


# Degree of Blood Glucose Control and Risk of Hypertension in Chinese Adults with T2DM: A Cross-Sectional Study

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**Background:** Diabetes mellitus and hypertension often coexist and share common risk factors. This study investigated the correlation between glycemic management and the prevalence of hypertension among Chinese adults diagnosed with type 2 diabetes mellitus (T2DM).

**Methods:** This study included 1715 patients with T2DM from four cities in Anhui Province, China. Sociodemographic characteristics of the sample participants were collected via questionnaires. A univariate analysis of variance (ANOVA) was utilized for continuous variables, and chi-square testing was used for categorical variables. Binary logistic regression was utilized to examine the relationship between blood pressure and variables including fasting plasma glucose (FPG), glycosylated haemoglobin (HbA1c), body mass index (BMI), waist circumference (WC), physical activity, dyslipidemia, and family history of hypertension.

**Results:** FPG levels did not increase the risk of hypertension, while HbA1c was significantly and negatively associated with hypertension risk. HbA1c levels ranged from 7.2 to 8.6%, with odds ratios (OR) of 0.68 and 95% confidence intervals (CI) of 0.48 to 0.97 and a significant  $p$  value of less than 0.05. For the HbA1c levels above 8.6%, the OR was 0.58 with a 95% CI of 0.39 to 0.87 and a significant  $p$  value of less than 0.01. Furthermore, advanced age, higher BMI, greater waist circumference, presence of dyslipidemia, and positive family history of hypertension were all found to be significantly and independently linked to a heightened risk of developing hypertension. These associations remain significant after further adjustment.

**Conclusion:** There was a negative association between HbA1c and the risk of hypertension, and the association remained significant after adjustment for antihypertensive drug use.

**Keywords:** FPG, HbA1c, T2DM, hypertension

## Introduction

Diabetes is a rapidly expanding global public health crisis, which is attributed to rising obesity, an aging population, and unhealthy lifestyle habits.<sup>1</sup> According to statistical projections, the incidence of diabetes worldwide across all age groups is projected to reach 12.2% by 2045, resulting in a staggering 783.2 million people affected.<sup>2</sup> As a result of the increasing prevalence of diabetes, type 2 diabetes mellitus (T2DM) accounts for over 90% of all diabetic cases.<sup>3</sup> Microvascular (including retinal and nervous system complications) and macrovascular (cardiovascular) complications are two common complications in diabetes.<sup>4</sup> An observational analysis of 28 countries across Europe, Asia, and Africa found that 27% of patients with T2DM experienced macrovascular complications, and nearly half had microvascular disorders.<sup>5</sup>

Hypertension constitutes a significant risk factor for vascular complications linked to T2DM. Multiple studies have demonstrated the co-occurrence of T2DM and hypertension.<sup>6–8</sup> Activated signalling pathways and cytokines in persons with T2DM cause vascular fibrosis, calcification, and damage.<sup>9</sup> Coexisting hypertension can worsen vascular lesions in individuals with diabetes.<sup>10</sup> Hypertension and T2DM are linked to an elevated likelihood of developing cardiovascular

and renal disorders, in addition to other severe health issues.<sup>11</sup> Hence, it is imperative to timely detect hypertension risk factors in patients with T2DM and prevent risk buildup.

A cohort study conducted in Japan identified high plasma glucose (FPG) at baseline as an independent risk marker for new-onset hypertension.<sup>12</sup> Mika et al validated this observation and reported an increased risk of hypertension among pre-diabetic individuals with elevated FPG levels.<sup>13</sup> Comparable results have been documented in studies on adult women with hypertension living in rural areas of China.<sup>14</sup> Furthermore, it has been found that glycosylated haemoglobin (HbA1c) is closely linked to hypertension.<sup>15</sup> Multiple prospective cohort and cross-sectional studies indicate a linear positive association between HbA1c and the occurrence of high blood pressure in non-diabetic populations.<sup>16–18</sup> However, the main focus of these studies is to investigate the correlation between elevated pressure and impaired glucose tolerance associated with prediabetes. Some scholars have suggested a significant correlation between the prevalence of hypertension and the risk of hypertension in patients with T2DM.<sup>19–21</sup> Randomized Mendelian analyses have also shown that genetic testing for T2DM is associated with the risk of hypertension.<sup>22</sup> Conversely, other scholars have claimed that there is no significant association between blood glucose levels and the risk of hypertension in patients with T2DM.<sup>23,24</sup> Some studies have explored the relationship between diabetes and hypertension risk in general,<sup>23,25</sup> and some have explored the relationship between blood glucose levels and hypertension in people with prediabetes or non-diabetes.<sup>15,17</sup> To our knowledge, there are few studies examining the association between blood glucose levels and hypertension risk in Chinese T2DM patients.

The correlation between elevated blood glucose levels and hypertension risk in the Chinese population with T2DM has not been thoroughly investigated, and the exact nature of this relationship is still unclear. Consequently, this research conducted patient chronic complications questionnaire screenings and serum laboratory tests to examine the connection between blood glucose control levels and hypertension incidence rate.

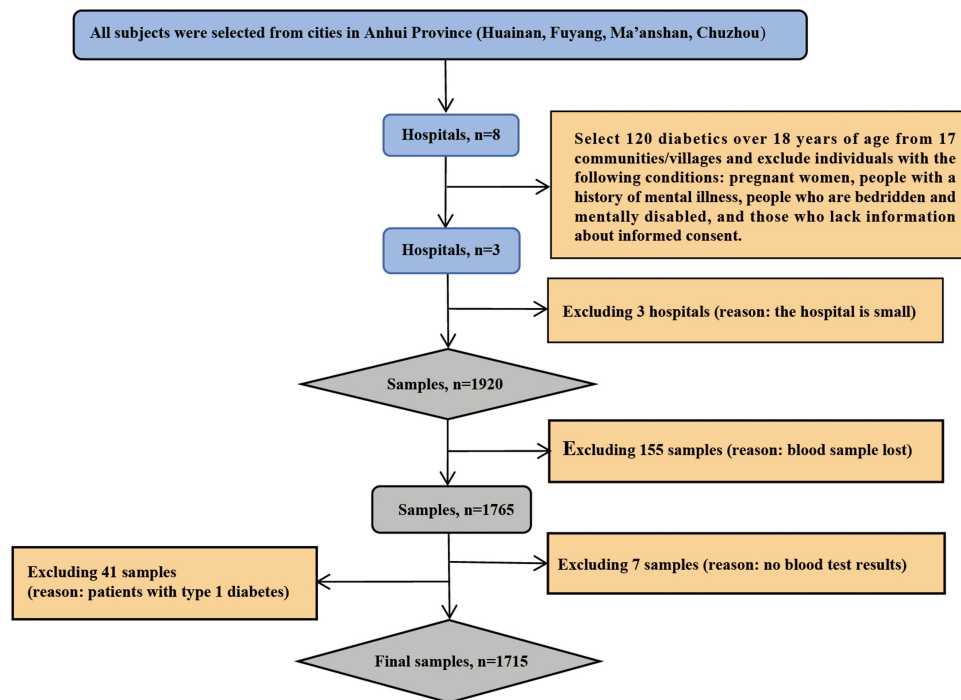
## Methods

### Study Design and Data Extraction

This is a cross-sectional descriptive study. The analysis of data relies on the China National Diabetic Chronic Complications Study (China DiaChronic Study), an extensively documented report.<sup>26</sup> The study screened for chronic diabetes complications in Anhui province, under the direct governance of the central government in China. It utilized a multi-stage sampling methodology (stratified, clustered, and random) to sample participants for the research. Standardized surveys were used to gather data on demographic characteristics and health-related factors, including age, gender, and lifestyle behaviors such as tobacco and alcohol use, and physical activity, and medical data such as family history and drug use. A physical examination was conducted to measure height, weight, and body mass index (BMI). BMI is calculated as weight (in kg) divided by height (in meters) squared. Individuals were split into three BMI groups: normal weight group (BMI <25 kg/m<sup>2</sup>), overweight group (BMI 25–30 kg/m<sup>2</sup>), and obese group (BMI >30 kg/m<sup>2</sup>).<sup>27</sup> Common laboratory tests used to assess metabolic health included FPG, HbA1c, total serum cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C). After fasting for 8–12 hours, a venous blood sample (12 mL) was collected from each participant by venipuncture at 7–12 am. Serum samples were immediately frozen to –20 °C and sent to a designated hospital or laboratory facility for biochemical analysis within 24 hours of collection. This study was conducted in accordance with the Helsinki Declaration. All data sources mentioned were collected by medical professionals and trained personnel from authorized medical institutions in nearby hospitals or community medical centers.

### Study Population

This research study enrolled 1765 participants from four cities located in Anhui Province, namely: Huainan, Fuyang, Ma'anshan, and Chuzhou. The flowchart depicted in Figure 1 illustrates the process by which the study population was selected. A total of 50 participants were excluded due to specific reasons. Ultimately, the analysis included 1715 patients who satisfied the research requirements. All participants voluntarily provided written informed consent forms.



**Figure 1** Flowchart of participants in the study.

## Criteria for Risk Factors

Impaired fasting glucose (IFG) is defined as an FPG level of between 100 and 125 mg/dL (5.6–7.0 mmol/L), diagnosed by a physician or managed as diabetes.<sup>28</sup> HbA1c levels increased by more than 6.5%, diagnosed by a doctor or treated as diabetes.<sup>29</sup> BMI is categorized as normal weight (BMI <25 kg/m<sup>2</sup>), overweight (BMI 25–30 kg/m<sup>2</sup>), or obese (BMI >30 kg/m<sup>2</sup>).<sup>27</sup> The diagnostic criteria for dyslipidemia include serum levels of TC exceeding 5.69 mmol/L or TG surpassing 1.68 mmol/L, HDL-C levels above < 1.0mmol/L, or use of lipid-lowering medication.<sup>30</sup> Complete the questionnaire to assess tobacco use and record alcohol consumption.

## Exposure of Interest and Outcomes

This study examines the effects of HbA1c, FPG, and blood pressure levels on T2DM. Fasting venous blood samples were taken to determine HbA1c and FPG levels. Impaired fasting glucose (IFG) is defined as an FPG level of between 100 and 125 mg/dL (5.6–7.0 mmol/L), diagnosed by a physician or managed as diabetes.<sup>28</sup> Impaired glucose tolerance (IGT): FPG less than 7.0 mmol/L and two-hour post-load blood glucose 7.8 to 11.0 mmol/L.<sup>31</sup> Diabetes was defined as FPG levels ≥ 7.0 mmol/L and/or HbA1c ≥ 6.5%, self-reported history of diabetes, or FPG ≥ 7.0 mmol/L (with insulin or oral hypoglycemic agents).<sup>32</sup> Hypertension was defined as SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg or current use of antihypertensive medication.<sup>33</sup> Blood pressure readings were obtained by trained professionals using either a standard mercury sphygmomanometer or an electronic sphygmomanometer. The blood lipid profile included measurements of TC, TG, LDL-C, and HDL-C.

## Inclusion and Exclusion Criteria

All inclusion and exclusion criteria were adhered to by participants in this study. Inclusion criteria included individuals aged 18 or older, with permanent residence and a diabetes diagnosis, and who had registered their household in the survey area for at least six months. Exclusion criteria applied to patients who: 1. Individuals who are pregnant or have severe health conditions, such as bedridden or intellectually disabled individuals, should refrain from attending. 2. Those who have experienced acute or chronic infections, mental illness, malignant tumors, adverse pregnancy outcomes, or

end-stage kidney disease within the last three months should also avoid attending. 3. It is advisable that individuals currently using immunosuppressants or glucocorticoids do not attend.

## Statistical Analysis

Continuous variable differences were analyzed through Kruskal–Wallis one-way ANOVA and posthoc tests, highlighting mean  $\pm$  SD. Meanwhile, chi-square tests were utilized to present categorical variable frequency and percentages. In addition, binary logistic regression was conducted to scrutinize blood pressure's relation with metabolic indicators, age, waist, and BMI. Finally, after organizing the preliminary data, we processed the missing data using version 23.0 of SPSS.

HbA1c was divided into quartile groups based on the following percentages: <6.3%, 6.3–7.2%, 7.2–8.6% and >8.6%. Similarly, FPG levels were classified into the following groups: <7.13 mmol/L, 7.13–8.72 mmol/L, 8.72–10.93 mmol/L, and >10.93 mmol/L. To create a binary logistic regression model, blood pressure was put as the dependent variable, with WC, BMI, physical activity, dyslipidemia, hypertension family history, waist group, FPG group, and HbA1c group as covariates. After adjusting the use of antihypertensive drugs, a new binary logistic regression model was established. The results for risk were presented using OR and 95% CI. GraphPad Prism 8.0.1 statistical software was utilized to assess changes in SBP and DBP, as well as mean arterial pressure (MAP), using FPG and HbA1c levels as covariates. Statistical significance was determined by a *p* value of less than 0.05.

## Results

### The Prevalence Characteristics of FPG

Table 1 shows, significant differences in various variables among different FPG categories. The participants with high FPG levels were mainly male, younger, had higher TC and TG levels, lower HDL-C levels, and had a higher likelihood of smoking during the baseline period. Individuals with high FPG levels have a higher probability of having diabetes for a longer duration a family history of diabetes. Among diabetics, individuals with FPG levels below 7.13 mmol/L had a higher incidence of hypertension than those with levels above 7.13 mmol/L. Additionally, participants with higher FPG levels displayed a lower frequency of utilization of antihypertensive medications during treatment. Patients with lower FPG levels exhibited a greater likelihood of having a family history of coronary heart disease. BMI, WC, additional family history, and medication history were not linked to FPG levels.

**Table 1** The Prevalence Characteristics of FPG

Variables	FPG, mmol/L				P value
	<7.13	7.13–8.72	8.72–10.93	>10.93	
Age, y	57.50 $\pm$ 9.81	58.43 $\pm$ 9.43	57.25 $\pm$ 9.82	55.58 $\pm$ 10.11	<0.001
Sex, n					0.023
Male	187 (43.5)	210 (49.0)	217 (50.7)	230 (53.7)	
Female	243 (56.5)	219 (51.0)	211 (49.3)	198 (46.3)	
BMI, kg/m <sup>2</sup>	26.04 $\pm$ 3.81	26.18 $\pm$ 3.73	25.92 $\pm$ 3.33	21.12 $\pm$ 3.69	0.759
WC, cm	88.87 $\pm$ 10.67	89.62 $\pm$ 9.28	90.17 $\pm$ 9.34	90.57 $\pm$ 9.97	0.062
Waist group, n	234 (54.4)	252 (58.7)	264 (61.7)	261 (61.0)	0.127
Years of diabetes, n	6.79 $\pm$ 5.11	7.51 $\pm$ 5.61	8.55 $\pm$ 6.03	9.53 $\pm$ 5.58	<0.001
Hypertension, n	241 (56.0)	239 (55.7)	194 (45.3)	185 (43.2)	<0.001
Dyslipidemia, n	264 (61.4)	293 (68.3)	271 (63.3)	294 (68.7)	0.057
Current smoking, n	73 (17.0)	66 (15.4)	91 (21.3)	107 (25.0)	0.002
Current alcohol drinking, n	102 (23.7)	123 (28.7)	122 (28.5)	133 (31.1)	0.109
Physical activity, n	283 (65.8)	288 (67.1)	270 (63.1)	287 (67.1)	0.564

(Continued)

Table 1 (Continued).

Variables	FPG, mmol/L				
	<7.13	7.13–8.72	8.72–10.93	>10.93	P value
Laboratory results, mmol/L					
TC	5.06 ± 1.1	5.06 ± 1.10	5.14 ± 1.17	5.46 ± 1.32	<0.001
TG	1.89 ± 1.39	2.03 ± 1.88	2.37 ± 1.76	3.04 ± 3.80	<0.001
LDL-C	3.03 ± 0.92	3.04 ± 0.98	3.02 ± 0.94	3.17 ± 1.02	0.075
HDL-C	1.50 ± 0.46	1.42 ± 0.40	1.42 ± 0.39	1.39 ± 0.42	0.003
Family history, n					
Family history of diabetes	174 (40.5)	168 (39.2)	210 (49.1)	215 (50.2)	0.001
Family history of obesity	123 (28.6)	136 (31.7)	143 (33.4)	151 (35.3)	0.192
Family history of coronary heart disease	110 (25.6)	78 (18.2)	75 (17.5)	84 (19.6)	0.013
Family history of stroke	112 (26.0)	98 (22.8)	90 (21.0)	93 (21.7)	0.309
Family history of malignant tumor	88 (20.5)	90 (21.0)	83 (19.4)	97 (22.7)	0.695
Family history of hyperlipidemia	110 (25.6)	89 (20.7)	95 (22.2)	109 (25.5)	0.243
Family history of hypertension	262 (60.9)	277 (64.6)	259 (60.5)	263 (61.4)	0.604
Insulin/oral medicine/no medication taken, n					0.52
Insulin	53 (12.3)	40 (9.3)	55 (12.9)	53 (12.4)	
Oral medicine	318 (74.0)	323 (75.3)	309 (72.2)	323 (75.5)	
No medication taken	59 (13.7)	66 (15.4)	64 (15.0)	52 (12.1)	
Reserpine, or other Chinese patent medicine	24 (5.6)	26 (6.1)	22 (5.1)	28 (6.5)	0.836
Antihypertensive drugs	199 (46.3)	208 (48.5)	169 (39.5)	164 (38.3)	0.004
Lipid-lowering drugs	73 (17.0)	66 (15.4)	52 (12.1)	54 (12.6)	0.137

**Notes:** Data are presented as means ± standard deviation, or numbers (percentage (%)). FPG indicates fasting plasma glucose.

**Abbreviations:** BMI, body mass index; WC, waist circumference; TC, total cholesterol; TG, triglycerides; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol.

## Analysis of Variations in Blood Pressure, Blood Lipids, and Other Parameters Based on HbA1c Classification

Epidemiological characteristics of abnormal HbA1c levels were displayed in Table 2. Younger participants with lower HbA1c levels generally had a narrower WC and higher HDL-C levels. On the other hand, individuals with higher HbA1c levels tended to have increased levels of TC, TG, and LDL-C, in addition to a greater likelihood of being smokers during baseline. Furthermore, the usage rates lipid-lowering and antihypertensive medications were comparatively low. Individuals with a longer duration of diabetes and a family history of the condition typically experience comorbid hypertension at low likelihood if their HbA1c levels exceed 8.6%. On the other hand, those with comorbid hypertension are usually found at HbA1c levels ranging from 6.3–7.2%. It is important to note that.

## Association Between Blood Glucose Control Levels and Hypertension Risk, with Further Adjustment for the Use of Antihypertensive Drugs

As shown in Table 3, in the crude model, no covariates were adjusted; in the adjusted model, the use of antihypertensive drugs was adjusted. In the crude model, based on the multivariable analysis, physical activity, WC and waist grouping, age, BMI, dyslipidemia, and family history of hypertension were significantly and independently positively related to hypertension risk. In contrast, FPG levels did not associated with blood pressure risk, while HbA1c exhibited a significant and negative correlation with hypertension risk. When HbA1c levels ranged from 7.2 to 8.6 mmol/L, the odds rate (OR) was 0.68, with a 95% confidence interval (CI) of 0.48 to 0.97 and *p* value <0.05. For level of HbA1c above 8.6 mmol/L, the OR was 0.58, with a 95% CI of 0.39 to 0.87 and *p* value <0.01. After adjusting the use of antihypertensive drugs, HbA1c was still negatively associated with the risk of hypertension. HbA1c levels ranged from 7.2 to 8.6%, with OR of 0.49 and 95% CI of 0.25 to 0.95 and a significant *p* value of less than 0.05. For the HbA1c levels above 8.6%, the OR was 0.45 with a 95% CI of 0.20 to 0.97 and a significant *p* value of less than 0.05. FPG levels did not associated with blood pressure risk, physical activity, waist

**Table 2** Analysis of Variations in Blood Pressure, Blood Lipids, and Other Parameters Based on HbA1c Classification

Variables	HbA1c, %				
	<6.3	6.3–7.2	7.2–8.6	>8.6	P value
Age, y	55.77 ± 10.08	59.0 ± 9.25	58.21 ± 9.64	55.86 ± 9.96	<0.001
Sex, n					0.085
Male	202 (44.8)	203 (48.1)	220 (52.0)	219 (52.3)	
Female	249 (55.2)	219 (51.9)	203 (48%)	200 (47.7)	
BMI, kg/m <sup>2</sup>	25.83 ± 3.85	26.04 ± 3.46	26.35 ± 3.45	26.06 ± 3.77	0.198
WC, cm	88.02 ± 9.67	89.67 ± 9.67	91.09 ± 9.58	90.57 ± 9.87	<0.001
Waist groups, n	234 (51.9)	255 (60.4)	269 (63.6)	253 (60.4)	0.003
Years of diabetes, n	5.94 ± 4.46	8.01 ± 5.75	8.92 ± 6.19	9.66 ± 5.56	<0.001
Hypertension, n	245 (54.3)	231 (54.7)	208 (49.2)	175 (41.8)	<0.001
Dyslipidemia, n	278 (61.6)	275 (65.2)	287 (67.8)	282 (67.3)	0.202
Current smoking, n	84 (18.6)	59 (14.0)	96 (22.7)	98 (23.4)	0.002
Current alcohol drinking, n	128 (28.4)	102 (24.2)	130 (30.7)	120 (28.6)	0.191
Physical activity	299 (66.3)	276 (65.4)	273 (64.5)	280 (66.8)	0.903
Laboratory results, mmol/L					
TC	5.13 ± 1.17	5.00 ± 1.08	5.11 ± 1.09	5.47 ± 1.35	<0.001
TG	2.17 ± 2.77	2.00 ± 1.54	2.28 ± 2.01	2.90 ± 3.70	<0.001
LDL-C	3.02 ± 0.94	2.99 ± 0.95	3.05 ± 0.93	3.20 ± 1.04	0.009
HDL-C	1.49 ± 0.42	1.42 ± 0.38	1.40 ± 0.40	1.41 ± 0.46	0.012
Family history, n					
Family history of diabetes	173 (38.4)	191 (45.3)	193 (45.6)	210 (50.1)	0.006
Family history of obesity	135 (29.9)	131 (31.0)	137 (32.4)	150 (35.8)	0.283
Family history of coronary heart disease	101 (22.4)	89 (21.1)	78 (18.4)	79 (18.9)	0.418
Family history of stroke	112 (24.8)	103 (24.4)	96 (22.7)	82 (19.6)	0.247
Family history of malignant tumor	92 (20.4)	87 (20.6)	80 (18.9)	99 (23.6)	0.394
Family history of hyperlipidemia	109 (24.2)	100 (23.7)	85 (20.1)	109 (26.0)	0.229
Family history of hypertension	282 (62.5)	259 (61.4)	263 (62.2)	257 (61.3)	0.979
Insulin/oral medicine/no medication taken, n					0.135
Insulin	54 (12.0)	47 (11.1)	40 (9.5)	60 (14.3)	
Oral medicine	342 (75.8)	306 (72.5)	316 (74.7)	309 (73.7)	
No medication taken	55 (12.2)	69 (16.4)	67 (15.8)	50 (11.9)	
Antihypertensive drugs, n	207 (45.9)	200 (47.4)	181 (42.8)	152 (36.3)	0.006
Lipid-lowering drugs, n	63 (14.0)	67 (15.9)	71 (16.8)	44 (10.5)	0.047

**Notes:** Data are presented as means ± standard deviation, or numbers (percentage (%)). HbA1c indicates glycosylated haemoglobin.

**Abbreviations:** BMI, body mass index; WC, waist circumference; TC, total cholesterol; TG, triglycerides; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol.

circumference grouping, age, BMI, abnormal lipids, dyslipidemia, and family history of hypertension were still positively associated with the risk of hypertension. These findings suggest that HbA1c has a protective effect against hypertension.

## Differences in Systolic, Diastolic, and Mean Arterial Pressure for Different FPG and HbA1c Levels

To investigate hypertension incidence across groups with different FPG levels, we categorized hypertension as SBP, DBP, and MAP. [Figure 2A](#) demonstrates the significance of SBP, DBP, and MAP at various FPG levels ( $p < 0.01$ ). Individuals with FPG levels between 7.13–8.72 mmol/L, 8.12–10.93 mmol/L, and >10.93 mmol/L had increased SBP in comparison to those with FPG levels <7.13 mmol/L. Furthermore, individuals with FPG levels >10.93 mmol/L had higher DBP than the other three groups. Moreover, the MAP was significantly higher in the group with FPG levels between 7.13–8.72 mmol/L and the group levels >10.93 mmol/L compared with FPG levels <7.13 mmol/L ( $p < 0.05$ ).



**Table 3** Association Between Blood Glucose Control Levels and Hypertension Risk, with Further Adjustment for the Use of Antihypertensive Drugs

Traits	Crude Model		Adjusted Model	
	OR (95% CI)	P value	OR (95% CI)	P value
FPG				
FPG <7.13 mmol/L	1 (reference)		1 (reference)	
7.13 ≤ FPG ≤ 8.72 mmol/L	0.93 (0.68–1.27)	0.657	1.03 (0.57–1.86)	0.919
8.72 < FPG ≤ 10.93 mmol/L	0.75 (0.53–1.06)	0.101	0.87 (0.44–1.72)	0.693
FPG >10.93 mmol/L	0.81 (0.54–1.20)	0.294	0.81 (0.37–1.76)	0.596
HbA1c				
HbA1c ≤ 6.3%	1 (reference)			
6.3 < HbA1c ≤ 7.2%	0.85 (0.62–1.16)	0.310	0.69 (0.39–1.22)	0.202
7.2 < HbA1c ≤ 8.6%	0.68 (0.48–0.97)	0.032	0.49 (0.25–0.95)	0.036
HbA1c > 8.6%	0.58 (0.39–0.87)	0.008	0.45 (0.20–0.97)	0.042
BMI				
BMI < 25 kg/m <sup>2</sup>	1 (reference)			
25 ≤ BMI < 30 kg/m <sup>2</sup>	1.53 (1.16–2.02)	0.002	1.61 (1.06–2.45)	0.026
BMI ≥ 30 kg/m <sup>2</sup>	2.22 (1.51–3.28)	<0.0001	2.04 (1.22–3.71)	0.019
Central obesity	1.12 (0.81–1.54)	0.501	0.81 (0.40–1.66)	0.087
Family history of hypertension	2.81 (2.26–3.50)	<0.0001	2.04 (1.34–3.10)	0.001
Dyslipidemia	1.75 (1.40–2.18)	<0.0001	2.36 (1.47–3.77)	<0.0001
Physical activity	1.06 (0.85–1.32)	0.613	0.93 (0.62–1.40)	0.736
WC	1.02 (0.99–1.04)	0.168	1.03 (0.10–1.09)	0.087
Age	1.06 (1.05–1.07)	<0.0001	1.04 (1.01–1.06)	0.003

**Note:** Adjusted for the use of antihypertensive drugs.

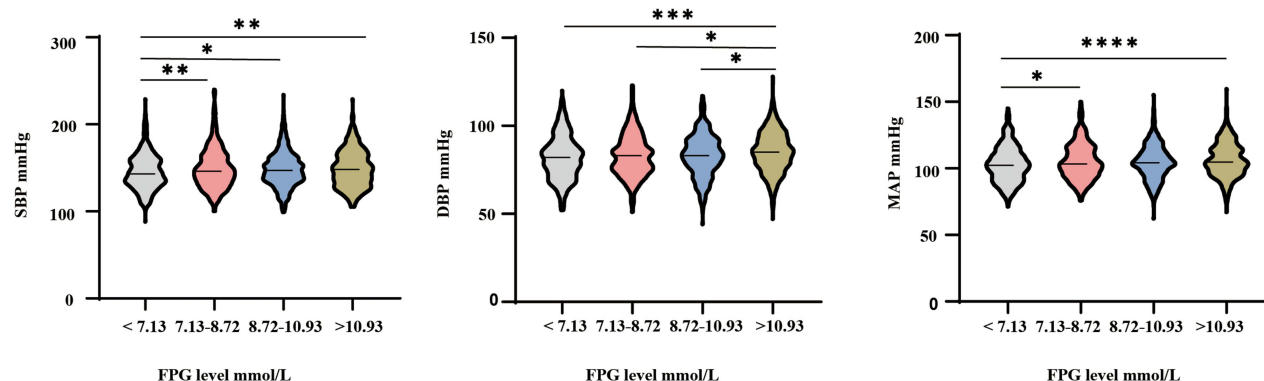
**Abbreviations:** FPG indicates fasting plasma glucose; HbA1c indicates glycosylated haemoglobin; BMI, body mass index; WC, waist circumference; Central obesity is defined as a sex-specific android to gynoid fat mass ratio (A/G ratio) above the median; Physical activity indicates aerobic exercise/resistance exercise.

To investigate hypertension differences across various HbA1c levels, the hypertensive cohort was divided into SBP, DBP, and MAP subgroups. **Figure 2B** reveals that DBP was higher in the HbA1c 6.3–7.2% group than in the HbA1c <6.3% group ( $p < 0.05$ ). Furthermore, the DBP of the HbA1c >8.6% group was higher than that of the HbA1c >6.3–7.2% group ( $p < 0.05$ ). Nevertheless, no significant correlation existed between changes in HbA1c levels and SBP and MAP.

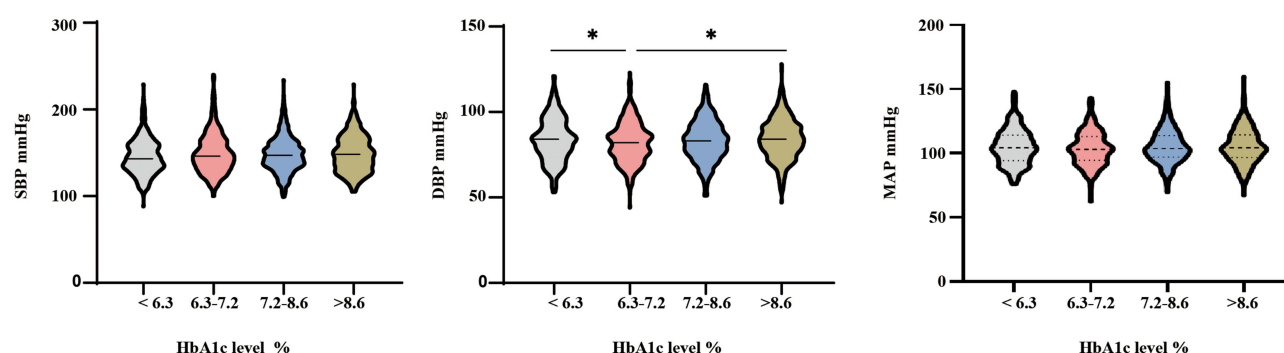
## Discussions

In this extensive cross-sectional study of 1715 Chinese adults aged 18–75 who had T2DM, we discovered that diabetic patients with elevated HbA1c levels had a reduced risk of hypertension development. In addition, there was a significant inverse correlation between HbA1c and the risk of hypertension, while FPG levels did not exhibit a comparable association. After adjusting the use of antihypertensive drugs, this conclusion remains significant. These findings not only fill the knowledge gap regarding the association of blood glucose control and hypertension prevalence patients with T2DM, but also corroborate the correlation between blood glucose levels and hypertension in the Chinese population.

### A. Differences in systolic, diastolic and mean arterial pressure for different FPG levels



### B. Differences in systolic, diastolic and mean arterial pressure for different HbA1c levels



**Figure 2** Differences in systolic, diastolic and mean arterial pressure for different FPG and HbA1c levels. **(A).** Differences in Systolic, Diastolic and Mean Arterial Pressure for Different FPG Levels. *p* values are from unpaired two-sided Student's *t*-test. \*Indicates *p* value <0.05. \*\*indicates *p* value <0.01. \*\*\*indicates *p*-value <0.001. \*\*\*\*indicates *p* value <0.0001. **(B).** Differences in Systolic, Diastolic and Mean Arterial Pressure for Different HbA1c Levels. *p* values are from unpaired two-sided Student's *t*-test. \*Indicates *p* value <0.05.

The mechanisms responsible for the plausible connection between HbA1c and FPG levels and the future risk of hypertension are not fully comprehended, but several different theories have been proposed. Various studies have revealed that FPG is an autonomous risk factor for future hypertension.<sup>12,14,34</sup> Additionally, a few studies have identified IFG as an independent of hypertension.<sup>13,14</sup> Every one mg/dL increase in FPG elevates the risk of hypertension by 4.6%, and the risk of hypertension doubles independent of IFG.<sup>13</sup> Furthermore, in men and individuals with normal baseline FPG, hypertension risk increases with changes in FPG trajectory.<sup>35</sup> However, some scholars refute this argument. An eleven-year prospective study conducted in Mauritius demonstrated that FPG was not to the hypertension development.<sup>23</sup> Furthermore, Lee et al and the Hong Kong Cardiovascular Risk Factor Prevalence Study both reported no significant association between FPG or IFG and the occurrence of hypertension.<sup>36,37</sup> Consistent with these findings, our study also reveals no noteworthy relationship between FPG levels and the risk of developing hypertension. The data suggest that FPG does not have a significant correlation with an increased likelihood of hypertension in individuals who have been diagnosed with T2DM. The influence of blood glucose on the development of hypertension may be attributed to various mechanisms. Hyperglycemia causes cell damage and vascular dysfunction by activating the vascular injury signaling and the polyol pathway. This activation leads to an immune response, production of proinflammatory transcription factors, and increased oxidative stress. A similar process occurs with high blood pressure.<sup>38</sup> High blood glucose levels can lead to inflammation, oxidative stress, production of advanced glycosylation end products and vascular dysfunction. They can also disrupt the stability and balance of endothelial and smooth muscle cells, and ultimately causing hypertension.<sup>39,40</sup>



Recent studies on the risk of HbA1c and hypertension have yielded conflicting results. Some studies have found a positive association between HbA1c levels and incident hypertension.<sup>41,42</sup> A study conducted in Sudan found that HbA1c levels were positively linked to the occurrence of newly diagnosed hypertension.<sup>18</sup> Some research has indicated that there is no correlation between HbA1c levels and the occurrence of hypertension.<sup>17,43</sup> A randomized Mendelian study using the UK Biobank analysis found no significant association between HbA1c levels and the risk of hypertension.<sup>44</sup> However, numerous studies have reported an inverse association between HbA1c levels and hypertension in individuals with T2DM.<sup>45,46</sup> A study conducted in Iran found a significant negative association between HbA1c and risk of hypertension in patients with T2DM.<sup>47</sup> The study found that for HbA1c levels ranging from 9.0–10.9% range, the OR was 0.88, with a 95% CI of 0.79–0.97; for those with HbA1c levels in the 11–12.9 range, the OR was 0.81, with a 95% CI of 0.71–0.92. Compared to HbA1c levels in the 11–12% group, HbA1c levels in the 13–14.9% group had a reduction OR to 0.73 and 95% CI of 0.62–0.86. Diabetics with HbA1c levels of 15% or higher had an OR of 0.67 and 95% CI of 0.53 to 0.85. Our study also found that HbA1c was significantly inversely associated with the risk of hypertension in patients with T2DM and showed a protective effect against hypertension. These findings provide new insights into the complex relationship between hypertension and HbA1c levels. The inverse relationship between HbA1c and hypertension may be due to the following mechanisms: Studies have shown that insulin could promote vasodilation through the augmentation of nitric oxide release (by stimulating nitric oxide synthase activity in endothelial cells) and by increasing acetylcholine-induced vasodilation.<sup>48,49</sup> Insulin promotes vasodilation,<sup>50</sup> resulting in a decrease in blood pressure as blood vessels dilate. In addition, elevated HbA1c and glucose levels affect the properties of red blood cells, reducing their flexibility, increasing aggregation, and increasing blood viscosity.<sup>51</sup> Increased blood viscosity increases shear stress, which stimulates NO production by endothelial cells. In addition, glycosylation of hemoglobin reduces oxygen carrying capacity, with compensates for the effect of viscosity on peripheral vascular resistance through vasodilation.<sup>52</sup>

Our study has the following strengths. First, this study is a cross-sectional study to present an association between the level of glycemic control and the incidence of hypertension in patients with T2DM. Second, this study represents the first investigation of the association between blood glucose levels and hypertension prevalence in individuals with T2DM, unlike most previous research that focused on individuals with pre-diabetes. Third, we used data from a large, well-designed cohort with elaborate measurements. Fourth, the strength of this study lies in its meticulous selection of patients with T2DM, along with the inclusion of age, family history of hypertension, hyperlipidemia, which provide a more comprehensive and nuanced assessment of the individual. Fifth, trained and certified personnel collected all data and followed quality control protocols. These findings add to current knowledge of the incidence of abnormal blood glucose and hypertension in Asian populations.

Inevitably, this article also has the following limitations. First, the study population was limited to individuals in four urban areas in Anhui, China, which limits the generalizability of the findings. Second, the sample of participants was relatively small, and large-scale population studies are needed to further understand and confirm the findings. Third, we did not consider other factors that could potentially affect HbA1c levels, such as hemoglobin levels, iron storage status, and red blood cell abnormalities.<sup>53</sup> Fourth, we did not follow up with the participants. Finally, there has yet not been a comprehensive assessment of the underlying factors contributing to hypertension, making it difficult to exclude the possibility of secondary hypertension.

## Conclusions

There was a negative association between HbA1c and the risk of hypertension, and the association remained significant after adjustment for antihypertensive drug use. T2DM patients with high levels of HbA1c have a lower risk of hypertension. These findings suggest that active glycemic control of is necessary to prevent the onset and development of hypertension. These results underscore the potential value of glucose monitoring in adults with hypertension or in hypertension prevention.

## Abbreviation

T2DM, Type 2 diabetes mellitus; FPG, Fasting plasma glucose; HbA1c, glycosylated haemoglobin; IFG, Impaired fasting glucose; IGT, Impaired glucose tolerance; WC, Waist circumference; BMI, Body mass index; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; MAP, Mean arterial pressure; TC, Total cholesterol; TG, Triglycerides; HDL-C,

High-density lipoprotein cholesterol; LDL-C, Low-density lipoprotein cholesterol; SD, Standard deviation; OR, Odds ratio; CI, Confidence interval; ANOVA, One-way analysis of variance.

## Data Sharing Statement

The original contributions presented and analyzed during the current study are available from the corresponding author on reasonable use.

## Ethics Statement

This study was approved by the Ethics Committee of the First Affiliated Hospital of Anhui Medical University Ethics Committee (Approval No: 2018-010) and was registered in the Chinese Clinical Trial Registry (ChiCTR1800014432). Each participant provided their written informed consent to participate in this study.

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## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors report no conflicts of interest in this work.

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