



Is there a relationship between body mass index and diabetic retinopathy in type II diabetic patients? A cross sectional study

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Abstract

Background Type 2 diabetes mellitus (T2DM) is one of the most important leading causes of disability, premature mortality and Diabetic Retinopathy (DR) that is one of the diabetes-related complications in diabetic patients and the most common cause of vision loss in diabetic patients. The aim of the study was to evaluate the association between DR and body mass index (BMI) in those patients with T2DM.

Methods This was a central-based, cross-sectional study on 518 diabetic patients. Their medical history and the laboratory data were collected. All the patients received examination of diabetic retinopathy by professional ophthalmologist. Based on their optic fundi findings, they were classified into five groups: No retinopathy, Mild Non-proliferative Diabetic Retinopathy (NPDR), Moderate NPDR, Severe NPDR, Proliferative diabetic retinopathy (PDR). To analysis data SPSS v18 software used. Frequency, percent, mean and standard deviation were used for population description. t test, spearman correlation, partial correlation, analysis of variance (ANOVA) and Chi-square test (χ^2) were used for analytic analysis. Multivariate logistic regression was used to estimate the odds ratio.

Results 518 patients with T2DM 198 male (38%), 320 female (62%) included in this study. The mean age of patients was 61.02 ± 10.18 years. The mean age at onset was $49.06 + 10.52$ years and the mean duration of diabetes was 12.09 ± 7.81 years. There was a strong relationship between duration of diabetes and DR ($P=0.001$). There were strong significant association between the development of DR and Insulin therapy (OR = 5.975). Correlation analysis between Retinopathy and BMI showed that BMI had inverse relationship with DR when BMI considered as a continuous variable (p -value = 0.009 and correlation coefficient = -0.467).

Conclusion BMI in diabetic patient is one of the most important clinical parameter for their health and disease progression. We conclude that BMI had inverse relationship with DR when BMI considered as a continuous variable.

Keywords Diabetic retinopathy · Body mass index · Type 2 diabetes mellitus

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Background

Type 2 diabetes mellitus (T2DM) is one of the most important leading causes of disability, quality of life reduction and premature mortality in the world [1, 2]. The number of people with T2DM is increasing rapidly worldwide [3, 4]. Based on the last update by the International Diabetes Federation (IDF) one of the regions that including emerging diabetes hotspot is Middle East [5]. On the other hand Diabetic Retinopathy (DR) is one of the diabetes-related complications in diabetic patients and the most common cause of vision loss in diabetic patients [6]. Some degree of diabetes-related eye disorder or retinopathy develops in one third of patients with diabetes mellitus (DM) and also in nearly 80% of patients with a history of over 20 years of diabetes [7]. In Iran, the most recent study showed that 34.6% of the diabetic patients already have diabetic retinopathy [8]. Some risk factors such as poor glycemic control, high blood pressure and long diabetes duration are strongly associated with diabetic retinopathy [9–11]. Studies demonstrated diabetes duration as an important risk factor for DR [12–14] and some studies have highlighted the effect of blood pressure and blood lipid level [14–17]. Up to now, the association between diabetic retinopathy and Body Mass Index (BMI) is completely unclear. Some studies have demonstrated direct relationship between obesity and DR [14, 18–21] whereas others have identified BMI as protective factor for diabetic retinopathy [14, 22–25]. In view of the increasing prevalence of DM, so will the number of DR throughout most of the world, the purpose of this paper was to investigate the association and quantify the relationship between DR and BMI in adult patients with DM.

Methods

By using similar study done by Kastelan [26], with two mean compare formula, using BMI mean and standard deviation for retinopathy group as 26.96 ± 2.7 and for control group 26.46 ± 3 , 0.05 error and 80% study power a total of 518 consecutive central-based patients with T2DM were recruited in this prospective cross-sectional study. Patients included in this study from Yazd Diabetes Research Center in year 2014. Inclusion criteria were patients older than 30 years of age, with T2DM on oral antidiabetic or insulin therapy. Exclusion criteria were pregnancy or lactation, type 1 diabetes, gestational diabetes, HbA1c <5 or $>11\%$, newly discovered uncontrolled DM.

This analytic cross-sectional study was performed in the Yazd Diabetes research center. The local institutional research ethics committee approved the study protocol, and all the patients included in the study received both written and oral information concerning the study and signed a written informed consent. Information concerning the age, gender,

duration of diabetes, HbA1c, medication, previous history of stroke or myocardial infarction (MI) and cigarette smoking status was obtained from the patients' medical records.

Blood pressure (BP) was measured by standard methods using a sphygmomanometer with the patient in a sitting position. Three measurements were made in all subjects at 5-min intervals, and the average of the second and third measurements was used in the analysis. Hypertension was defined as a systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg or taking antihypertensive medications.

Anthropometric measurements including weight and height measurements were obtained using standardized techniques. Height was measured in centimeters using a wall-mounted measuring tape to the nearest centimeter [25]. Subjects were requested to stand upright without shoes with their back against the wall, heels together and eyes directed forward. Weight was measured in kilograms using a digital scale that was kept on a firm horizontal surface [27]. Subjects were asked to wear light clothing and weight was recorded to the nearest 0.5 kg. BMI was calculated as weight in kilograms divided by height in meters squared (Kg/m^2). The guideline of the United States National Institute of Health (NIH) use the following BMI classification: BMI < 18.5 kg/m^2 , underweight; BMI 18.5 to 24.9 kg/m^2 , normal weight; BMI 25.0–29.9 kg/m^2 , overweight; BMI 30–34.9 kg/m^2 , obesity class I; BMI 35–39.9 kg/m^2 , obesity class II; and BMI ≥ 40.0 kg/m^2 , obesity class III [28].

Ophthalmologic examination including visual acuity (by means of snellen charts), intraocular pressure (using Applanation Tonometry), funduscopy (utilizing slit lamp and non-contact lenses) and indirect ophthalmoscopy were also completed. If required, fluorescein angiography was ordered. All the relevant examinations were completed by an ophthalmologist. Based on their optic fundi findings, they were classified into five groups: No retinopathy, Mild NPDR, Moderate NPDR, Severe NPDR, PDR [29].

Availability of data and material Please contact corresponding author for data requests.

Statistical analyses

Data were analyzed using the SPSS version 20.0 for windows computer software package (SPSS Inc., Chicago, IL, USA). Frequency, percent, mean and standard deviation were used for population description. The normal distributions of data were checked and t test, spearman correlation, analysis of variance (ANOVA) and Chi-square test (χ^2) were used for analytic analysis. Multivariate logistic regression was used to estimate the odds ratio with a 95% confidence interval

Table 1 Basic characteristics of type II diabetic patients (총 = 518) divided into five groups according to diabetic retinopathy status

Variables	Group1 (n = 306)	Group2 (n = 38)	Group3 (n = 58)	Group4 (n = 30)	Group5 (n = 86)	P value*
Age, y	59.35 ± 10.46	62.66 ± 9.45	63.98 ± 10.06	63.8 ± 8.47	63.27 ± 8.86	0.001
Male, n (%)	118(59.9)	9(4.6)	23(11.7)	11(5.6)	36(18.3)	0.39
Diabetes Duration, n (%)	8.85 ± 6.17	15.96 ± 7.14	16.96 ± 7.39	13.73 ± 6.07	18.28 ± 8.03	0.001
<5 years	116 (92.8)	0 (0)	2 (1.6)	2 (1.6)	5 (4)	
5–10 years	56 (67.5)	7 (8.4)	7(8.4)	6(7.2)	7 (8.4)	0.001
≥10 years	119 (41.9)	29 (10.2)	44 (15.5)	22 (7.7)	70 (24.6)	
Insulin use, n (%)	64(39.3)	14(8.6)	23(14.1)	16(9.8)	46(28.2)	0.001
BMI, (kg/m ²)	27.97 ± 4.47	28.05 ± 4.29	27.92 ± 3.24	27.7 ± 4.02	27.68 ± 4.75	0.99
Patient weight, (kg)	73.98 ± 13.94	72.6 ± 11.67	72.92 ± 9.76	7.12 ± 10.13	72.35 ± 13.63	0.72
Patient height, (cm)	162.06 ± 10.14	159.64 ± 7.78	161.56 ± 9.3	160.3 ± 7.07	161.78 ± 9.8	0.62
	129.4 ± 16.56	123.43 ± 14.67	135.29 ± 16.79	136.55 ± 17.98	139.43 ± 22.12	0.001
Diastolic blood pressure, (mmHg)	77.15 ± 7.82	78.29 ± 8.99	77.12 ± 7.1	75 ± 6.68	78.72 ± 9.03	0.25
Systemic hypertension, n (%)	131(58.5)	16(7.1)	23(10.3)	11(5.6)	36(18.3)	0.11

Data presented are means (SD) or number (%), as appropriate

Group 1: no retinopathy, Group 2: mild non-proliferative diabetic retinopathy; Group 3: moderate non-proliferative diabetic retinopathy, Group 4: severe non-proliferative diabetic retinopathy Group 5: proliferative diabetic retinopathy

*P-value for linear trend in mean characteristics across quartiles based on 2 or ANOVA. Bold denotes a significant trend

(CI) for the risk of DR. Statistical significance was accepted at the $p < 0.05$ level. Data are expressed as mean ± SD values when referred to in the text.

Results

This study is a central-based, cross-sectional study that included 518 patients with T2DM .most of patients were female 320 (62%) according the Yazd diabetes research center gender distribution of patients (60%/40%). The mean age of patients was 61.02 ± 10.18 years. The mean age at onset was 49.06 + 10.52 years and the mean duration of diabetes was 12.09 ± 7.81 years. About 45.3% of the patients were treated with insulin and 54.7% of them without insulin. In addition 9.7% of patients have macular edema and 66.1% of patients are hypertensive. Table 1 presents descriptive statistics of basic characteristics of T2DM patients divided into the following five groups: group I (no retinopathy; 총 = 306), group II (mild NPDR; 총 = 38), group III (moderate NPDR; 총 = 58), group IV (severe NPDR; 총 = 30) and group V (PDR; n = 86). There was difference in age ($P = 0.001$) and gender ($P = 0.358$) between the investigated groups. Figure 1 shows the retinal screening results. Overall frequency of any form of retinopathy was present in 41%.The frequency of NPDR was 24.5% and the frequency of PDR was 16.5%. The frequency of mild, moderate, and severe NPDR was 7.4%, 11.3%, and 5.8%, respectively. There was a strong relationship between duration of diabetes and DR ($P = 0.001$). Diabetes duration was longer in groups with moderate NPDR (83%) and PDR (85.4%) (Fig. 2). However, there were no significant difference in

BMI between the five groups (총 = 0.99). Also between DR and patients weight was not observed ($P = 0.72$). It should be noted that none of these patients was underweight (BMI lower than 18.5). Compared with normal weight and obese patients, overweight participants were more likely to had NPDR but there were no significant relation between them ($P = 0.42$). Correlation analysis between retinopathy and BMI showed that BMI had inverse relationship with DR when BMI considered as a continuous variable (p -value = 0.009 and spearman bivariate correlation coefficient = -0.467). Due to significant relation between age of insulin usage and SBP, with minimal correlation coefficient; we control impaction of these two parameters and again correlation analysis between retinopathy and BMI was showed a significant relation ($p = 0.038$ and $r = -0.115$) As shown in Fig. 3, BMI is higher among diabetic patients with mild NPDR. Compared with NDR and NPDR participants, PDR participants were more likely to had longer diabetes duration, previous MI, higher SBP, higher mean of HbA1c, and poor glycemic control (Table 2). Demographic

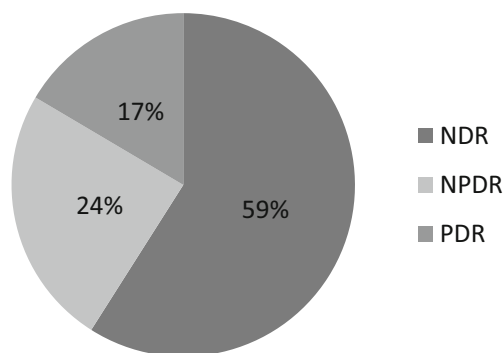
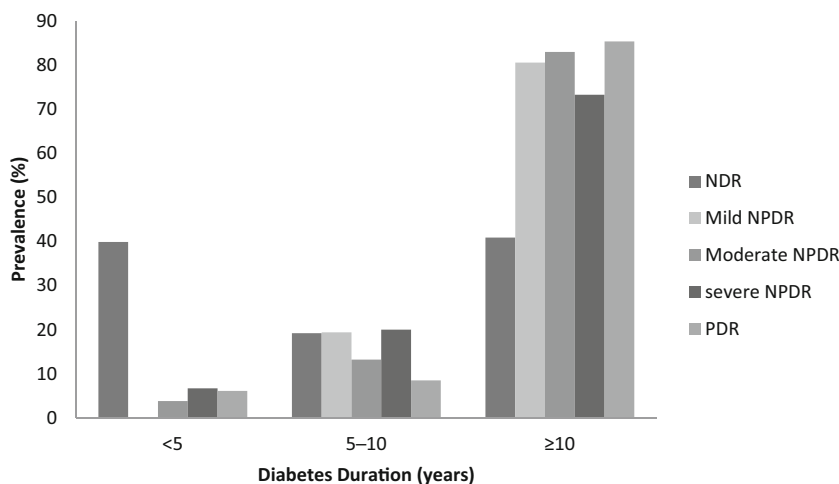


Fig. 1 Prevalence of DR among 518 T2DM patients

Fig. 2 Prevalence of any stage of DR for the Diabetes Duration



data and metabolic profile of patients from NDR to PDR were shown in Table 3. We observed a significant deterioration of HbA1c ($P = 0.001$), microalbuminuria ($\chi^2 = 0.001$), and a significant increase in triglycerides (0.016) with the progression of retinopathy. The correlations between DR and total cholesterol, low-density lipoprotein (LDL) and high-density lipoprotein (HDL) were not significant. In addition, the correlation between DR and stroke was not positive ($\chi^2 = 0.124$). There was no correlation between BMI with triglycerides ($\chi^2 = 0.82$) and total cholesterol ($P = 0.36$), HDL ($P = 0.59$) and LDL cholesterol levels ($P = 0.38$).

Diabetes duration, insulin therapy, weight, SBP, HbA1c and previous history of MI were entered into a logistic regression model. Results of Odd’s ratio obtained by multivariate logistic regression analysis are shown in Table 4. There were strong significant association between the development of DR and Insulin therapy (OR = 5.975) and SBP (OR = 1.057). But HbA1c was negatively associated with DR. Weight, presence of previous MI and diabetes duration were not associated with DR.

Discussion

DR is one of the microvascular complications of DM and is the most frequent causes of new-onset blindness between adults (31). In Iran, DR is among the leading causes of visual impairment after cataract, amblyopia, vitreo-retinal disease and corneal problems (32). The global prevalence of DR is 34.6% (33) and in Iran is 23.6% (9). In Yazd, a city in center of

Iran that has high rates of DM (34), DR prevalence is 39.3% (35). The present study showed that the frequency of DR in Yazd diabetes research center- 2014 was 41% among patients with T2DM. (consisting of 24.5% of NPDR and 16.5% PDR).

On the other hand, overweight and obesity is increasing worldwide in recent years [30] and its prevalence among Iranian children and adults increased during previous decade [31]. High BMI is an important risk factor for most of non-communicable disease such as DM, however its effect on DR is not defined precisely. Some of earlier studies identified BMI as predisposing factor for DR [32–34] and some studies noted overweight and obesity is protective for DR in Asian population [35, 36]. Recently, Lu and et al. [37] found U-shaped association between BMI and DR in Chinese type 2 diabetic patients. In our study, BMI had inverse relationship with DR when BMI considered as a continuous variable. Moreover, overweight patients in comparison with normal-weight and obese patients had the highest rate of NPDR, but different situation seen for PDR. PDR prevalence was minimal in overweight diabetics, and lower than normal-weight and obese patients.

Similar association between BMI and mortality in T2DM patients has been reported [38]. The exact mechanism of inverse relationship between BMI and DR is not established yet. It may be secondary to poor glycemic control and weight loss in some patients that put them in normal-weight group. However, subgroup analysis ruled-out this hypothesis because patients with poor controlled diabetes were more prevalent in groups with higher BMI and BMI was not correlated significantly with diabetes duration. We can use a new

Fig. 3 BMI of T2DM ($n = 518$) divided into five groups according to DR status

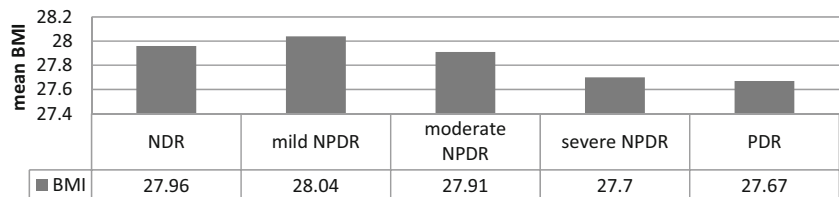


Table 2 Comparisons between patients with NDR and DR, patients with NPDR and PDR

Variables	NDR (n = 306)	NPDR (n = 126)	PDR (n = 86)	p-value*
Age, y	59.35 ± 10.46	63.5 ± 9.47	63.27 ± 8.86	0.001
Male, n (%)	118 (59.9)	43 (21.8)	36 (18.3)	0.46
BMI, (kg/m ²)	27.97 ± 4.47	27.9 ± 3.74	27.68 ± 4.75	0.88
Patient weight (kg)	73.98 ± 13.94	72.38 ± 10.39	72.35 ± 13.63	0.42
Patient height (cm)	162.06 ± 10.14	160.68 ± 8.34	161.78 ± 9.8	0.42
Systemic hypertension, n (%) ^{htn}	131(58.5)	53(23.7)	40(17.9)	0.04
Systolic blood pressure, (mmHg)	129.4 ± 16.56	134.74 ± 16.43	139.43 ± 22.12	0.001
Diastolic blood pressure, (mmHg)	77.15 ± 7.82	76.94 ± 7.65	78.72 ± 9.03	0.27
HbA1c level (%)	8.1 ± 1.47	8.88 ± 1.59	8.91 ± 1.64	0.001
Poor glycemic control (%)** ^{hba1c > 7}	64(83.1)	8(10.4)	5(6.5)	0.001
Previous MI, n (%)	43(47.3)	26(28.6)	22(24.2)	0.002
Previous stroke, n (%)	10(45.5)	7(31.8)	2(22.7)	0.28
Total cholesterol, (mmol/L)	182.49 ± 42.58	180.8 ± 41.94	191.62 ± 73.24	0.42
LDL cholesterol, (mmol/L)	106.03 ± 36.8	106.3 ± 31.63	101.48 ± 40.39	0.78
HDL cholesterol, (mmol/L)	44.32 ± 12.24	42.89 ± 14.18	42.49 ± 10.42	0.61
Diabetes duration, n (%)	8.85 ± 6.17	15.84 ± 7.07	18.28 ± 8.03	0.001
<5 years	116 (92.8)	4 (3.2)	5 (4)	
5–10 years	56 (67.5)	20 (24.1)	7 (8.4)	0.001
≥10 years	119 (41.9)	95 (33.5)	70 (24.6)	

Data presented are means (SD) or number (%), as appropriate

NDR, no retinopathy, NPDR, non-proliferative diabetic retinopathy; Group 3: proliferative diabetic retinopathy

*P-value for linear trend in mean characteristics across quartiles based on 2 or ANOVA. Bold denotes a significant trend

**Poor glycemic control defines as HbA1c up to 7

hypothesis, high BMI can be a protective factor for DR. Regression analysis in this study was shown the association between SBP with DR, which was consistent with the results from Bin-Bin He et al. study [39]. Moreover, subgroup analyses revealed that there was no significant association between BMI and DR stratified by gender, glycemic control and

microalbuminuria. The inverse relationship between BMI and DR was significant only in insulin users-subgroup that supports the probability of protective effect of higher BMI for DR in more severe cases of T2DM.

Diabetes duration is a very important risk factor for DR. In this study, 40.9% of patients with NDR had more than 10 years

Table 3 Metabolic and clinical parameters of type 2 diabetic patients (n = 518) divided into five groups according to diabetic retinopathy status

Variables	Group1 (n = 306)	Group2 (n = 38)	Group3 (n = 58)	Group4 (n = 30)	Group5 (n = 86)	P value
HbA1c level, (%)*	8.1 ± 1.47	8.79 ± 1.61	8.77 ± 1.5	9.21 ± 1.78	8.91 ± 1.64	0.001
Poor glycemic control, n (%)**	170(59.6)	21(7.4)	34(11.9)	16(5.6)	44(15.4)	0.005
Previous MI, n (%)	43(47.3)	8(8.8)	13(14.3)	5(5.5)	22(24.2)	0.01
Previous stroke, n (%)	10(4.5)	3(13.6)	1(4.5)	3(13.6)	5(22.7)	0.18
Total cholesterol, (mmol/L)	182.49 ± 42.58	188.67 ± 35.43	174.08 ± 42.06	184.84 ± 48.11	191.62 ± 73.24	0.53
LDL cholesterol, (mmol/L)	106.03 ± 36.8	102.13 ± 23.55	103.19 ± 30.13	120.09 ± 43.38	101.48 ± 40.39	0.65
HDL cholesterol, (mmol/L)	44.32 ± 12.24	45.71 ± 20.54	43.24 ± 10.43	37.73 ± 8.16	42.49 ± 10.42	0.44
Triglyceride, (mmol/L)tg	180.68 ± 102.45	181.24 ± 74.91	136.44 ± 65.01	179.89 ± 72.16	228.87 ± 212.77	0.02
Microalbuminuria, (mg/g)ma	19.18 ± 33.74	60.11 ± 97.58	59.99 ± 88.23	68 ± 81.87	125.02 ± 145.23	0.001

Data presented are means (SD) or number (%), as appropriate

Group 1: no retinopathy, Group 2: mild non-proliferative diabetic retinopathy; Group 3: moderate non-proliferative diabetic retinopathy, Group 4: severe non-proliferative diabetic retinopathy Group 5: proliferative diabetic retinopathy

*P-value for linear trend in mean characteristics across quartiles based on 2 or ANOVA. Bold denotes a significant trend

**Poor glycemic control defines as HbA1c up to 7

Table 4 Multiple logistic regressions of diabetic retinopathy

Items	B	S.E	Wald	Sig.	OR
Diabetes duration	0.15	0.03	30.49	0.001	1.17
Insulin therapy	0.81	0.36	5.02	0.02	2.24
Weight	−0.011	0.015	0.61	0.43	0.99
SBP	0.011	0.01	1.18	0.28	0.011
MI	0.16	0.42	0.14	0.71	1.17
HbA1c	0.38	0.12	9.53	0.002	1.46

of diabetes duration but in NPDR and PDR group, diabetes duration more than 10 years was 79.8% and 85.4%, respectively.

In present study, DR was correlated with systolic hypertension (p value <0.001), previous MI, age of lower than 40 years at diabetes diagnosis (p value = 0.004) and Microalbuminuria that is in line with other studies [12–17, 40].

In our study, HbA1c had a negative correlation with DR, in David Rooney et al., study they also showed that there was a negative correlation between HbA1c and DR because HbA1c shows the poor control diabetes in patient and it cause eye problems in patients [35].

Several limitations should be noted. Firstly, is that our method for diagnosing and grading of DR was based on physical examination and not retinal photographs. Secondly, the study design was cross-sectional and these kinds of studies cannot establish causal relationship between variables. Thirdly, the fact that it was a single-center study, which may reduce the generalizability of this study. Finally, because of the absence of an underweight group, we are unable to compare the DR prevalence between this group with another.

Conclusions

BMI in diabetic patient is one of the most important clinical parameter for their health and disease progression. We conclude that BMI had inverse relationship with DR when BMI considered as a continuous variable. Patients with T2DM should be careful about their BMI.

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Authors' contributions All authors contribute in this study equally.

Compliance with ethical standards

Ethics approval and consent to participate This analytic cross-sectional study was performed in the Yazd Diabetes research center.

Consent for publication All the authors consent for publication.

Competing interests The authors declare that they have no conflict of interest.

Human and animal rights disclosure All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 [5].

Informed consent disclosure Informed consent was obtained from all patients for being included in the study.

Abbreviations DR, diabetic retinopathy; T2DM, type 2 diabetes mellitus; BMI, body mass index; NPDR, Non-proliferative Diabetic Retinopathy; PDR, Proliferative diabetic retinopathy; HbA1c, Glycosylated hemoglobin; DM, diabetes mellitus; IDF, International Diabetes Federation; MI, myocardial infarction; BP, Blood pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; NIH, National Institute of Health; LDL, low-density lipoprotein; HDL, high-density lipoprotein

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