those aged 40–49 years to a peak of 4.8% in participants aged ≥80 years (95% CI 0.0% to 11.3%). No significant difference was found in the prevalence of macular oedema (DME and CSME) between different age groups.

Among those diabetic patients, the standardised prevalence rates of DR were 32.8% for known diabetic patients and 12.6% for newly diagnosed diabetic patients. Compared with the newly diagnosed diabetic patients, the prevalence rate 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 DR

Univariable logistic regression showed that compared with participants without DR, those with DR were significantly associated with male gender, education level, duration of DM, SBP, waist:hip ratio, fasting blood glucose (FBG) and glycosylated haemoglobin (HbA1c) (table 5). Multivariable logistic regression showed that DR was significantly associated with male gender (OR (OR)=1.765, 95% CI 1.267 to 2.459; p=0.001), higher education level (OR=0.683, 95% CI 0.471 to 0.988; p=0.043), longer duration of DM (>10 years vs ≤5 years; OR=8.037, 95% CI 3.467 to 18.631; p<0.001), higher SBP (OR=1.113, 95% CI 1.028 to 1.205; p=0.008) and higher HbA1c (OR=1.237, 95% CI 1.142 to 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 the univariable logistic regression analysis indicated that those with DR were significantly associated with male gender, FBG, HbA1c, SBP, DBP, TG and BMI compared with subjects without DR (table 7). Multivariable logistic regression indicated that DR was significantly associated with male gender (OR=2.750, 95% CI 1.747 to 4.329; p<0.001), greater BMI (OR=1.075, 95% CI 1.014 to 1.139; p=0.015), higher SBP (OR=1.147, 95% CI 1.028 to 1.279; p=0.014) and higher HbA1c (OR=1.295, 95% CI 1.166 to 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 to 1.271; p<0.001) and higher HbA1c (OR=1.278, 95% CI 1.095 to 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 lifestyle and medical conditions, and the content and results of the questionnaire are summarised in online supplementary file 2. For lifestyle, 94.2% of the participants with T2DM ate fresh fruits and vegetables daily, and 67.8% had exercise more than 30 min daily. For the clinical history, 21.2% of the participants with a prior diagnosis of T2DM (known diabetes) had hypertension, while 32.0% of the participants with newly diagnosed T2DM had hypertension. More than one-fourth of the participants (28.8%) had a 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 underwent blood glucose monitoring, and 13.5% of diabetic patients never underwent routine BP monitoring.

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

Variables	Non-DR (n=1077)	DR (n=233)	Statistics	P value
Age (years)	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 (years)			−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 (mm Hg)	140.7 (19.9)	143.5 (20.1)	−1.941	0.052
DBP (mm Hg)	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

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

DISCUSSION

The current study provides data on the prevalence of DR for an adult population in a rural area of southern China. The prevalence rate of age-standardised 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 rates of NPDR, PDR and VTDR were 16.9%, 0.9% and 2.5%, respectively. The prevalence rates of DME and CSME were 2.8% and 0.9%, respectively. Significant independent risk factors of

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

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

*Multifactorial logistic regression analysis with backward selection procedure was performed by including significant factors identified in univariate analyses (ie, p<0.1).
HbA1c, glycosylated haemoglobin; SBP, systolic blood pressure.

Table 7 Univariate logistic regression analysis of the occurrence of DR among newly diagnosed diabetic patients

	Non-DR (n=832)	DR (n=104)	Statistics	P value
Age (years)	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 (mm Hg)	140.9 (20.1)	146.6 (21.3)	–2.645	0.008
DBP (mm Hg)	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

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

any DR were male gender, longer duration of DM, higher education level and higher SBP and HbA1c.

Previous worldwide studies have reported a prevalence rate 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 rates were 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 rate of any DR in Chinese (26.2%) is lower than that in Indians (30.7%) but comparable with that in Malays (25.5%).

A meta-analysis including 19 studies in China found that the prevalence rates of DR, NPDR and PDR in the diabetic group were 23%, 19.1% and 2.8%, respectively. The prevalence rate of DR was higher in the rural diabetic group compared with the urban diabetic group (29.1% vs 18.1%). In addition, the prevalence rate 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 the northern China rural region. The study observed that the age-standardised prevalence rate of DR in patients over 40 years in Handan city (Hebei Province) was 45.6%,[11] markedly higher than our finding of 18.2%. In addition, a Yangxi eye study conducted in rural areas of Yangxi of Guangdong Province showed that the prevalence of DR in individuals over 50 years old was low (8.19%).[8] The

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

Variables	β	SE	OR (95% CI)	P value
Gender (male vs female)	1.011	0.232	2.750 (1.747 to 4.329)	<0.001
Age (per 10 years)	0.143	0.110	1.154 (0.930 to 1.432)	0.195
BMI (kg/m^2)	0.072	0.030	1.075 (1.014 to 1.139)	0.015
SBP (per 10 mm Hg)	0.137	0.056	1.147 (1.028 to 1.279)	0.014
HbA1c (%)	0.259	0.054	1.295 (1.166 to 1.439)	<0.001

BMI, body mass index; HbA1c, glycosylated haemoglobin; SBP, systolic blood pressure.

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

Variables	β	SE	Wald	df	P value	OR (95% CI)
Gender (male vs female)	0.298	0.386	0.596	1	0.440	1.348 (0.632 to 2.874)
Age (years)	0.023	0.018	1.631	1	0.202	1.024 (0.988 to 1.061)
Diabetes duration (years)	0.175	0.033	28.558	1	<0.001	1.192 (1.117 to 1.271)
HbA1c (%)	0.245	0.079	9.663	1	0.002	1.278 (1.095 to 1.492)

HbA1c, glycosylated haemoglobin.

different prevalence of DR between the previous study and our observation may be due to different lifestyles (dietary habits and exercise), socioeconomic status and economic levels in North and South China.[2 4 16] Another possible reason of the differences may be related to selected diagnosis criteria. FBG was only used to define DM in the Handan Eye Study, while FBG, oral glucose tolerance test and HbA1c were used further 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 that were identified in the current study were similar to those reported in other studies of Caucasians.[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 had a 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 a duration of DM of >10 years was approximately eight times that of participants with a duration of <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 that patients with risk factors be tracked clinically.

In addition to duration of diabetes, hyperglycaemia 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 two clinical trials, the United Kingdom Prospective Diabetes Study (UKPDS) and the Diabetes Control and Complications Trial reported that the strict control of glycaemia (HbA1c, 7 %) decreases the incidence rate of DR in type 1 and type 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 per cent of HbA1c is lowered (eg, 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 glycaemic control versus 12.7% receiving standard control (adjusted OR=0.42, 95%, CI 0.28 to 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 mm Hg 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 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 is 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] 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 threefolds for those whose BMI is low (<20 kg/m^2).[24 27 28]

The current study found a higher prevalence of DR in men, while other studies had the opposite result. A study of rural residents in India also found a higher frequency of DR in men.[31] On the contrary, female gender was an independent risk factor for the development of DR in Japanese patients with T2DM,[32] and women 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 were found in men, suggesting that HbA1c may be an influence factor on the occurrence and development of DR. The exact role of gender as a possible determinant of DR remains to be determined.

The analysed results of the 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 patients with DM 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 to consider the importance and high prevalence of DR. In addition, the sample size was big and the demographic characteristics of the participants were simple to reflect the actual results. This is because this study focused on a rural area that has experienced economic development and urbanisation 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 standardised 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 for DR. Male gender, 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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