

BMJ Open Prevalence and associated factors of diabetic retinopathy in Beijing, China: a cross-sectional study

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To cite: Cui J, Ren J-P, Chen D-N, *et al.* Prevalence and associated factors of diabetic retinopathy in Beijing, China: a cross-sectional study. *BMJ Open* 2017;**7**:e015473. doi:10.1136/bmjopen-2016-015473

► Prepublication history for this paper is available online. To view these files please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2016-015473>).

Received 7 December 2016
Revised 6 May 2017
Accepted 24 May 2017



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ABSTRACT

Objectives The study aimed to determine the exact risk factors for diabetic retinopathy (DR) in the Chinese population using a cohort of 17 985 individuals from Beijing, China.

Design Cross-sectional study.

Setting A hospital.

Participants 17 985 individuals from Beijing, China.

Primary and secondary outcome measures This was a cross-sectional study of permanent residents from the Changping area (Beijing, China) recruited from July 2010 to March 2011 and from March 2014 to February 2015 during a routine health examination at the Tongren Hospital of Beijing. Eye examinations were conducted by experienced ophthalmologists. Medical history, height, weight, body mass index (BMI) and blood pressure were recorded. Routine laboratory examinations were performed.

Results The prevalence of DR was 1.5% in the general study population and 8.1% among individuals with diabetes. Compared with the non-DR group, individuals in the DR group in the diabetes population had longer disease duration, higher systolic blood pressure (SBP), fasting plasma glucose (FPG) and uric acid (UA) (in men) and lower UA (in women) (all $p < 0.05$). The multivariate analysis showed that disease duration ($p < 0.001$), BMI ($p = 0.046$), SBP ($p = 0.012$), creatinine clearance rate (CCR) ($p = 0.014$), UA ($p = 0.018$) and FPG ($p < 0.001$) were independently associated with DR in patients with diabetes.

Conclusion The prevalence of DR was 8.1% among patients with diabetes. Disease duration, BMI, SBP, CCR, UA and FPG were independently associated with DR.

INTRODUCTION

Diabetic retinopathy (DR) is an important cause of vision impairment and blindness.¹ With the increasing prevalence of diabetes in the world,¹ DR has become a disease that severely threatens public health. Vision deterioration can be prevented and the risk of blindness can be reduced if fundus screening and early intervention are performed in patients with diabetes.¹

A systematic review based on the global census of population from 1980 to 2008 has

Strengths and limitations of this study

- The present study identified risk factors of diabetic retinopathy (DR) in a large sample of patients with diabetes. The results could help identify patients at high risk of DR and allow preventive measures to be taken early.
- There is a possibility of a selection bias because the recruited individuals were visiting the hospital for a routine health examination.
- Not all subjects underwent an oral glucose tolerance test, which could underestimate the prevalence of diabetes.
- Compared with multiview fundus examination, single-view fundus examination may underestimate the prevalence of DR.
- Some individuals were excluded because of other eye diseases.

shown that the prevalence of DR is 34.6%.² In fact, there are great differences in the prevalence of DR among various countries. Specifically, the highest prevalence of DR is 49.6% in African groups in the USA, while the lowest is 19.9% in Asian groups in host countries; in between is China with 25.1%.² A systematic review of studies published between 1986 and 2009 suggested that the prevalence of DR in mainland China was 23%.³

Diabetes duration, blood glucose and blood pressure are widely accepted risk factors for DR,² and some studies indicated that blood lipids,² body mass index (BMI) and renal function² also affect the occurrence of DR. Since the reported prevalence of DR in Chinese individuals is low despite the increasing prevalence of diabetes (but regional variations do exist) and considering the balance of disease and economic benefits, specific screening strategies have to be developed according to the actual situation in China. In China, healthcare is available to treat diabetic complications (such as retinopathy, foot

ulcers, kidney diseases, etc) but there is no screening programme for diabetes. Therefore, most patients become aware of their diabetic status once serious complications occur, hence the importance of a screening programme.

Therefore, in order to determine the exact risk factors for DR in the Chinese population, a cohort of 17985 individuals in Beijing (China) was recruited. These individuals underwent screening for diabetes and a survey for the prevalence of DR. This study aimed to analyse the risk factors for DR.

METHODS

Study design and subjects

This was a cross-sectional study of permanent residents from the Changping area (Beijing, China) recruited from July 2010 to March 2011 and from March 2014 to February 2015 during a routine health examination at the Tongren Hospital of Beijing. The inclusion criterion was being 18–79 years of age. The exclusion criteria were: (1) reluctant respondents; (2) did not complete the questionnaire, physical examination, oral glucose tolerance test (OGTT) or blood tests; (3) cataract, glaucoma or any other eye diseases; or (4) fundus examination could not be completed for any reason.

The permanent resident population of the Changping area (suburb) of Beijing was 1 660 500. A total of 8155 people were selected and invited to participate in the study by using a multistage, stratified random sampling method. During the study periods, 2551 individuals who participated in the Changping Epidemiological Study and whose fasting plasma glucose was >5.6 mmol/L completed the OGTT and ophthalmic examination. Among 15 671 individuals receiving routine health check-up, 237 individuals were excluded for eye diseases, and 15 434 people were included in this analysis. Therefore, the overall study population (from the Changping Epidemiological Study and from health examinations) was 17 985 individuals.

The present study was approved by the ethics committee of the Tongren Hospital of Beijing. Each subject provided a written informed consent.

Diagnostic criteria

The diagnosis criteria for diabetes were: (1) fasting plasma glucose (FPG) ≥ 7.0 mmol/L; (2) history of diabetes; (3) taking antidiabetes medication; or (4) OGTT results consistent with the criteria of the 1997 American Diabetes Association (ADA).⁴ According to the Early Treatment Diabetic Retinopathy Study, those with the following lesions in fundus image were diagnosed with DR: (1) microaneurysms; (2) haemorrhage; (3) hard exudates; (4) cotton wool spots; (5) retinal vein beaded change; (6) microvascular abnormalities in the retina; and/or (7) neovascularisation.

Fundus examination

Eye examinations were conducted by experienced ophthalmologists. Mydriasis of both eyes was conducted and a Topcon TRC-NW7SF fundus camera (Topcon, Tokyo, Japan) was used to capture 45°C colour digital images of the fundus of both eyes. A double-blind diagnosis was performed by two ophthalmologists from the Eye Institute of the Affiliated Beijing Tongren Hospital of Capital Medical University. In case of disagreement, a third ophthalmologist was consulted.

Data collection and laboratory examinations

Medical history, height and weight were recorded. BMI was calculated as weight in kilograms divided by height in metres squared. A standard mercury sphygmomanometer was used to measure the blood pressure three times in the sitting position after 5 min rest; the average value was used for analysis.

Fasting antecubital venous blood was sampled to measure FPG. If FPG was ≥ 5.6 mmol/L, a standard 75 g glucose OGTT was performed within 8–10 hours. All measurements were performed in laboratories submitted to the quality control process of the Chinese Ministry of Health. A glucose oxidase method was used for the measurement of blood glucose. A Hitachi 7600 analyzer was used to detect creatinine, uric acid (UA) and blood lipids (total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C)). Creatinine clearance rate (CCR) (mL/min) = $((140 - \text{age}) \times \text{weight (kg)}) / (\text{creatinine } (\mu\text{mol/L}) \times 0.82 \text{ (men) or } 0.85 \text{ (women)})$. All blood samples were centrally analysed within 24 hours.

Statistical analysis

Continuous data were presented as mean \pm SD, and categorical data were presented as frequencies. Normally distributed continuous data were analysed using the independent t-test, while the rank sum test was used for non-normally distributed data. The χ^2 test was used for categorical data. After adjusting for age and gender using binary logistic regression, the evaluation of ORs and 95% CI of the risk factors for DR was performed. In the binary logistic regression analysis, the continuous variables were FPG, UA, TC, TG, LDL-C and HDL-C. The patients were grouped as diabetes, pre-diabetes and normal glucose tolerance (NGT), according to the 1997 ADA guidelines.⁴ For the multivariate analyses performed in patients with diabetes and pre-diabetes, the continuous data were transformed into categorical data for the logistic regression: (1) age was divided into 10-year groups; (2) blood pressure was divided into 10 mm Hg groups; (3) the course of the disease was divided into three groups: <5 , 5–9 and >9 years; (4) BMI: <24 and ≥ 24 kg/m²; (5) CCR <90 mL/min (abnormal) and CCR ≥ 90 mL/min (normal); (6) abdominal obesity: men, waist circumference ≥ 85 cm,

Table 1 Characteristics of the study population

	All n=17 985	DM n=1749	Pre-DM n=1633	NGT n=14 603
Age	44.1±13.9	55.7±11.2*†	51.4±11.8‡	41.8±13.4
Men (%)	46.2%	55.5%†	52.5%‡	44.4%
BMI (kg/m ²)	24.2±3.1	26.3±3.7†	26.1±3.6‡	23.7±3.5
SBP (mm Hg)	120.9±18.2	134.8±20.6†	134.9±19.8‡	117.7±16.1
DBP (mm Hg)	76.9±11.4	83.0±11.8*†	84.2±11.4‡	75.4±10.8
CCR (mL/min)	99.8±26.4	94.1±32.0*†	96.8±26.4‡	100.8±25.5
UA (men) (mmol/L)	358.6±73.0	340.1±79.1*†	362.2±81.1	360.9±70.5
UA (women) (mmol/L)	265.8±59.3	288.5±73.6*†	278.8±67.1‡	262.4±56.3
FPG (mmol/L)	5.6±1.4	8.4±2.6*†	6.4±0.3‡	5.2±0.4
TC (mmol/L)	4.8±0.9	5.0±1.1†	5.1±1.0‡	4.7±0.9
TG (mmol/L)	1.5±1.3	2.2±2.0*†	1.9±1.4‡	1.3±1.2
HDL-C (mmol/L)	1.3±0.4	1.3±0.4*†	1.3±0.3‡	1.3±0.4
LDL-C (mmol/L)	2.9±0.8	2.9±0.8	2.9±0.8	2.9±0.8
DR	266/1.5%	142/8.1%*†	22/1.4%	102/0.7%
Abdominal obesity	37.3%	69.0%*†	57.9%	31.3%

*DM vs pre-DM, $p < 0.05$.

†DM vs NGT, $p < 0.05$.

‡Pre-DM vs NGT, $p < 0.05$.

BMI, body mass index; CCR, creatinine clearance rate; DBP, diastolic blood pressure; DM, diabetes mellitus; DR, diabetic retinopathy; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; NGT, normal glucose tolerance; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides; UA, uric acid.

women, waist circumference of ≥ 80 cm, or waist-to-hip ratio ≥ 0.93 . SPSS V.22.0 for Windows (IBM) was used for statistical analysis. Two-sided p -values < 0.05 were considered statistically significant.

RESULTS

Characteristics of the study population

All patients had type 2 diabetes, based on medical history, patient age and drug history. The average age of the overall study population (17 985 individuals) was 44.1 ± 13.9 years (range, 18–79 years), and 1749 people were identified to be with diabetes. The average age of the patients with diabetes was 55.7 ± 11.2 years. Age, BMI, blood pressure, FPG, TC and TG in the diabetes group were all significantly higher than in the non-diabetes group, while the CCR in the diabetes group was lower than that in the non-diabetes group (table 1).

Prevalence and characteristics of DR

There were 261 patients with DR in the general study population, for a prevalence of 1.5%. There were 141 patients with DR in patients with diabetes, for a prevalence of 8.1% (the prevalence of known diabetes was 11.8%, and the prevalence of newly diagnosed diabetes was 2.8%). There were 120 patients with DR in individuals without diabetes, for a prevalence of 0.7% (cases with abnormal OGTT or increased FPG were 1.4%, and cases with normal OGTT or normal FPG were 0.7%).

Compared with the non-DR group, individuals in the DR group in the diabetes population had longer disease duration, higher systolic blood pressure (SBP), FPG, and UA (in men) and lower UA (in women). There was no significant difference in CCR, TC, TG, HDL-C and LDL-C levels between the two groups (table 2).

Multivariate analysis of the risk of DR among patients with diabetes

The risk factors for retinopathy were analysed in the patients with diabetes. The multivariate analysis showed that disease duration (OR 1.74, 95% CI 1.37 to 2.20, $p < 0.001$), BMI ≥ 24 kg/m² (OR 1.58, 95% CI 1.01 to 2.48, $p = 0.046$), SBP (for 10 mm Hg increases; OR 1.13, 95% CI 1.03 to 1.24, $p = 0.012$), CCR < 90 mL/min (OR 1.61, 95% CI 1.10 to 2.36, $p = 0.014$), UA (OR 0.997, 95% CI 0.995 to 0.999, $p = 0.018$) and FPG (OR 1.22, 95% CI 1.15 to 1.29, $p < 0.001$) were independently associated with DR (table 3).

Multivariate analysis of the risk of DR among patients with pre-diabetes

The risk factors for retinopathy were analysed in the individuals with pre-diabetes. The multivariate analysis showed that SBP (for 10 mm Hg increases; OR 1.14, 95% CI 1.06 to 1.21, $p < 0.001$) and FPG (OR 1.38, 95% CI 1.33 to 1.44, $p < 0.001$) were independently associated with DR.

Table 2 Comparison of the characteristics between subjects with or without DR

	DR		p Value
	Negative (1608)	Positive (141)	
Age	55.9±11.3	57.1±10.3	0.202
Men (%)	55.5%	55.6%	0.979
Diabetes duration	4.5±4.2	7.1±4.6	<0.001*
BMI (kg/m ²)	26.3±3.7	25.9±2.9	0.090
SBP (mm Hg)	134.4±20.3	139.7±23.2	0.007*
DBP (mm Hg)	82.9±11.8	82.6±12.2	0.757
CCR (mL/min)	94.5±32.7	90.3±27.4	0.132
UA (men) (mmol/L)	341.8±79.6	321.4±72.3	0.029*
UA (women) (mmol/L)	290.7±73.7	263.5±68.9	0.005*
FPG (mmol/L)	8.2±2.5	10.2±3.4	<0.001*
TC (mmol/L)	5.0±1.1	5.1±1.2	0.662
TG (mmol/L)	2.2±2.1	2.2±2.2	0.740
HDL-C (mmol/L)	1.3±0.4	1.3±0.3	0.486
LDL-C (mmol/L)	2.9±0.8	2.9±0.9	0.967
Abdominal obesity (%)	68.9%	70.2%	0.744

*p<0.05.

BMI, body mass index; CCR, creatinine clearance rate; DBP, diastolic blood pressure; DM, diabetes mellitus; DR, diabetic retinopathy; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; NGT, normal glucose tolerance; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides; UA, uric acid.

Table 3 Univariate and multivariate analyses of factors associated with DR in patients with diabetes

Variables	Univariate		Multivariate	
	p Value	OR (95% CI)	p Value	OR (95% CI)
Age (category)	0.077	1.136 (0.972 to 1.328)	0.270	0.882 (0.706 to 1.102)
Gender	0.979	1.005 (0.711 to 1.419)	0.183	1.311 (0.880 to 1.952)
Duration (category)	<0.001	1.503 (1.201 to 1.882)	<0.001	1.735 (1.368 to 2.202)
BMI (category)	0.593	1.116 (0.747 to 1.666)	0.046	1.579 (1.007 to 2.475)
SBP (category)	0.005	1.133 (1.039 to 1.236)	0.012	1.127 (1.027 to 1.238)
DBP (category)	0.644	0.965 (0.828 to 1.124)	0.085	0.842 (0.692 to 1.024)
CCR (category)	0.059	1.395 (0.987 to 1.972)	0.014	1.613 (1.103 to 2.358)
UA	0.001	0.996 (0.994 to 0.998)	0.018	0.997 (0.995 to 0.999)
FPG	<0.001	1.215 (1.154 to 1.279)	<0.001	1.220 (1.152 to 1.291)
TC	0.662	1.035 (0.886, 1.211)	0.365	1.290 (0.744 to 2.239)
TG	0.740	0.985 (0.902,1.076)	0.289	0.908 (0.761 to 1.085)
HDL-C	0.486	1.188 (0.731,1.931)	0.687	0.836 (0.349 to 2.000)
LDL-C	0.967	1.004 (0.819,1.232)	0.363	0.767 (0.434 to 1.357)
Abdominal obesity (category)	0.581	1.111 (0.764 to 1.618)	0.486	1.198 (0.721 to 1.992)

The continuous data were transformed into categorical data: (1) age was divided into 10-year groups; (2) blood pressure was divided into 10mm Hg groups; (3) the course of the disease was divided into three groups: <5, 5–9 and >9 years; (4) BMI: <24 kg/m² (normal), >24 kg/m² (overweight); (5) CCR <90 mL/min (abnormal), CCR >90 mL/min (normal); (6) abdominal obesity: men, waist circumference >85 cm, women, waist circumference of >80 cm, or waist-to-hip ratio >0.93.

BMI, body mass index; CCR, creatinine clearance rate; DBP, diastolic blood pressure; DR, diabetic retinopathy; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides; UA, uric acid.

DISCUSSION

The prevalence of DR in Chinese individuals is low despite the increasing prevalence of diabetes (but regional variations do exist). This study aimed to determine the exact risk factors for DR in the Chinese population using a cohort of 17985 individuals from Beijing, China. The prevalence of DR was 1.5% in the general study population or 8.1% among patients with diabetes. Disease duration, BMI, SBP, CCR and FPG were independently associated with DR.

In the present study, the prevalence of DR in the patients with diabetes was 8.1%, which was significantly lower than in other countries such as Norway (34.6%),⁵ the USA (28.5%),⁶ Iceland (25.2%)⁷ and Africa (30.2%–31.6%),⁸ and also lower than the worldwide prevalence (34.6%).² Studies indicate that ethnic differences are the main factors leading to differences of the prevalence among different populations after adjusting for general risk factors,⁹ and still, the prevalence of DR in Asians remains the lowest, at 19.9%.²

Nevertheless, some studies have suggested that South Asians are more likely to have DR compared with white Europeans, but Asians with DR are younger, the course of disease is shorter and blood pressure and FPG are higher.¹⁰ Although there is no ethnic difference among Asian countries,¹¹ the prevalence observed in the present study is still far lower than in other Asian countries such as Bangladesh (21.6%),¹² India (21.7%)¹³ and Singapore (35%),¹⁴ and even lower than the results of other mainland cities such as Shanghai (22.9%),¹⁵ Beijing (37.1%)¹⁶ and Handan (43.1%),¹⁷ but it is similar to the prevalence observed in a study in Shanghai (9.6%).¹⁸ These differences among studies may be caused by the sample size, the type of study population, age, course of disease, the average levels of various variables and different methods for fundus examination.

This study confirmed the commonly accepted risk factors for DR such as the course of diabetes, SBP and FPG.² In the present study, the prevalence of DR was 11.8% in individuals with a known history of diabetes and 2.8% in individuals with newly diagnosed diabetes. In addition, disease duration was independently associated with DR, as supported by a previous study.¹⁹ Of course, there is a high probability that undiagnosed patients before study participation were at the beginning of the disease, before onset of diabetic symptoms. Therefore, a less severe diabetes should be associated with fewer complications such as DR. Patients without known diabetes but with high suspicion or diagnosis of DR on fundus examination should undergo screening for diabetes. In addition, the present study found that the risk of DR increased in overweight people compared with people with normal BMI, which is consistent with studies in China²⁰ and abroad.²¹ On the other hand, a Chinese study²² reported that individuals with low BMI were more prone to DR, which was also confirmed in other Asian countries.²³ The above studies were cross-sectional surveys, while some Western cohort studies indicated that high BMI was associated

with the progression of DR,²⁴ and a Korean study also confirmed that weight reduction strategies could reduce the occurrence of DR.²⁵ The discrepancies may be due to differences in study design and in the study population. Studies showing no association between BMI and DR could suffer from a reverse causality/survival bias. In addition, a Chinese study suggested that the relationship between BMI and DR prevalence was actually a U-shaped distribution.²⁶ The association between BMI and DR needs further study using larger sample size.

Although some studies indicated that serum creatinine was an independent risk factor for DR,¹¹ the results of this study did not reveal any association between serum creatinine and DR. After converting the serum creatinine values into CCR, it was found that the prevalence of DR increased with decreasing CCR, and that CCR was an independent risk factor for DR, which is supported by previous studies.²⁷ In addition, the severity of DR is related to decreased glomerular filtration rate.²⁷

The present study suggested that blood lipids were not independently associated with DR, which is supported by previous studies,²⁰ but a previous Chinese study showed that hyperlipidaemia (TC ≥ 6.2 mmol/L), very low-density lipoprotein cholesterol and TG were independent risk factors for DR,²⁸ and a study confirmed the correlation between DR and TC and TG.²¹ American studies found that the occurrence of hard infiltration in the population with high TC and LDL was twice as much as that in the normal population, suggesting that TC and LDL are associated with the increasing risk of hard infiltration in the fundus.²¹ Therefore, further studies are needed for the relationship between blood lipids and DR.

The growth of the prevalence of diabetes in developing countries is higher than that in developed countries.¹ In China, as a developing country with a large population, the prevalence of diabetes is steadily increasing and diabetes is diagnosed at a younger age.¹ The present study was mainly conducted in young people (individuals <60 years of age accounted for 85% of the study population), and it was found that the prevalence of diabetes and prevalence of DR had the most important growth between 30 and 60 years of age. It can be seen from this study that although the prevalence of DR was low in the Chinese people, the frequency of diagnosis of diabetes and the prevalence of DR were significantly increased after 30 years of age. Therefore, screening programmes for diabetes in the general population and for DR in the population of patients with diabetes should be implemented, especially in individuals who have risk factors for diabetes and diabetic complications (eg, overweight, obesity, high blood pressure, dyslipidaemia and high FPG).

The present study has some strengths. The sample size was large. Fundus examinations were performed by experienced ophthalmic technicians and ophthalmologists. Screening of diabetes in the natural population was determined by OGTT. Nevertheless, there were some limitations. First, there is a possibility of a selection

bias because the recruited individuals were visiting the hospital for a routine health examination. Second, not all subjects underwent an OGTT, which could underestimate the prevalence of diabetes. Third, Vujosevic *et al.*²⁹ showed that one-field examination does not necessarily reliably estimate the severity of retinopathy when compared with seven-field examination. Fourth, some individuals were excluded because of other eye diseases. Finally, fundus examinations without mydriasis could result in inaccurate diagnosis of DR. The selection criteria and the limitations of the study could limit the generalisability of the study. Nevertheless, the study population was from what could be considered the general Beijing population. Since the Beijing population is composed of Han people as well as minorities from the country, it could be considered as representative of the Chinese population.

In conclusion, we found that the prevalence of DR was 8.1% among patients with diabetes in our study population. Disease duration, BMI, SBP, CCR, UA and FPG were independently associated with DR.

Acknowledgements We acknowledge the Diabetes Prevention and Control Bureau of Beijing, the Center for Disease Control of Changping area and the Ophthalmic Research Institute of Beijing Tongren Hospital for their assistance in completing this project.

Contributors JC and JKY contributed to conception and design; JC, JPR, DNC, ZX, MX, JX, QSY and JKY contributed to acquisition of data, or analysis and interpretation of data; JC, JPR, DNC, ZX, MX, JX, QSY and JKY were involved in drafting the manuscript or revising it critically for important intellectual content; all authors gave final approval of the version to be published.

Funding This work was supported by grants from the National Natural Science Foundation of China (8151101058) and Beijing Municipal Science and Technology Project (D171100002817005) to JKY.

Competing interests None declared.

Patient consent Obtained.

Ethics approval Ethics committee of the Tongren Hospital.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement Technical appendix, statistical code and dataset are available from the corresponding author.

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