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Association Analysis Between Different Diabetic Family History and Gender with Diagnosed Age of Type 2 Diabetes Mellitus: A Cross-Sectional Study in Tianjin, China

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Abstract

Background: Type 2 diabetes mellitus (T2DM) was previously considered a common disease in middle-aged and older people, but the age of diagnosis of T2DM is advancing every year, and the trend toward a younger age is obvious. Early-onset T2DM is a clinical syndrome caused by genetic and environmental factors. This study aimed to investigate the association between diabetic family history and gender with the diagnosed age of T2DM.

Methods: The newly diagnosed T2DM patients admitted to the diabetes identification center of Tianjin 4th Central Hospital (TJ4thch) from October 2017 to June 2020 were registered. According to whether the diagnosis age is over 40 years old, patients were divided into 2 groups (early-onset T2DM group and late-onset T2DM group). In the study, the T2DM family history was divided into 5 types: (*a*) Father T2DM: father with T2DM, but not the mother; (*b*) Mother T2DM: mother with T2DM, but not the father; (*c*) Both parents with T2DM; (*d*) Another relative(s) (other than the parents) with a history of T2DM; and (e) Without a family history of T2DM. The diagnosed age with different genders and diabetic family history was compared. Multivariate logistic regression analysis was used to investigate the association factors of early-onset T2DM.

Results: A total of 3725 patients completed the survey. There were 589 patients (15.8%) with early-onset T2DM, and 2469 patients (66.3%) had a diabetic family history. The T2DM-diagnosed age in males was lower than in females (51.7 ± 11.2 vs 54.0 ± 10.2, P = .000). The result was also reflected in the different T2DM family histories (with Both parents T2DM, 46.7 ± 11.1 vs 48.5 ± 10.3, *P* = .271; with Father T2DM, 46.8 ± 10.8 vs 49.8 ± 11.3, *P* = .005; with Mother T2DM, 50.4 ± 10.6 vs 52.3 ± 10.2, *P* = .019; with Other T2DM family history, 54.0 ± 10.8 vs 55.7 ± 9.5, *P* = .008; with no T2DM family history, 53.0 ± 11.0 vs 55.9 ± 9.3, *P* = .000). The order of the T2DM-diagnosed age in the different groups was Both parents T2DM (47.5 ± 11.0) and Father T2DM (47.9 ± 11.1) family history < that with Mother T2DM family history (51.1 ± 10.5) < that with Other T2DM family history (54.7 ± 10.3) and no T2DM family history (54.1 ± 10.5). Logistic regression analysis indicated that gender (OR, 1.733; *P* = .000), Father T2DM history (OR, 2.738; *P* = .000), Mother T2DM history (OR, 1.536; *P* = .001), Both parents T2DM (OR, 2.866; *P* = .000) and body mass index (OR, 1.108, *P* = .000) were correlated with early-onset T2DM.

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Conclusion: Patients with early-onset T2DM tend to have a more obvious T2DM family history in China. This survey shows that when a parent has a T2DM family history, especially the father with T2DM, male patients are diagnosed with T2DM earlier. We need more intensive screening for diabetes in children with a family history of diabetes, especially in male children.

Keywords
type 2 diabetes mellitus, early-onset type 2 diabetes mellitus, diabetic family history, gender

What Do We Already Know About This Topic?
T2DM patients have an obvious family genetic background. It is unknown if a correlation between paternal diabetes mellitus, maternal diabetes, and other family histories with the onset age of patients with diabetes in Chinese people.

How does your research contribute to the field?
We investigated the newly diagnosed T2DM patients in our hospital to explore the correlation between different family histories of diabetes, gender, and the diagnosed age of T2DM.

What are your research's implications towards theory, practice, or policy?
We hope to have a more detailed care for the younger generation of diabetes.

Introduction

Type 2 diabetes mellitus (T2DM) has become an important public health problem.[1] In 2017, China had 114.4 million people with T2DM, ranking first globally.[2] T2DM was previously considered a common disease in middle-aged and older people, but the age of diagnosis of T2DM is advancing every year, and the trend toward a younger age is obvious.[3] According to an epidemiological survey in China, the prevalence of pre-diabetes in people younger than 40 years of age in 2013 was significantly higher than that in 2010 (28.8% vs 9.0%), and the prevalence of T2DM in people younger than 40 years of age was 3.2% in 2010, rising to 5.8% in 2013.[4-5] A survey showed that T2DM had also increased significantly in British adolescents.[6] The proportion of T2DM patients diagnosed ≤ 40 years of age reached 24%.[6] Compared with the late-onset T2DM group, adolescents with T2DM have a longer exposure time to hyperglycemia, a higher risk of T2DM-related complications, and a higher risk of cardiovascular disease.[7-8] Compared with late-onset T2DM, the function of the β cell is worse in young people with T2DM.[9] T2DM in young people increases all-cause mortality, CVD mortality, stroke, and ischemic heart disease mortality.[10-14] In diabetic nephropathy, diabetic retinopathy (DR), and peripheral neuropathy, the incidence rate of T2DM in young people is higher than in T1DM.[15] In the observation of newly diagnosed T2DM patients, the age of onset of T2DM is significantly correlated with the occurrence of DR.[16]

At present, T2DM is usually divided into early-onset and late-onset T2DM according to the diagnosed age of 40 years.[3] Sixty percent of early-onset T2DM had one of their parents with diabetes, and 30% had one of their grandparents with diabetes.[1] Family history of diabetes reflects both genetic as well as environmental factors and can lead to better prediction of incidence of type 2 diabetes than only genetic factors and environmental factors alone. Youth with T2DM were more likely to have been exposed to maternal diabetes or obesity in utero than were nondiabetic control youth. After adjusting for offspring age, sex, and race/ethnicity, exposure to maternal diabetes (odds ratio, 5.7) and exposure to maternal obesity (2.8) were independently associated with T2DM.[17] Early-onset T2DM is a clinical syndrome caused by genetic and environmental factors, but its etiology and pathogenesis have not been fully elucidated. In studies on the correlation between sex and early-onset T2DM, the current conclusions are inconsistent.[13,14,18] Many studies[19-20] have shown that the prevalence of T2DM in adult men is higher than in adult women. It is unknown if a correlation between paternal diabetes mellitus, maternal diabetes, and other family histories with the onset age of patients with diabetes in Chinese people. Due to the insidious onset of T2DM, the exact age of onset is not easy to determine. In this study, we investigated the newly diagnosed T2DM patients in Tianjin 4th Central Hospital (TJ4thch) to investigate the association between different family histories of diabetes and diagnosed age of T2DM.

Patients and Methods

This was a single-center cross-sectional study in the TJ4thch. The Metabolic Disease Management Center (MMC) was responsible for the diagnosis and treatment of newly diagnosed T2DM patients. The diabetes-nursing team measured height, weight, and blood pressure, and gathered information about smoking, drinking, disease history, and T2DM family history. Electronic medical records were generated at the same

time. Only one patient could be enrolled per family. Study participants were patients with newly diagnosed T2DM who visited MMC from October 2017 to June 2020. The patient information came from an electronic database of the hospital's diabetes identification center. The information included the patient's name, gender, age, race, contact information, urban/rural household registration, and date of T2DM diagnosis. The clinical study protocol was approved by the Institutional Review Board (IRB) of Tianjin 4th Central Hospital (IRB approval NO.2019-SZXLL068), and all steps were conducted in accordance with the principles of the World Medical Association Declaration of Helsinki (trial registration code: ChiCTR2000036881). Written informed consent was obtained from each patient.

Inclusion Criteria. (*a*) The study enrolled participants newly diagnosed with T2DM within the past three months; (*b*) age ≥ 18 years; (*c*) patients without mental disorders who can communicate independently; and (*d*) patients can accurately describe their family history of diabetes. According to the Chinese guidelines for the prevention and treatment of diabetes, all patients must be diagnosed with an oral glucose tolerance test. The diagnostic criteria during the execution were as follows[21]: (1) fasting plasma glucose ≥ 7.0 mmol/L, fasting was defined as no caloric intake for at least 8 h, or (2) 2-h plasma glucose ≥ 11.1 mmol/L during an OGTT. The test was performed as described by WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water. The hemoglobin A1c (HbA1c) test was not standardized in China, so it could not be used as a diagnostic standard.[22]

Exclusion Criteria. (*a*) Type 1 and other special types of diabetes, gestational diabetes, or diabetes mellitus with pregnancy; (*b*) patients with severe mental illness and unclear consciousness; and (*c*) patients with active tuberculosis and other infectious diseases.

Information about the patients' names, sex, phone numbers, body mass index (BMI), age, smoking history, drinking history, family history of T2DM, 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 meters. Weight was measured using the same scale on an empty stomach at the MMC clinic in the morning and recorded. Smoking status assessment: according to the WHO (1997) smoking survey method, smoking at least one cigarette per day for > 6 months was considered a smoking history.[23] Drinking history: the alcohol consumption of women should not exceed 15 g/day and that of men should not exceed 25 g/day, and should not exceed twice a week.[21] If the above situation was exceeded, the drinking history was considered.

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). All patient identifiers were removed before analysis.

Evaluation of Clinical Variables. In this study, family histories of diabetes include parents, grandparents, maternal grandparents, siblings, and children. Classification of family history of T2DM: according to the prevalence of diabetes in parents and other relatives, the family history of T2DM can be divided into 5 types: (*a*) Father T2DM: Father with T2DM, but not the mother; (*b*) Mother T2DM: Mother with T2DM, but not the father; (*c*) Both parents T2DM: Both parents with T2DM; (*d*) Other family T2DM: Family members other than the parents with T2DM; and (*e*) Without a family history of T2DM. Other family histories of diabetes include grandparents, maternal grandparents, siblings, and children. (2) Diagnostic age of early-onset T2DM: the demarcation line between early-onset and late-onset T2DM is not completely consistent. Recently, several large-scale studies in Asia, such as the JADE project group, defined early-onset T2DM as the diagnosis age < 40 years in the study of "metabolic profile and treatment gap of Asian youth with type 2 diabetes."[3] A study in China on cardiovascular disease risk of early-onset T2DM also takes the age of 40 years as the boundary.[24] In this study, early-onset T2DM was defined as age < 40 years at the time of diagnosis, and late-onset T2DM was defined as age ≥ 40 years. The study did not include pre-diabetes among the subjects and family members.Observation

Indexes. The main observation indices included (*a*) diagnostic age of T2DM patients with a different family history, (*b*) age of diagnosis in male and female T2DM patients, and (*c*) association between early-onset T2DM with gender and different family history of DM.

Statistical Analysis

SPSS 20.0 statistical software package (IBM Corp, Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp) was used for data collection and analysis. GPower software was used to calculate the sample size. 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 such variables' distribution. Mean ± standard deviation was used for statistical descriptions of variables conforming to a normal distribution, median (P50) was used for those not conforming to a normal distribution, and percentage (%) was used to count data. When comparing the age at diagnosis of patients with different family history and gender of diabetes, one-way ANOVA was first adopted, and further comparison between groups was conducted using the Student-Newman-Keuls test. We examined the factors using multivariate logistic regression analysis to evaluate the factors associated with early-onset T2DM and adjust for potential confounding effects. All statistical tests were performed using a bilateral test with alpha = .05.

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

Table 1. The Characteristics of the Study Participants.

Items	All Subjects	Male	Female
N (%)	3725	2288	1437
With smoking history	1670 (44.8%)	1541 (67.4%)	129 (9.0%)
With drinking history	846 (22.7%)	819 (35.85)	27 (1.9%)
With hypertension	2025 (54.4%)	1191 (52.1%)	834 (58.0%)
With CHD history	785 (21.1%)	463 (20.2%)	322 (22.4%)
With cerebral infarction history	411 (11.0%)	292 (12.8%)	119 (8.3%)
With T2DM family history	2469 (66.3%)	1475 (64.5%}	994 (69.2%)
Father T2DM	453 (12.2%)	286 (12.5%)	167 (11.6%)
Mother T2DM	696 (18.7%)	425 (18.6%)	271 (18.9%)
Both parents T2DM	190 (5.1%)	108 (4.7%)	82 (5.7%)
Other T2DM family history	1130 (30.3%)	656 (28.7%)	474 (33.0%)

Note. T2DM = type 2 diabetes mellitus; CHD = coronary heart disease history.

Table 2. Type 2 Diabetes Mellitus Diagnosed Age Comparison of Patients with Different Types of Family History.

	Both Parents T2DM	Father T2DM	Mother T2DM	Other T2DM Family History	No T2DM Family History
N	190	453	696	1130	1256
Diagnosed age	47.5 ± 11.0[a]	47.9 ± 11.1[a]	51.1 ± 10.5[b]	54.7 ± 10.3[c]	54.1 ± 10.5[c]

Note. a, b, and c indicate a statistical difference between different labels using the SNK test (P < .05), but there is no statistical difference in the same label. T2DM = type 2 diabetes mellitus.

obtained from the health records at the institution. The information included the patient's name, gender, age, race, contact information, urban/rural household registration, and date of T2DM diagnosis. All patient identifiers were removed before the analysis was conducted. There was no direct patient or public involvement.

Results

Demographic and Clinical Characteristics of the Study Population

A total of 3725 patients with T2DM participated and completed the survey. All were of Han nationality. 2288 (61.4%) were male. The population with high school education or above was 1938 (52.0%). 2174 (58.4%) were urban population. Their arithmetic mean age was 52.6 ± 10.8 years. The systolic blood pressure (SBP) was 142.4 ± 20.1 mmHg, the diastolic blood pressure (DBP) was 81.7 ± 11.4 mmHg, the waist circumference (WC) was 96.2 ± 10.7 cm, the body weight was 76.1 ± 13.7 kg, and the BMI was 27.3 ± 4.0 kg/m^2. The fasting peripheral blood glucose (FBP) was 8.98 ± 2.76 mmol/l, the 2-hour postprandial blood glucose (P2BG) was 17.58 ± 4.41 mmol/l, and the HbA1c was 8.73 ± 1.81%. Patients' characteristics were shown in Table 1.

Age of Type 2 Diabetes Mellitus Diagnosis With Different Type 2 Diabetes Mellitus Family History and Gender

The age comparison of patients with different family history of T2DM was shown in Table 2. The F value of analysis of variance was 54.382, $P = .000$. The SNK test showed that patients with a family history of diabetes in Both parents were diagnosed at the earliest age. Patients with only a family history of maternal diabetes were the second youngest to be diagnosed with diabetes, P < .05. The age at diagnosis of T2DM was 51.7 ± 11.2 years for males and 54.0 ± 10.2 for females. The age of males was lower than that of females (t = −6.283, P = .000).

In patients with different T2DM family history, we compared the T2DM-diagnosed age in different genders. Among patients from the Father T2DM, Mother T2DM, Other T2DM family history, and Without T2DM family history groups, the diagnosed age in males was lower than in females, which was shown in Table 3.

The average diagnosed age of male patients in different types of family history was compared between groups (F = 32.375, $P = .000$), and that in female patients was compared (F = 671, P = .000). The order of the T2DM-diagnosed age in the different groups was Both parents T2DM and Father T2DM family history < mother T2DM family history < Other types of T2DM family history and no T2DM family history in Table 3 (SNK test, P < .05).

Univariate Comparison Between Early-Onset Type 2 Diabetes Mellitus and Non-Early-Onset Type 2 Diabetes Mellitus Patients

In this study, 589 patients (15.8%) with early-onset T2DM were used as the observation group, and 3136 patients (84.2%) with non-early-onset T2DM were used as the control

Table 3. Comparison of Diagnosed Age with Different Family History Between Male and Female Patients.

Sex		Both Parents T2DM	Father T2DM	Mother T2DM	Other T2DM Family History	No T2DM Family History
Male	N	108	286	425	656	813
	Diagnosed age	46.7 ± 11.1[a]	46.8 ± 10.8[a]	50.4 ± 10.6[b]	54.0 ± 10.8[c]	53.0 ± 11.0[c]
Female	N	82	167	271	474	443
	Diagnosed age	48.5 ± 10.3[1]	49.8 ± 11.3[1]	52.3 ± 10.2[2]	55.7 ± 9.5[3]	55.9 ± 9.3[3]
t value		−1.105	−2.825	−2.342	−2.652	−4.738
P-value		.271	.005	.019	.008	.000

Note. (a, b, c) and (1, 2, 3) indicate that there is a statistical difference between different labels using the SNK test (P < .05), but there is no statistical difference in the same label. T2DM = type 2 diabetes mellitus.

Table 4. Univariate Comparison Between the 2 Groups.

Item	Early-Onset T2DM	Nonearly-onset T2DM	χ^2/t Value	*P*
Sex (male)	415 (70.5%)	1873 (59.7%)	24.106	.000
BMI (kg/m^2)	28.8±5.2	27.0 ± 3.7	9.937*	.001
Smoking history	269 (45.7%)	1401 (44.7%)	.199	.656
Drinking history	113 (19.2%)	733 (23.4%)	4.956	.026
DM family history	429 (72.8%)	2040 (65.1%)	13.445	.000
HbA1c (%)	9.26 ± 1.89	8.63 ± 1.78	7.413*	.001

Note. *, Independent sample *t*-test; the remainder are χ^2 tests. BMI = body mass index; T2DM = type 2 diabetes mellitus.

Table 5. Logistic Regression Analysis of Related Factors of Early-Onset Type 2 Diabetes Mellitus.

Items	β	Wald χ^2	p	OR	95% CI
BMI	.103	88.807	.000	1.108	1.085–1.132
SEX	.550	29.372	.000	1.733	1.421–2.115
DM family history*		97.003	.000		
Other T2DM family history	.136	1.085	.298	.873	.676–1.127
Mother T2DM history	.429	10.367	.001	1.536	1.183–1.995
Father T2DM history	1.007	53.182	.000	2.738	2.089–3.590
Both parents T2DM	1.053	31.805	.000	2.866	1.988–4.132

Note. *, family history of diabetes mellitus was used as a dummy variable, and patients without a family history of diabetes mellitus were taken as a reference. BMI = body mass index; T2DM = type 2 diabetes mellitus.

group. The univariate differences in sex, smoking history, family history of T2DM, BMI, and WC were compared (Table 4). There were statistically significant differences in sex composition, BMI, family history of T2DM, and HbA1c between the 2 groups.

Logistic Regression Analysis of Related Factors of Early-Onset Type 2 Diabetes Mellitus

Taking diagnostic age of T2DM (early-onset/non-early onset) as the dependent variable, family history of diabetes, sex, and BMI as independent variables, multiple logistic regression analysis was used to analyze early-onset-related factors of T2DM in Table 5. Sex, Father T2DM history, Mother T2DM history, Parents T2DM, and BMI were all correlated with early-onset T2DM.

Discussion

T2DM is a complex disease caused by the joint action of genetic and environmental factors. Large-scale studies on the risk factors of T2DM in China show that weight gain, WC, dietary pattern, family history of diabetes, hypertension, family history of hypertension, and depression are the main risk factors of diabetes.[2] Among the newly diagnosed T2DM in the United States, 11.4% of the patients were under 45 years of age.[25] In the outpatient survey in Hong Kong, 29% of patients were diagnosed with T2DM before the age of

35 years.[26] In this study, 2469 (66.3%) of the 3725 patients had a family history of diabetes. There were 589 cases of early-onset T2DM, accounting for 15.8%. With the prolongation of disease, the attenuation rate of islet β cell function in early-onset T2DM patients was 15% per year, while that of late-onset patients was 6% per year.[27] To study the clinical characteristics of early-onset T2DM is of great significance for the mechanism research and prevention of the disease.

The study showed that early-onset T2DM patients against the control group had a higher proportion of family history of T2DM, and the HbA1c was higher at the time of diagnosis. Nakanishi et al. followed 960 people without T2DM for up to 7 years and found a significant increase in the incidence of T2DM among people with a family history of diabetes.[28] Studies have shown that approximately 84% of adolescents with T2DM have a family history of T2DM.[29] Some studies have investigated the population with a family history of T2DM in India. It was found that the average age of onset of T2DM in the first generation is 55.95 years and that of the second generation is 38.4 years.[30] To further compare the correlation between different family histories and early-onset diabetes, different from previous studies, we further refined the family history of diabetes according to parents' incidence. Multiple factor analysis showed that the father's and mother's T2DM family history was related to early-onset T2DM. The OR values were 2.866 (Both parents T2DM), 2.738 (Father T2DM), and 1.536 (Mother T2DM). At present, studies have shown that the onset age of T2DM is earlier when the mother's blood glucose is abnormal during pregnancy, which may be related to heredity and the intrauterine environment of T2DM.[31] There are few studies on the influence of paternal diabetes on offspring. Our study suggests that fathers with T2DM may be more associated with early-onset T2DM in their offspring than mothers with T2DM. In addition to genetic factors, the familial aggregation of diabetes may also be related to a similar living environment, and these families tend to be more vigilant and more aware of diabetes.[31]

In this study, the proportion of male patients in the early-onset T2DM group was significantly higher than in the late-onset T2DM group. The diagnosed age in males was earlier than in females. In different family history background, except when Both parents have diabetes, male patients are diagnosed earlier than female patients. In multivariate logistic regression analysis, it was also found that male sex was significantly correlated with the early-onset of T2DM. An increasing amount of attention has been paid to the impact of gender on common chronic diseases.[19] Studies outside China[32] and within China[20] have reported more males than females with T2DM in adults. Some European epidemiological surveys also show that more men are diagnosed with T2DM at an earlier age, 3–4 years earlier than women.[31] The analysis of the causes showed a possible relationship with social progress, improvement of automation, reduction of activities requiring high-intensity physical labor of men, and the level of sex hormone-binding globulin, and sex hormone.[31] Androgen can increase body weight and visceral fat, leading to or aggravating insulin resistance.[33] Estrogen is closely related to insulin sensitivity and can affect many aspects of the insulin signaling pathway.[34] It can enhance IGF signal transduction and alleviate insulin resistance by inducing various regulatory molecules of IGF.[35] However, a study of 7706 subjects (3896 women) for an average of 13.8 years of follow-up found that low testosterone levels predicted high risk of T2DM in men (HR = 2.66; 95% CI, 1.91−3.72; P < .001), while in women, this relationship was opposite (HR, .53; 95% CI, .37−.77; P = .003).[36] It is now becoming increasingly evident that the mammalian Y chromosome functions are not circumscribed to the induction of the male sex.[37] Animal studies have shown that variations in the Y chromosome are strongly accountable for blood pressure (BP), which is paralleled by studies in humans showing that the Y chromosome haplogroup is a significant predictor of coronary artery disease by influencing immunity pathways.[38] Whether the Y chromosome is associated with early-onset T2DM needs further studies.

The study also found significant correlation between BMI and early onset of T2DM (OR = 1.108). A Danish study on the correlation between male childhood weight and adult diabetes mellitus included 62,565 subjects, who were screened for diabetes at the age of 30, and found that obesity from age 7 to early adulthood was significantly associated with an increased risk of early T2DM.[39] More than 80% of patients with early-onset T2DM are complicated with obesity, while less than 50% of patients with late-onset T2DM are obese.[40] Patients with early T2DM have more fat content in liver and muscle than patients with late T2DM.[41] The obesity-related mechanisms, including circulating fatty acid level and chronic inflammation, are involved in the occurrence and development of diabetes, which needs further study.

Conclusions and Limitations

In conclusion, in China, patients with early-onset T2DM tend to have a more obvious T2DM family history. This survey shows that the T2DM family history of the parents, especially a father with diabetes family history, predicts an early diagnosis of T2DM in male patients. We need more intensive screening for diabetes in children with a family history of diabetes, especially in male children.

The findings of this study must be seen considering its limitations. First of all, although we analyzed all the newly diagnosed type 2 diabetic patients who came to the MMC department of our hospital during the period, the proportion of female patients in the group reached 38.6%, which may bias the result. Second, part of the family history of diabetes was gathered from the memories of patients and their families, so this might have an important effect on the outcome. Thirdly, the study was a single-center survey, and the research participants were mainly from the urban population of Tianjin. In this study, we did not investigate the diagnosed age of onset of T2DM of the patients. Finally, in this survey, the

level of glycosylated hemoglobin was 9.26% in early-onset T2DM and 8.63% in late-onset T2DM, which were significantly higher than the normal range (4–6%), indicating that the diagnosed age may be considerably delayed with respect to the onset time, and the actual situation of early-onset T2DM could be even more serious. Therefore, long-term cohort studies are needed to elucidate the correlation.

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Authors' Contribution

Zhaohu Hao wrote the manuscript. Xiao Huang was responsible for basic information collection and statistical analysis. Xiaohui Liu was responsible for keeping patients in order and basic information collection and statistical analysis. Feng He proposed the necessity and design of the study. Hailin Shao was in charge of the Metabolic Disease Management Center of Tianjin 4th Central Hospital. All authors read and approved the final manuscript.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical Approval

The clinical study protocol was approved by the Institutional Review Board (IRB) of Tianjin 4th Central Hospital, and all steps were conducted according to the principles of the World Medical Association Declaration of Helsinki (trial registration code: ChiCTR2000036881). According to regulations for clinical trials in humans, the IRB approved the collection and use of patients' records (IRB approval no. 2019-SZXLL068). Written informed consent was obtained from each patient.

Informed Consent

Written informed consent was obtained from each patient.

Data Availability

All data are available from the corresponding author upon request.

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