The Interaction Between Age and Risk Factors for Diabetes and Prediabetes: A Community-Based Cross-Sectional Study

Zihui Yan 1, Mengjie Cai¹, Xu Han², Qingguang Chen², Hao Lu^{1,2}

Department of Endocrinology, Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine, Shanghai, 201203, People's Republic of China; ²Diabetes Research Institute, Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine, Shanghai, 201203, People's Republic of China

Correspondence: Qingguang Chen; Hao Lu, Email ruiqi3721@163.com; tangniaobing107@163.com

Objective: This study aimed to investigate the interaction between age groups and risk factors for diabetes and prediabetes in Shanghai communities and to identify the effect of age on other risk factors for diabetes and prediabetes.

Methods: This study recruited 3540 participants with undiagnosed diabetes or prediabetes in 14 communities in Shanghai from February to August 2019. All participants underwent a comprehensive examination, including filling out a detailed questionnaire, physical examination, 75 g oral glucose tolerance test, and blood sample collection. In addition, logistic regression was used to analyze the interaction between age and risk factors for prediabetes and diabetes.

Results: The statistical analysis included 2776 people. In this study, the prevalence of diabetes and prediabetes were 15.1% and 52.3%, respectively. The prevalence of diabetes and prediabetes is higher in the elderly than in the middle-aged group. Among the risk factors for diabetes, overweight was associated with higher age (P-interaction 0.028). In addition, among the risk factors for prediabetes, a high level of education was associated with higher age (P-interaction 0.039) and elevated serum cholesterol level was associated with lower age (P-interaction 0.019).

Conclusion: This study confirmed an interaction between age and other influencing factors, which may be important in explaining differences in risk factors for diabetes and prediabetes in the middle-aged and elderly populations. Community health facilities can provide health guidance to people of different age groups to prevent and control prediabetes and diabetes.

Keywords: diabetes, prediabetes, risk factors, age, interaction

Introduction

Diabetes, a chronic disease with a high prevalence, has attracted worldwide attention. Surveys indicate that the global prevalence of diabetes in the adult population was 10.5% in 2021, with approximately 6.7 million adult deaths attributed to diabetes and its complications. According to the statistics, the prevalence of diabetes in China increased from 10.9% in 2013 to 12.4% in 2018, making China the country with the highest number of people with diabetes worldwide because of its large population.² The latest epidemiological survey revealed a 38.1% prevalence of prediabetes among Chinese adults, with much more patients having prediabetes than diabetes.² Prediabetes development is bidirectional, worsening into diabetes or returning to normal glucose metabolism. Therefore, early detection and appropriate intervention are key measures to prevent the deterioration of prediabetes.³

As society improves by leaps and bounds, population aging has become an obvious problem affecting public health. In China, most people with diabetes and prediabetes are over 40 years. According to a survey, the prevalence of diabetes and prediabetes among people aged 40-49 is 11.1% and 40.3%, respectively, while the prevalence of diabetes and prediabetes among people aged 60-69 has increased to 23.9% and 47.6%, respectively.² Advanced age is a major risk factor for diabetes and prediabetes.^{4,5} Therefore, the elderly has a higher prevalence of diabetes and prediabetes than the young and middle-aged and are more likely to develop complications in the cardiovascular, retinal, and renal systems.^{6,7}

Age differences cause changes in socio-demographic features and clinical characteristics; therefore, age may be an important variable influencing the role of risk factors for diabetes and prediabetes. Hence, clarifying the interaction between age and factors influencing the abnormal state of glucose metabolism is essential for healthcare organizations to develop precise prevention and control programs for diabetes. Given that few studies have examined the interaction between age and other risk factors, this study focused on analyzing differences in risk factors for diabetes and prediabetes between age groups, exploring the interaction between age and the main risk factors for the disease, and identifying differential factors. With the data, community health workers can make more targeted management and prevention of diabetes and prediabetes, achieving better tertiary prevention of diabetes.

Methods

Participants and Research Design

A cluster random sampling method was used to survey residents aged 40 and above in 14 communities in four administrative districts of Shanghai. We recruited 3540 participants with undiagnosed diabetes or prediabetes from February to August 2019. All participants underwent a comprehensive examination, including filling out a detailed questionnaire, physical examination, 75 g oral glucose tolerance test (OGTT), and blood sample collection. After excluding participants whose questionnaires were incomplete or who did not meet the age requirements, the data from 2776 participants were eventually included in the statistical analysis. All participants were divided into two groups according to the following criteria: middle-aged (40–59 years old) and elderly (60–80 years old) (Figure 1).

The Ethics Committee of Shuguang Hospital, affiliated with the Shanghai University of Traditional Chinese Medicine, approved this study, and all participants signed written informed consent. The entire procedure adopted in this study was in accordance with the World Medical Association Declaration of Helsinki.

Procedures and Measurements

The questionnaires were used to collect information on socio-demographic characteristics (age, sex, and education level), lifestyle characteristics (smoking and alcohol consumption), personal medical history (hypertension and dyslipidemia), and family history of diabetes. In physical examinations, systolic blood pressure (SBP), diastolic blood pressure (DBP),

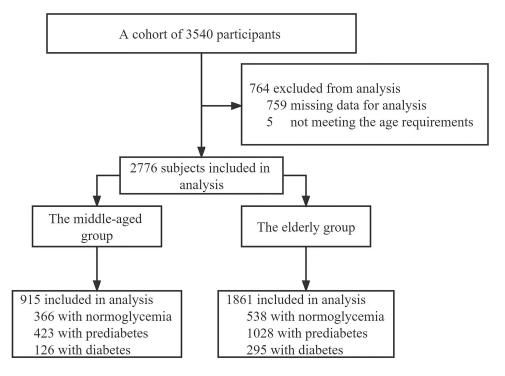


Figure I Participants selection flow diagram.

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weight, and height were measured according to standard protocols.⁸ Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared (kg/m²).

The laboratory indexes comprise fasting plasma glucose (FPG), 2-h postprandial plasma glucose (2-h PG), glycated hemoglobin A1c (HbA1c), fasting insulin (FINS), triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), serum creatinine (SCr), and serum uric acid (SUA). HbA1c was measured using high-performance liquid chromatography performed on an automatic analyzer (Tosoh HLC-723 G8, Japan). The remaining items were measured using an automatic biochemistry analyzer (Roche Cobas E602/E702, Switzerland). The homeostasis model assessment of insulin resistance was used to determine the insulin resistance, which could be defined as [fasting insulin (mIU/l) * fasting glucose (mmol/l)]/22.5.

Diagnostic Criteria

Diagnosis of diabetes mellitus: The diagnostic criteria issued by the American Diabetes Association (ADA) were used to identify: 9 FPG ≥ 7.0 mmol/l, OGTT 2-h PG ≥ 11.1 mmol/l, and HbA1c $\geq 6.5\%$.

Diagnosis of prediabetes mellitus: Based on the definition of prediabetes of the ADA, ¹⁰ any of these three aspects could be used to judge: either impaired fasting glucose (IFG) (FPG \geq 5.6 and \leq 6.9 mmol/l and glucose tolerance test 2-h PG < 7.8 mmol/l) or impaired glucose tolerance (IGT) (glucose tolerance test 2-h PG \geq 7.8 and < 11.1 mmol/l and FPG < 5.6 mmol/l) or HbA1c 5.7%–6.4%. Hypertension was defined ¹¹ as SBP \geq 140 mmHg and DBP \geq 90 mmHg, both of which should be measured repeatedly and the average calculated separately. Reference range of FINS: 17.80–173.00 pmol/l and SCr: 57–97 µmol/l. According to the Chinese national standard, overweight was defined as 24 \leq BMI < 28, and obesity, BMI \geq 28 for statistical analysis. ² Dyslipidemia: TC > 5.18 mmol/L, TG > 1.70 mmol/L, HDL-C < 1.04 mmol/L, and LDL-C > 3.37 mmol/L. ¹² Hyperuricemia was defined as a uric acid level of > 420 µmol/L. ¹³

Statistical Analysis

SPSS 25.0 was used to process and analyze all statistics. Measurement data for normally distributed continuous variables were expressed as means ± standard deviations, and the Student's *t*-test method was used for inter-group comparison. Data for other continuous variables were indicated as medians with interquartile ranges in parentheses, and comparisons between groups were made non-parametrically. In addition, categorical variables were expressed as frequencies and composition ratios, and intergroup comparison was conducted using a chi-square test. Considering the possible confounding factors in the sample, we used propensity score analysis to control the interference of confounding factors on the study's results and reduce bias. Multivariate logistic regression analysis was used to assess the risk factors for diabetes and prediabetes in middle-aged and elderly groups separately. Variables with *P*-values < 0.05 in the baseline analysis were first diagnosed for multicollinearity, and those with strong covariance with other variables were excluded. Then, the rest were included in the regression model using the stepwise regression method. In addition, when performing logistic regression analysis, the continuous variables TG, TC, HDL-C, LDL-C, and SUA were stratified and converted into categorical variables for analysis. Finally, the interaction between age and other risk factors was analyzed to identify differences in risk factors between age groups. Statistical significance was set at *P*-values < 0.05.

Results

Analysis of Baseline Data

This study recruited 3540 participants. After eliminating participants without complete information or meeting the age requirement, 2776 participants were finally analyzed statistically (Table 1). This study included 915 (33.0%) middle-aged and 1861 (67.0%) elderly people. Distributional differences were observed in the normoglycemic, prediabetic, and diabetic groups in socio-demographic factors and clinical characteristics (P < 0.05).

Table I General Characteristics of Study Participants

Variable	Normoglycemic	Prediabetic	Diabetic	P value
n (%)	904 (32.6)	1451 (52.3)	421 (15.1)	
Age groups****###				<0.001
Middle-aged group	366 (40.5)	423 (29.2)	126 (29.9)	
Elderly group	538 (59.5)	1028 (70.8)	295 (70.1)	
Gender(female)##	616 (68.1)	1022 (70.4)	253 (60.1)	<0.001
Educational level*##				0.015
Junior high school and below	651 (72.0)	972 (67.0)	270 (64.1)	
Senior high school and technical college	195 (21.6)	368 (25.4)	124 (29.5)	
University and above	57 (6.3)	111 (7.6)	27 (6.4)	
Family history of diabetes****###	208 (23.0)	460 (31.7)	246 (58.4)	<0.001
Alcohol drinking****	420 (46.5)	832 (57.3)	244 (58.0)	<0.001
Cigarette smoking****###	426 (47.1)	840 (57.9)	247 (58.7)	<0.001
Clinical characteristics				
Body mass index (BMI)***###				<0.001
BMI<24 kg/m ²	483 (53.4)	645 (44.5)	138 (32.8)	
24 kg/m²≤BMI <28 kg/m²	376 (41.6)	700 (48.2)	218 (51.8)	
BMI≥28 kg/m ²	45 (5.0)	106 (7.3)	65 (15.4)	
Hypertension***********************************	276 (30.5)	564 (38.9)	223 (53.0)	<0.001
FPG (mmol/l)****###	4.70 (4.41–4.95)	4.98 (4.67–5.35)	6.15 (5.45–7.12)	<0.001
2hPG (mmol/l)****###	5.68 (4.91–6.45)	7.02 (5.84–8.33)	12.30 (10.41–14.19)	<0.001
FINS (mIU/I)****###	6.29 (4.41–8.96)	7.60 (5.40–10.45)	9.51 (6.43–13.60)	<0.001
HOMA-IR****###	1.31 (0.91-1.90)	1.65 (1.16–2.38)	2.65 (1.78–3.93)	<0.001
HbA1c(%)****###	5.40 (5.30–5.50)	5.90 (5.70–6.00)	6.60 (6.25–7.10)	<0.001
TC(mmol/I)****#	4.92±0.91	5.09±0.90	5.01±0.99	<0.001
HDL-C (mmol/l)**###	1.45 (1.21–1.76)	1.40 (1.17–1.68)	1.26 (1.07–1.53)	<0.001
LDL -C (mmol/l)***	2.77±0.80	2.89±0.83	2.76±0.80	<0.001
TG (mmol/l)****###	1.19 (0.88–1.70)	1.37 (1.02–1.95)	1.68 (1.23–2.38)	<0.001
SCr (µmol/l)	66.0 (58.0–77.0)	66.0 (58.0–77.0)	66.0 (57.5–78.0)	0.705
SUA (μmol/l)*****###	288.5 (245.0–343.0)	306.0 (261.0–359.0)	319.0 (270.0–375.0)	<0.001

Notes: ****P < 0.001; **P < 0.01; *P < 0.05 for comparison of the prediabetic and normoglycemic. *##P < 0.001; *#P < 0.01; *P < 0.05 for comparison of the diabetic and normoglycemic.

The Effect of Age on the Prevalence of Diabetes and Prediabetes

We used propensity score matching to reduce confounding interference from random sampling (Table 2). In the unmatched state, there were differences between the elderly and middle-aged groups in terms of sexual composition, education levels, hypertension, dyslipidemia, and SCr levels. Univariate logistic regression suggested that the risk of diabetes and prediabetes was significantly higher in the elderly than in the middle-aged group (P < 0.001). After matching other influencing factors, the risk of prediabetes in the elderly group dramatically increased than the middle-aged group (Odds ratio = 2.537; 95% confidence interval, 2.015–3.194, P < 0.001). However, the risk of diabetes was not different between the two groups after matching (P > 0.05) (Table 3).

The Interaction Between Age and Risk Factors for Diabetes and Prediabetes

Logistic regression analysis indicated that females, a higher level of education, overweight and obesity, and a family history of diabetes significantly increased the risk of prediabetes in the elderly group. In contrast, hypertension, a higher level of education, and TC correlated with a greater risk of prediabetes in the middle-aged group (Table 4). In addition, the analysis demonstrated that hypertension, overweight and obesity, a family history of diabetes, a higher level of education, and TG significantly increased the risk of diabetes in the elderly group. Alcohol drinking, hypertension, and a family history of diabetes were associated with a higher risk of diabetes in the middle-aged group (Table 5).

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Table 2 Characteristics of Participants in Middle-Aged and Elderly Groups

Variable	Unmatched			Matched		
	Middle-Aged Group	Elderly Group	P value	Middle-Aged Group	Elderly Group	P value
n (%)	915 (33.0)	1861 (67.0)		755 (50.0)	755 (50.0)	
Glucose metabolism status			<0.001			<0.001
Normoglycemic	366 (40.0)	538 (28.9)		305 (40.3)	170 (22.5)	
Prediabetic	423 (46.2)	1028 (55.2)		367 (48.6)	519 (68.7)	
Diabetic	126 (13.8)	295 (15.9)		83 (10.9)	66 (8.7)	
Gender (female)	655 (71.6)	1236 (66.4)	0.006	549 (72.7)	549 (72.7)	1.000
Educational level			<0.001			1.000
Junior high school and below	555 (60.7)	1338 (71.9)		495 (65.5)	495 (65.5)	
Senior high school and	252 (27.5)	436 (23.4)		205 (27.1)	205 (27.1)	
technical college						
University and above	108 (11.8)	87 (4.7)		55(7.2)	55(7.2)	
Family history of diabetes	280 (30.6)	634 (34.1)	0.068	206 (27.3)	206 (27.3)	1.000
Alcohol drinking	513 (56.1)	983 (52.8)	0.107	418 (55.3)	418 (55.3)	1.000
Cigarette smoking	517 (56.5)	996 (53.5)	0.138	419 (55.5)	419 (55.5)	1.000
Clinical characteristics						
BMI (kg/m ²)			0.134			1.000
BMI<24	442 (48.3)	824 (44.3)		368 (48.7)	368 (48.7)	
24 ≤BMI <28	405 (44.3)	889 (47.8)		350 (46.3)	350 (46.3)	
BMI≥28	68 (7.4)	148 (8.0)		37 (4.9)	37 (4.9)	
Hypertension	267 (29.2)	796 (42.8)	<0.001	220 (29.1)	220 (29.1)	1.000
FPG (mmol/l)	4.92 (4.60–5.36)	4.95 (4.60–5.42)	0.195	4.91 (4.59–5.32)	4.95 (4.62–5.35)	0.205
2hPG (mmol/l)	6.27 (5.29–7.99)	6.87 (5.67–8.70)	<0.001	6.25 (5.32–7.72)	6.78 (5.68–8.29)	<0.001
FINS(mIU/I)	7.32 (5.02–10.30)	7.33 (5.19–10.52)	0.308	7.33 (5.08–10.09)	7.29 (5.19–10.32)	0.499
HOMA-IR	1.64 (1.08–2.38)	1.63 (1.11–2.44)	0.264	1.63 (1.08–2.35)	1.60 (1.09-2.39)	0.455
HbA1c(%)	5.70 (5.40–6.00)	5.80 (5.50-6.10)	<0.001	5.70 (5.40–5.90)	5.80 (5.60-6.00)	<0.001
TC > 5.18 (mmol/l)	360 (39.3)	829 (44.5)	0.009	262 (35.3)	262 (35.3)	1.000
HDL-C < 1.04 (mmol/l)	140 (15.3)	248 (13.3)	0.158	86 (11.6)	86 (11.6)	1.000
LDL -C > 3.37 (mmol/l)	210 (22.9)	480 (25.7)	0.103	150 (20.2)	150 (20.2)	1.000
TG > 1.70 (mmol/l)	292 (31.9)	654 (35.1)	0.091	210 (28.3)	210 (28.3)	1.000
SCr (μmol/l)	65.0 (57.0–75.0)	67.0 (59.0–79.0)	<0.001	65.0 (57.0–75.0)	65.0 (58.0–75.0)	0.517
SUA ≥ 420 (μmol/l)	75 (8.2)	178 (9.5)	0.239	58 (7.4)	58 (7.4)	1.000

We analyzed the interaction between age and other risk factors to illustrate further the effect of age on prediabetes and diabetes risk factors. The results revealed that a high level of education and being overweight influenced the increased risk of diabetes and prediabetes in the elderly group compared to the middle-aged group, respectively (*P*-interaction 0.039; *P*-interaction 0.028). In addition, elevated serum cholesterol level was an important factor influencing the increased risk of prediabetes in the middle-aged group compared to the elderly group (*P*-interaction 0.019) (Table 6).

Table 3 The Effect of Age on the Risk of Prediabetes and Diabetes

Variable	Prediabetic vs Normoglycemic		Diabetic vs Normoglycemic		
	OR (95% CI)	P value OR (95% CI)		P value	
Unmatched					
Middle-aged	Reference		Reference		
Elderly	1.653 (1.389–1.969)	<0.001	1.593 (1.244–2.040)	<0.001	
Matched					
Middle-aged	Reference		Reference		
Elderly	2.537 (2.015–3.194)	<0.001	1.427 (0.982–2.073)	0.062	

Table 4 Risk Factors for Prediabetes in Different Age Groups

Variable	Middle-Aged Group ^a Elderly G		iroup ^b	
	OR (95% CI)	P value	OR (95% CI)	P value
Female	-		1.284 (1.023–1.614)	0.031
Senior high school and technical college	2.091 (1.470-2.975)	< 0.001	-	
University and above	1.656 (1.040-2.638)	0.034	3.045 (1.637–5.667)	< 0.001
24 kg/m² ≤ BMI < 28 kg/m²	-		1.464 (1.174-1.825)	0.001
BMI ≥ 28 kg/m ²	-		1.755 (1.095–2.814)	0.020
Family history of diabetes	-		1.571(1.232–2.004)	< 0.001
Hypertension	1.451 (1.041-2.022)	0.028	-	
TC > 5.18 mmol/l	2.243 (1.631–3.087)	< 0.001	-	
TG > 1.70 mmol/l	-		1.517 (1.195–1.925)	0.001

Notes: Model ^aadjusted for educational level, family history of diabetes, BMI, hypertension, TC, LDL-C, TG, SUA; Model ^badjusted for gender, educational level, family history of diabetes, BMI, hypertension, TC, HDL-C, TG, SUA.

Table 5 Risk Factors for Diabetes in Different Age Groups

Variable	Middle-Aged Group ^a		Elderly Group ^b		
	OR (95% CI)	P value	OR (95% CI)	P value	
Senior high school and technical college	-		2.749 (1.830–4.130)	< 0.001	
Alcohol drinking	3.307 (1.851-5.908)	< 0.001	-		
$24 \text{ kg/m}^2 \le \text{BMI} < 28 \text{ kg/m}^2$	-		2.098 (1.473-2.998)	< 0.001	
BMI ≥ 28 kg/m ²	-		4.670 (2.541-8.583)	< 0.001	
Family history of diabetes	4.676 (2.900–7.541)	< 0.001	5.666 (4.009-8.009)	< 0.001	
Hypertension	3.113 (1.895–5.112)	< 0.001	1.703 (1.213-2.390)	0.002	
TG > 1.70 mmol/l	-		3.491 (2.424–5.027)	< 0.001	

Notes: Model ^aadjusted for educational level, alcohol drinking, family history of diabetes, BMI, hypertension, TC, HDL-C, TG, SUA; Model ^b adjusted for gender, educational level, family history of diabetes, BMI, hypertension, HDL-C, TG, SUA.

Table 6 Interaction of Age with Other Risk Factors

Variable	Prediabetic				Diabetic	
	Middle-Aged	Elderly	P Interaction	Middle-Aged	Elderly	P Interaction
University and above 24 kg/m ² ≤ BMI < 28 kg/m ²	Reference	2.216 (1.043–4.711)	0.039	- Reference	- 1.820 (1.068–3.102)	- 0.028
TC > 5.18 mmol/l	1.539 (1.073–2.209)	Reference	0.019	-	-	-

Discussion

This study was based on a cross-sectional community survey to analyze the interaction between age and risk factors for diabetes and prediabetes and identify differences in risk factors for diabetes in different age groups. The findings suggested that in Shanghai communities, the prevalence of prediabetes (55.2%) and diabetes (15.9%) was higher in the elderly than in the middle-aged group, which was consistent with previous studies.² Age is an important factor that affects the increased risk of prediabetes and diabetes, based on previous national and international studies.¹⁴ After excluding other confounders, age significantly affected the risk of prediabetes.

Similar to previous studies, ^{15,16} our study results revealed that a higher level of education in the elderly group increases the risk of prediabetes and diabetes. However, some studies have presented the opposite conclusion: lower education level as a risk factor for prediabetes and diabetes. ^{17,18} People with high levels of education mostly had a better understanding of the disease and could control their blood glucose adequately. Moreover, the various education level also

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influenced patients' jobs and income, so these socioeconomic factors affected the participant's health. ^{19,20} Therefore, different results might occur when variables interfere with each other.

Being overweight and obese, defined by BMI, are risk factors for prediabetes and diabetes.²¹ Previous studies have reported that high BMI increases the risk of developing type 2 diabetes in the elderly,^{22,23} consistent with our study results. In addition, due to increased age, hormonal changes, and a sedentary lifestyle, the elderly population are more prone to sarcopenic obesity and increased insulin resistance than the middle-aged group, increasing the risk of diabetes.²⁴

Diabetes is closely related to dyslipidemia; hence, patients with type 2 diabetes usually present with low HDL, increased TG, and elevated levels of small, dense LDL.²⁵ As a serum indicator, TG could be used to predict the risk of diabetes;²⁶ hence, elevated TG levels increase the risk of prediabetes.²⁷ In our study, elevated TG levels only increased the risk of prediabetes and diabetes in the elderly group because aging caused elevated serum TG levels and changed TG metabolism in the body. This made the elderly more likely to develop metabolic-related diseases than younger people, including diabetes, metabolic syndrome, and non-alcoholic fatty liver disease.²⁸ In addition, our study discovered that abnormally elevated TC levels in the blood are a risk factor for increased risk of prediabetes in the middle-aged group. However, the related association was not observed in the elderly group. A longitudinal analysis revealed that TC increased with age, peaking around middle age and then declining.²⁹ Therefore, we speculated that abnormal TC levels had a negligible effect on diabetes in the elderly because their TC levels presented an overall downward trend with age in physiological conditions.

In conclusion, this study demonstrated the relationship between age and risk factors for diabetes and prediabetes, comparing differences in the characteristics of middle-aged and elderly groups, unlike most previous epidemiological investigations on diabetes and prediabetes in Shanghai. However, this study had some limitations. First, this study was a cross-sectional survey; therefore, it could not assess the causal relationship between risk factors and diabetes. Second, there were some omissions in the socio-demographic information and clinical characteristics of the participants, and there was still room to improve the analytical model for risk factors. Finally, the models relating to interaction studies could be further deepened and improved. Therefore, we will conduct a community-based prospective cohort study to determine the effect of different exposure factors on different age groups with prediabetes and diabetes.

Conclusion

We confirmed an interaction between age and other influencing factors, which may be important in explaining the differences in risk factors for diabetes and prediabetes in the middle-aged and elderly populations. Based on our findings, community health facilities can provide health guidance for different age groups to achieve precise prevention and control of prediabetes and diabetes.

Data Sharing Statement

The data that support the findings of this study are available within the article.

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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 declare that they have no conflicts of interest.

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