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Analysis of factors related to diabetic retinopathy in patients with newly diagnosed type 2 diabetes: a cross-sectional study

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ABSTRACT

Aim To investigate the related factors of diabetic retinopathy (DR) and explore the correlation between smoking and DR in patients with newly diagnosed type 2 diabetes mellitus (T2DM).

Design A single-centre cross-sectional study.

Setting Tianjin 4th Central Hospital.

Participants Patients with newly diagnosed T2DM who visited the outpatient department of the hospital from December 2018 to April 2019.

Methods A total of 947 patients were enrolled in the study. They were divided into two groups according to whether they were diagnosed with DR (diabetic retinopathy group, DR group; non-diabetic retinopathy group, NDR group). The smoking index (SI) was calculated to assess smoking status. Factors such as sex, age, hypertension, T2DM diagnosed age, family history of diabetes, drinking history, haemoglobin A1c (HbA1c), body mass index (BMI) and smoking status were compared between the two groups. Logistic regression was used to analyse the relationship between DR and the above factors.

Results There was no statistically significant difference between the two groups in sex, age, hypertension, DM diagnosed age, family history of diabetes, drinking history and HbA1c. BMI was significantly higher in DR patients (27.7±4.2 vs 26.7±4.4, p=0.004). Smoking status was also different between the two groups (χ^2=6.350, p=0.042). BMI was shown to be a related factor for DR in patients with newly diagnosed diabetes (OR=0.592, p=0.004). When BMI was ≥28 kg/m^2, heavy smoking was significantly associated with DR (OR=2.219, p=0.049), and there was a negative correlation between DR and the age of diagnosis of diabetes ≥60 years (OR=0.289, p=0.009).

Conclusions Heavy smoking was an important related factor for DR in patients with newly diagnosed diabetes mellitus when BMI was ≥28 kg/m^2. Delaying the age of diabetes might prevent the occurrence of DR. To elucidate the correlation, long-term cohort studies with large samples are needed.

Strengths and limitations of this study

- This study is a representative population-based study.
- There are few studies on the factors related to newly diagnosed diabetic retinopathy in patients with type 2 diabetes mellitus in China.
- This study was the first to use the smoking index to assess smoking severity to study diabetic retinopathy.
- The study is a single-centre cross-sectional study.

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disease characterised by hyperglycaemia. It has various aetiologies, and the incidence is increasing yearly worldwide. According to the report of the International Diabetes Federation (IDF) in 2017, about 425 million people were affected by DM, and that number is expected to reach 629 million by 2045.[1] China has the highest number of patients with DM, and the prevalence has increased from 0.67% in 1980 to 10.4% in 2013.[2] A epidemiological-based meta-analysis conducted in 35 research centres around the world showed that the prevalence of diabetic retinopathy (DR) in the total diabetic population was 35.4%.[3] DR is a highly specific microvascular complication caused by diabetes, and its prevalence is significantly correlated with the course of DM and blood glucose levels.[4] DR is the most important cause of irreversible blindness in working-age adults.[4] Chronic hyperglycaemia causes not only retinal vascular diseases but also damage to retinal neurons, both of which are factors that lead to vision loss.[5] Twenty per cent of patients with newly diagnosed type 2 diabetes mellitus (T2DM) are diagnosed with DR.[3] The explanation for this phenomenon is that the onset of T2DM is often insidious, and patients may have a long history of untreated hyperglycaemia before diagnosis.[3] Are there any other risk factors for DR in these newly diagnosed patients? There is no relevant research report at present.

Smoking is harmful to health, and it is an important risk factor for cardiovascular, cerebrovascular and respiratory diseases and also for malignant tumours.[6] Smoking is one of the most serious public health issues throughout the world, and it is responsible for about 7 million deaths per year worldwide.[6] In a 14-year prospective cohort study, Jee *et al* found that people smoking >20 cigarettes a day had a 1.55-fold higher incidence of diabetes than non-smokers.[7] It is well known that smoking may cause an increase in proteinuria.[8] However, many studies have shown that smoking has no significant correlation with DR.[9] Even some studies in China have shown that smoking is a protective factor for DR.[10] Many patients with DM had started smoking before they were diagnosed with diabetes. Does smoking contribute to the complications of DR in newly diagnosed patients? Little research has been done on the relationship between smoking and DR in patients with newly diagnosed diabetes. The present study investigated the factors related to DR and explored the correlation between smoking and DR in patients with newly diagnosed T2DM who visited the outpatient department of the hospital from December 2018 to April 2019.

Research design and methods

The present study was a single-centre cross-sectional study of factors associated with DR in patients with newly diagnosed T2DM in Tianjin 4th Central Hospital. The hospital is a regional medical centre in Tianjin. The hospital had a diabetes identification centre. The patients in the region are identified by the department before they can enjoy more preferential health insurance policies in the clinic. The Metabolic Disease Management Center (MMC) was responsible for the screening for complications in patients with newly diagnosed diabetes, such as urinary protein, fundus examination, peripheral vascular and neuropathy. The diabetes nursing team undertook the measurement of height, weight and blood pressure, and gathered information about smoking, drinking and disease history. Electronic medical records were generated at the same time.

Participants

Study participants were patients with newly diagnosed T2DM who visited MMC from December 2018 to April 2019. The patient information came from an electronic database of the hospital's diabetes identification centre. All the patients who underwent fundus examination were enrolled in this study. All patient identifiers were removed prior to analysis. All the steps of this clinical study protocol were conducted in accordance with the principles of the World Medical Association Declaration of Helsinki.[11] Written informed consent was obtained from each patient.

Inclusion criteria

The study enrolled participants with a baseline of being newly diagnosed with T2DM within the past 6 months; patients who could communicate independently and describe their smoking status; none of the smokers had given up smoking before the study; and all patients underwent DR screening in the study.

According to the Chinese guidelines for the prevention and treatment of diabetes, all patients with diabetes in our hospital are required to be diagnosed with an oral glucose tolerance test. The diagnostic criteria during the execution were as follows: (1) fasting plasma glucose ≥7.0 mmol/L. Fasting was defined as no caloric intake for at least 8 hours; or (2) 2-hour plasma glucose ≥11.1 mmol/L during an oral glucose tolerance test. The test was performed as described by the WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water. A haemoglobin A1c (HbA1c) test was not standardised in China, so it could not be used as a diagnostic standard.[12]

Exclusion criteria

Type 1 diabetes and other specific types of diabetes; acute complications of diabetes, such as diabetic ketoacidosis or lactic acidosis; hypovolaemia; subjects with diabetic nephropathy complications, rheumatic diseases, autoimmune diseases, pregnancy, malignant tumours, infection, foot ulcer, severe mental illness, thyroid dysfunction, severe hepatic insufficiency or renal insufficiency, severe anaemia, heart failure or respiratory insufficiency; cognitive impairment and communication disorders.

Evaluation of clinical variables

Information about the patients' names, sex, phone numbers, body mass index (BMI), age, smoking history, drinking history, family history of DM, hypertension and HbA1c was collected using a uniform information table. The formula for BMI was weight in kilograms divided by the square of height in metres. BMI (≥28 kg/m^2) met obesity criteria according to Chinese standards.[13]

Table 1 Baseline characteristics of 947 participants with newly diagnosed T2DM

Items	N	%
Sex		
Male	566	59.8
Female	381	40.2
With a family history of DM	580	61.2
Age, years		
<50	309	32.5
≥50 to <60	318	33.4
≥60	325	34.1
With hypertension	498	52.6
With drinking history	195	20.6
Smoking status		
Non-smoking	517	54.6
Light and moderate smoking	212	22.4
Heavy smoking	218	23.0

DM, diabetes mellitus; T2DM, type 2 diabetes mellitus.

Hao Z, *et al*. *BMJ Open* 2020;**10**:e032095. doi:10.1136/bmjopen-2019-032095

Venous blood samples were collected in EDTA tubes from fasting patients in the morning. The level of HbA1c was determined by affinity chromatography in the hospital standard laboratory (Tosoh Corporation, Japan). Smoking status assessment: according to the WHO (1997) smoking survey method, smoking at least one cigarette per day for >6 months was considered as a smoking history.[14] The smoking index (SI) was calculated by multiplying the number of cigarettes smoked per day by the number of years the person had smoked. In our study, according to the SI, 0 meant non-smoking, ≤500 meant light and moderate smoking, and >500 meant heavy smoking.

Screening for DR was carried out according to EURODIAB guidelines using one 45° field retinograph centred on the fovea. If DR was suspected, the other two 45° retinographs were obtained.[15] Ophthalmologists judged whether the patient had DR according to the results of the funduscopic examination and guidelines. In the study, the results were reported as either positive or negative (DR or non-diabetic retinopathy (NDR)), and the patients were divided into two groups (DR group and NDR group). NDR here included a normal fundus and other retinopathy that may be caused by other causes (non-diabetic) such as fundus arteriosclerosis.

Statistical analysis

Descriptive analysis was used to illustrate the basic demographic characteristics. For continuous variables, a one-sample Kolmogorov-Smirnov normality test was used to check the normality of the distribution of such variables. Once normal distribution and homogeneity of variance were satisfied, values were represented by the $\bar{x}\pm SD$ and Student's t-test was used. For categorical variables, a χ^2 test was performed. The occurrence of DR was identified as the dependent variable, and the related factors (sex, hypertension, age at DM diagnosis, family history of diabetes, drinking history, HbA1c, BMI and smoking status) were listed as independent variables. To analyse the factors associated with DR and adjust for potential confounding effects, we examined the factors associated with DR using multivariable logistic regression analysis. All the analyses conducted using SPSS V.16.0 software with $p<0.05$ (two-sided) indicated statistical significance.

Patient and public involvement

Patients were not involved in setting the research questions or planning the study. Investigators did not know the identities of the study participants. In this study, the electronic data were obtained from the health records at the institution. All patient identifiers were removed

Table 2 Comparison of clinical data between DR and NDR groups

Items		NDR (n=755)	DR (n=192)	T/χ^2	P value
Sex	Male	447 (79.0%)	119 (21.0%)	0.490*	0.510
	Female	308 (80.8%)	73 (19.2%)		
Age	years	53.3±11.7	52.9±11.1	0.350†	0.726
Family history of DM	No	288 (78.5%)	79 (21.5%)	0.580*	0.456
	Yes	467 (80.5%)	113 (19.5%)		
Drinking history	No	608 (80.9%)	144 (19.1%)	2.863*	0.109
	Yes	147 (75.4%)	48 (24.6%)		
Hypertension‡	No	349 (81.2%)	81 (18.8%)	1.457*	0.265
	Yes	392 (78.7%)	106 (21.3%)		
Age of DM diagnosis (years)	<50	247 (79.9%)	62 (20.1%)	2.382*	0.304
	≥50 to <60	243 (77.1%)	72 (22.9%)		
	≥60	265 (82.0%)	58 (18.0%)		
HbA1c	%	9.51±2.13	9.60±2.12	−0.546†	0.585
BMI (	kg/m^2	27.7±4.2	26.7±4.4	2.921†	0.004
Smoking history	No	424 (82.0%)	93 (18.0%)	3.682†	0.062
	Yes	331 (77.0%)	99 (23.0%)		
Smoking status	Non-smoking	424 (82.0%)	93 (18.0%)	6.350*	0.042
Light and moderate smoking		170 (80.2%)	42 (19.8%)		
Heavy smoking		161 (73.9%)	57 (26.1%)		

There was no statistically significant difference if p >0.05.
*χ^2 test.
†Student's t-test.
‡19 cases of patients with missing data.
BMI, body mass index; DM, diabetes mellitus; DR, diabetic retinopathy; HbA1c, haemoglobin A1c; NDR, non-diabetic retinopathy.

Table 3 Analysis of related factors with DR, adjusted for age, BMI and smoking status

Factors	B	SE	Wald χ^2	P value	OR	95% CI
Sex	0.099	0.228	0.190	0.663	1.104	0.707 to 1.726
Hypertension	0.252	0.175	2.080	0.149	1.287	0.914 to 1.812
Drinking history	0.131	0.222	0.351	0.554	1.140	0.739 to 1.761
HbA1c	0.006	0.038	0.022	0.882	1.006	0.934 to 1.083
BMI (≥28 vs <28 kg/m^2)	−0.524	0.183	8.230	0.004	0.592	0.414 to 0.847
Family history of DM	−0.162	0.173	0.877	0.349	0.850	0.606 to 1.194
Age of DM diagnosis (years)			6.126	0.047		
<50	–	–	–	–	1	–
50–60	−0.092	0.216	0.183	0.669	0.912	0.597 to 1.393
≥60	−0.518	0.229	5.124	0.024	0.596	0.381 to 0.933
Smoking status			4.658	0.097		
Non-smoking	–	–	–	–	1	–
Light and moderate smoking	0.097	0.252	−0.149	0.700	1.102	0.673 to 1.806
Heavy smoking	0.509	0.251	4.104	0.043	1.664	1.017 to 2.724
Constant	−1.407	0.574	6.016	0.014	0.245	

BMI, body mass index; DM, diabetes mellitus; DR, diabetic retinopathy; HbA1c, haemoglobin A1c.

before the analysis was conducted. There was no direct patient or public involvement.

RESULTS

Characteristics of the study population

In this survey, 952 patients entered the study initially and 5 were excluded because their fundus could not be seen clearly. Finally, a total of 947 patients were enrolled in the study. Their average age was 53.2±11.6 years. The average HbA1c level was 9.53%±2.13%. The average BMI of the patients was 27.5±4.3 kg/m^2. A total of 430 patients had a history of smoking. The average smoking age was 27.8±12.2 years (2–60 years). They smoked 21.8±12.3 cigarettes per day. Baseline characteristics are shown in table 1.

Comparison of clinical data between the DR and NDR groups

A total of 755 patients (79.7%) were in the NDR group, and 192 patients were in the DR group. Among the

Table 4 Comparison of clinical data between patients (BMI ≥28 vs <28 k g/m^2)

Items		BMI ≥28 kg/m^2 (n=379)	BMI <28 kg/m^2 (n=573)	t/χ^2	P value
Sex, n (%)	Male	230 (60.7)	338 (59.0)	0.273*	0.637
	Female	149 (39.3.8)	235 (41.0)		
Age (years)		50.4±12.4	55.2±10.5	−6.184†	<0.001
Family history of DM, n (%)	No	141 (37.2)	228 (39.8)	0.643*	0.455
	Yes	238 (62.8)	345 (60.2)		
Drinking history, n (%)	No	305 (80.5)	452 (78.9)	0.567*	0.305
	Yes	74 (19.5)	121 (21.1)		
Hypertension‡, n (%)	No	148 (40.1)	284 (50.4)	9.419*	0.002
	Yes	221 (59.9)	280 (49.6)		
HbA1c (%)		9.38±2.10	9.63±2.30	−1.744†	0.082
Smoking history, n (%)	No	217 (57.3)	303 (52.9)	1.763†	0.206
	Yes	162 (42.7)	270 (47.1)		

There was no statistically significant difference if p>0.05.
*χ^2 test.
†Student's t-test.
‡19 cases of patients with missing data.
BMI, body mass index; DM, diabetes mellitus; HbA1C, hemoglobin A1c.

Table 5 The incidence of DR in patients with different smoking statuses

Items		Non-smoking, n (%)	Light and moderate smoking, n (%)	Heavy smoking, n (%)	χ^2	P value
BMI (kg/m^2)	≥28	27 (12.4)	11 (12.1)	20 (28.2)	11.163	0.004
	<28	66 (22.0)	31 (25.6)	37 (25.2)	0.901	0.637
Age (years)	<50	37 (21.8)	15 (13.8)	10 (33.3)	6.300	0.043
	≥50,<60	23 (14.6)	17 (35.4)	32 (29.4)	13.080	0.001
	≥60	33 (17.5)	10 (18.2)	15 (19.0)	0.090	0.956

BMI, body mass index; DR, diabetic retinopathy.

patients in the DR group, there were 12 patients with PDR. The comparison of clinical data between the DR and NDR groups is shown in table 2. There were no statistically significant differences between the two groups in sex, age, hypertension, family history of diabetes, drinking history and HbA1c. The BMI was significantly higher in NDR patients (27.7±4.2 vs 26.7±4.4, p=0.004). Smoking status was different between the two groups (χ^2=6.350, p=0.042).

The occurrence of DR was identified as the dependent variable, and the related risk factors were listed as independent variables. Both of the variables were progressed through multivariate logistic regression analysis; age, BMI and smoking status were adjusted, as shown in table 3. Patients with BMI ≥28 kg/m^2 were less likely to have DR in patients with newly diagnosed diabetes (OR=0.592, p=0.004). The age of DM diagnosis was also statistically significant in the regression analysis (p=0.047). The incidence of DR in patients over 60 years of age who were diagnosed with diabetes was significantly lower than that in patients under 50 years of age (OR=0.596, p=0.024). The incidence of DR in severe smokers was significantly higher than that in non-smokers (OR=1.664, p=0.043).

Did obesity have a protective effect on DR?

Our study compared the age, HbA1c, smoking and drinking history, family history of DM and complications between the obese and non-obese patients, as shown in table 4 (BMI ≥28 vs <28 kg/m^2). There was no statistically significant difference between the two groups in sex, family history of DM, drinking history, smoking history and HbA1c. The age of obese patients with diabetes was significantly lower than that of non-obese patients (50.4±12.4 vs 55.2±10.5, t=−6.184, p<0.001). Because the onset of T2DM was insidious, patients might have a long history before diagnosis.[3] BMI could be a possible confounding variable.

After adjustment for BMI and age, DR-related factors were further analysed. First, the participants were divided into two groups according to whether the BMI was ≥28 kg/m^2. The incidence of DR in patients with different smoking statuses was compared (table 5). The incidence of DR in heavy smoking patients was significantly higher in obese patients. There was no significant difference in the incidence of DR with different smoking statuses among patients over 60 years (table 5). Then after adjustment for age, multiple logistic regression analysis was used to analyse the related factors of DR (table 6). When BMI was ≥28 kg/m^2, heavy smoking was significantly associated with DR (OR=2.219, p=0.049), and there was a negative correlation between DR and the age of diagnosis of diabetes at ≥60 years (OR=0.289, p=0.009).

DISCUSSION

Summary of results

In our study, among the patients newly diagnosed with T2DM, 20.3% presented with DR. After analysing the related factors of DR, the present study found that obese patients may have a lower incidence of DR (OR=0.592, p=0.004). Many researchers have shown that duration of DM, blood glucose, blood pressure and blood lipids are important risk factors for DR.[16–18] The duration is the most important factor.[19] The subjects of the present study were all patients with newly diagnosed T2DM. Our study showed that DR was related to BMI, smoking status and age of DM diagnosis. To the best of our knowledge, the present study is the first that was designed to investigate the correlation between the smoking level and DR in patients with newly diagnosed T2DM. The results of the study suggested that heavy smoking was associated with DR in obese (BMI ≥28 kg/m^2) patients with newly diagnosed T2DM (OR=2.219, p=0.049), and there was a negative correlation between DR and the age of diagnosis of diabetes ≥60 years (OR=0.289, p=0.009). Those correlations did not exist in non-obese (BMI <28 kg/m^2) patients.

The relationship between BMI and DR

In our study, DR was negatively correlated to BMI. This was not consistent with other research results. Grey *et al* followed up with 14 657 patients with diabetes for an average of 6.68 years and found that increased risk of DR was associated with higher BMI.[20] It has also been reported that BMI was not correlated or even negatively correlated with DR.[21] The subjects in our study had newly diagnosed T2DM. The average age of patients with newly diagnosed T2DM with obesity (BMI ≥28 kg/m^2) was 50.4±12.4 years, whereas that of patients without obesity was 55.2±10.5 years. The former was significantly lower than the latter

Table 6 Logistic regression analysis of related factors for DR (BMI <28 kg/m^2; ≥28 kg/m^2)

	Factors	B	SE	Wald χ^2	P value	OR	95% CI
BMI <28 kg/m^2	Sex	0.168	0.290	0.334	0.563	1.183	0.670 to 2.089
	Hypertension	0.138	0.213	0.421	0.517	1.148	0.756 to 1.744
	Drinking history	−0.015	0.279	0.003	0.958	0.986	0.571 to 1.701
	HbA1c	0.001	0.045	0.000	0.9983	1.001	0.917 to 1.093
	Family history of DM	−0.406	0.208	3.815	0.051	0.666	0.443 to 1.001
	Age (years)			1.535	0.464		
	<50	–	–	–	–	1	–
	50–60	0.071	0.279	0.065	0.799	1.074	0.621 to 1.856
	≥60	−0.221	0.281	0.621	0.431	0.801	0.462 to 1.390
	Smoking status			1.595	0.450		
	Non-smoking	–	–	–	–	1	–
	Light and moderate smoking	0.380	0.328	1.345	0.246	1.463	0.769 to 2.781
	Heavy smoking	0.342	0.321	1.136	0.286	1.408	0.751 to 2.640
BMI ≥28 kg/m^2	Sex	0.040	0.392	0.010	0.919	1.040	0.483 to 2.242
	Hypertension	0.400	0.318	1.578	0.209	1.492	0.799 to 2.784
	Drinking history	0.593	0.384	2.378	0.123	1.809	0.852 to 3.842
	HbA1c	0.000	0.071	0.000	0.995	1.000	0.869 to 1.150
	Family history of DM	0.398	0.340	1.374	0.241	1.489	0.765 to 2.898
	Age (years)			7.195	0.027		
	<50	–	–	–	–	1	–
	50–60	−0.149	0.358	0.173	0.678	0.862	0.427 to 1.739
	≥60	−1.241	0.474	6.838	0.009	0.289	0.114 to 0.733
	Smoking status			6.920	0.031		
	Non-smoking	–	–	–	–	1	–
	Light and moderate smoking	−0.330	0.435	0.573	0.449	0.719	0.306 to 1.688
	Heavy smoking	0.797	0.404	3.884	0.049	2.219	1.004 to 4.903

BMI, body mass index; DM, diabetes mellitus; DR, diabetic retinopathy; HbA1c, haemoglobin A1c.

(t=−6.184, p<0.001). As the onset of T2DM is insidious, patients may have had a long history before diagnosis.[3] Based on the usual clinical experience and their different diagnostic ages, our study suggested that the diagnostic age of patients with T2DM with obesity might be closer to the real age of onset. Perhaps because non-obese patients might be confused with more complex diabetic course factors, we did not find any factors in the analysis of the related factors of DR in these patients. In conclusion, we do not think that a high BMI is a protective related factor for DR. It is very likely that there are confounding factors, such as an unobserved course of T2DM.

The relationship between smoking and DR

Cigarette smoking is a well-known risk factor for many chronic diseases, including cardiovascular diseases and various malignancies.[6] Many researchers have reported the negative effects of smoking on DM.[22 23] A 14-year prospective cohort study in South Korea showed that the risk of DM among men and women who smoked 20 or more cigarettes a day was 1.55 times higher than that in non-smokers.[7] Cigarette smoking is independently associated with the incidence of T2DM.[24] Although the mechanisms involved are not clear yet. Smoking is associated with insulin resistance, inflammation and dyslipidaemia.[25 26] When BMI was ≥28 kg/m^2, we found that the incidence of DR was 12.4% in non-smokers, 12.1% in light and moderate smokers and 28.2% in heavy smokers (χ^2=11.163, p=0.004). Some studies have reported that no association was found between smoking and DR in patients with T2DM.[27 28] Smoking cessation is one of the important targets for diabetes control and the prevention of chronic diabetes complications.[29 30]

Studies have shown that cigarette smoking impairs nitric oxide-mediated endothelial function via increased generation of superoxide anions, which may increase the risk of DR in patients with diabetes and could cause eye tissue ischaemia, eye tissue hypoxia, retinal arteriosclerosis and a decrease in choroidal blood flow, eventually leading to retinal ischaemia.[30 31] When BMI was ≥28 kg/m^2, the present study showed that the incidence of DR was

28.2% in heavy smokers. Heavy smoking was significantly associated with DR. Smoking may aggravate retinopathy damage by increasing arteriosclerosis.[32] DR remains the leading cause of acquired blindness in working-age adults.[4] Although cutting-edge research in the field has identified many molecular, functional and structural abnormalities, the exact molecular mechanism of this devastating disease remains obscure.[33] A diabetic environment drives the dysfunction of the power generator of the cell and disturbs the homeostasis of the mitochondrial dynamic. Mitochondria seem to have a significant role in the development of DR, and unravelling the mechanism responsible for their damage as well as the role of epigenetic modifications in mitochondrial homeostasis should identify novel therapeutic targets.[33] Further research is needed to determine whether smoking affects mitochondrial DNA function.

In the present study, DR was found in 20.3% of patients with newly diagnosed T2DM. This was consistent with other findings.[3] The study suggested that smoking may be an important related factor for the occurrence of DR in patients with newly diagnosed diabetes. Tyrberg *et al* investigated 794 patients diagnosed with diabetes in 1987–1988 and found that smoking history could increase the risk of DR during 9–17 years after diagnosis.[34] Because smoking behaviour occurred before the diagnosis of T2DM in this study, heavy smoking is very likely to be a risk factor for DR.

When BMI was ≥28 kg/m^2, there was a negative correlation between DR and the age of diagnosis of diabetes ≥60 years (OR=0.289, p=0.009). Wong *et al* investigated >1400 patients with T2DM and found that the risk of DR in young patients was significantly higher than that in old patients.[35] After adjusting for factors such as the course of diabetes, the risk of DR was increased two times in those with T2DM who were <45 years.[35] Our report agrees with other studies. Age at onset of diabetes was strongly associated with an increasing number of complications.[36] In other regions, studies that have looked at the age of onset of diabetes have found that early onset diabetes increases disease severity. Genetic determinants of diabetes are likely to be more common in patients with early onset of diabetes.[37] This observation suggests that patients with early onset of diabetes have a more aggressive disease and are prone to develop more complications at an earlier age.[38] Delaying the age of diabetes might prevent the occurrence of DR.

Limitations of the study

The study was a single-centre cross-sectional study. The results only showed a correlation between smoking and DR. Prospective cohort studies are needed to confirm whether there is a causal relationship between smoking and DR in patients with newly diagnosed T2DM. Because of the large number of patients with newly diagnosed T2DM, we have set relatively wide exclusion criteria for the population, which may affect external validity. Although our department is responsible for the first diagnosis and identification of diabetes in Tianjin, it is still unable to achieve a timely diagnosis for all those patients who newly develop diabetes. Because the patients are all from Tianjin, China, the conclusion has regional limitations.

CONCLUSIONS

The study found that heavy smoking and the age of T2DM diagnosis were related factors for the occurrence of DR in newly diagnosed patients when BMI was ≥28 kg/m^2. Although the subjects were all newly diagnosed patients, it is known that the onset of T2DM is relatively insidious. It is of great importance for people in populations at high risk of diabetes mellitus to quit smoking. Delaying the age of diabetes may prevent the occurrence of DR. Therefore, long-term cohort studies are needed to elucidate the correlation.

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