Dose-Response Association Between Dietary Folate and Niacin Intakes With Diabetes Among Chinese Adults: A Cross-Sectional Study

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Abstract

Background

This study aimed to examine the relationships between dietary vitamin intakes and the risk of diabetes among Chinese adults.

Methods

This is a cross-sectional observational study. Demographic and anthropometric data along with information on dietary vitamin intakes were collected and eligible participants were recruited to complete a questionnaire. Binary logistic regression analysis was conducted to examine the associations between dietary vitamin intakes and the risk of diabetes, with adjustment for potential confounders. We also evaluated non-linear dose-response relationships between dietary vitamin intakes and diabetes using adjusted restricted cubic splines.

Results

Of the 3106 eligible participants, 15.9% had prevalent diabetes, 19.0% in male and 13.7% in female, respectively. The median folate was significantly higher in diabetic patients than in controls (32.030 vs 27.600 µg), while median niacin was significantly lower (7.000 vs 7.900 mg). The binary logistic regression analysis also showed a significant association between dietary folate (Odds ratio (OR)=1.002; 95% confidence interval (CI): 1.000-1.004; P=0.022) and niacin intakes (OR=0.965; 95% CI: 0.944-0.986; P=0.001) with the risk of diabetes after controlling for potential confounders. The plots of restricted cubic splines presented an atypical inverted U-shaped association between dietary folate intake and diabetes.

Conclusions

The data presented here showed that diabetics had a low intake of vitamins, especially B group vitamins. Dietary folate and niacin intakes tended to be independently related to the risk of diabetes. Nevertheless, this study is observational, and there yet to be large-scale randomized controlled trials which would increase the evidence of the findings.

Background

Diabetes is one of the fastest growing health challenges of the 21st century, with the number of adults with diabetes having more than tripled over the past twenty years ^[1]. Diabetes has the potential to cause numerous debilitating health complications and increases the risk of early death ^[1]. Investment in effective diabetes prevention and management has become necessary to prevent disability and death.

It is well-known that diabetes is recognized as a multifactorial chronic disease that can be related to dietary factors ^[2]. Economic growth and environmental transitions have led to drastic changes in food production, processing, and distribution systems and have increased the accessibility of unhealthful foods. ^[3] With nutritional transitions, people have experienced increased diabetes incidence and mortality. ^[4]

Several epidemiological studies ^[2, 5–6] have shown that diet plays an important role in the development of diabetes, and reported the association between nutrients intakes and the risk of diabetes ^[5–6]. In addition, people with diabetes should be informed about the importance of acquiring daily vitamin requirements through a well-balanced diet because people with poorly controlled diabetes often experience micronutrient deficiencies. ^[7] Adequate B vitamins intakes are a general

requirement for healthy growth and nucleic acid synthesis in all cells. A few studies ^[8–15] have reported that B group vitamins, especially folate (vitamin B9) and niacin (vitamin B3), may be involved in the pathogenesis of glucose intolerance and inversely associated with the risk of diabetes. However, the conclusions are inconsistent. Moreover, most of the previous studies were either for the vitamin status ^[16–17] or supplemental ^[18–20] rather than dietary intakes ^[10–11].

Thus, it makes sense to explore the vitamin intakes in the diet and its association with the risk of diabetes. In view of this, the present study aimed to characterize dietary vitamin intakes in Chinese adults and to evaluate the associations between dietary vitamin intakes and the risk of diabetes, and hopefully to be able to provide a scientific rationale for formulating dietary guidelines.

Methods

Study population

A survey was conducted to explore the epidemiological characteristics of major chronic noncommunicable diseases among residents living in communities for more than 6 months selected by using a multistage random sampling design in Bengbu, China ^[21]. Individuals with severe mental illness or cognitive impairment and who were pregnant or breastfeeding were excluded. This cross-sectional study was reviewed and approved by the Ethics Committee of Bengbu medical college. All participants were required to complete the whole survey and sign informed consent.

Data collection

Demographic information was obtained through a questionnaire by trained staffs. The standardization of techniques and personnel training was performed before the start of the survey to reduce the inter-observer variations. Gender (male and female), age (years), educational level (elementary level or lower, junior high school level, high school level, and college level or higher), marital status (unmarried, currently married, and other), place of residence (urban and rural), cigarette smoking (current smoking and no smoking) were collected.

Anthropometric data were collected by trained staffs with uniform instruments. The height (m) and weight (kg) were ascertained in light indoor clothing, while the waist circumference (cm) in a fasting state as well as an upright position. Body mass index (BMI) was calculated using weight (kg) divided by squared height (m), and $BMI \geq 28 \text{ kg/m}^2$ was set as general obesity ^[22]. Males with waist circumference (WC) $\geq 90 \text{ cm}$ and females with WC $\geq 85 \text{ cm}$ were considered abdominal obesity, respectively ^[23].

Assessment of Diabetes

Blood samples were collected after an overnight fast of more than eight hours. The individuals with diagnosed diabetes previously or fasting plasma glucose (FPG) value $\geq 7.0 \text{ mmol/L}$ in this survey were defined as diabetes ^[24].

Assessment of vitamin intakes

For the assessment of the vitamin intakes from diet, the three-day food record was used and the amounts of vitamins were calculated using the Food Nutrition Calculator V2.65 developed and recommended by National Institute of Nutrition and Food Safety, Chinese Center for Disease Control and Prevention.

Statistical analyses

The Kolmogorov-Smirnov test was applied to verify the normality of the data. Data for continuous variables were expressed as median (interquartile range), and categorical variables were expressed as number (percentages). Mann-Whitney U tests and chi-square tests were used to compare the averages of continuous variables and the percentages of

categorical variables between diabetes and normoglycemia group, respectively. Binary logistic regression models were used to examine the associations between dietary vitamin intakes and the risk of diabetes, adjusting for potential confounding variables. Variables included in the models were checked for multi-collinearity. We also used restricted cubic splines with four knots at the 25th, 50th, 75th, and 95th percentiles of the exposures distribution in fully adjusted model to flexibly model the association between dietary vitamin intakes and diabetes. All statistical analyses were undertaken using SPSS 23.0 (IBM, Armonk, NY, USA) and Stata 12.0 software (StataCorp., College Station, TX, USA). $P < 0.05$ was considered statistically significant.

Results

Characteristics of the study population

A total of 3115 participants were recruited. Excluding 9 who did not complete the questionnaire regarding dietary vitamin intakes, 3106 were eventually included. The prevalence of diabetes was 15.9%, 19.0% in male and 13.7% in female, respectively. Diabetics had a higher median age (64y), compared with normoglycemia controls (57y, $P < 0.001$). Statistically significant differences of educational level ($\chi^2 = 19.731$, $P < 0.001$), marital status ($\chi^2 = 11.508$, $P = 0.003$) and place of residence ($\chi^2 = 8.467$, $P = 0.004$) between diabetics and normoglycemia controls were observed. There was a significantly higher proportion of smoking ($\chi^2 = 9.968$, $P = 0.002$), general obesity ($\chi^2 = 18.914$, $P < 0.001$) and abdominal obesity ($\chi^2 = 58.254$, $P < 0.001$) in the diabetes group compared with control group.

In terms of dietary vitamin intakes, median folate and vitamin E intakes were significantly higher in diabetic patients than in controls, while median thiamine, riboflavin, niacin and vitamin C intakes were significantly lower. Nevertheless, for vitamin A and vitamin B6, no significant differences were observed. The similar results were observed in women. Intake of niacin was lower in male diabetics than the controls. However, no other significant differences were observed in men.

Table 1
Characteristics of participants by diabetes status

Variables	Normoglycemia (n=2611)	Diabetes (n=495)	χ^2/Z value	P value
Gender (Female)	1556 (59.6%)	247 (49.9%)	16.061	<0.001
Age (years)	57 (45, 66)	64 (56, 72)	-11.434	<0.001
Educational level			19.731	<0.001
Elementary level or lower	735 (28.2%)	187 (37.9%)		
Junior high school level	963 (37.0%)	170 (34.4%)		
High school level	646 (24.8%)	99 (20.0%)		
College level or higher	258 (9.9%)	38 (7.7%)		
Marital status			11.508	0.003
Unmarried	92 (3.5%)	6 (1.2%)		
Currently married	2198 (84.8%)	411 (83.5%)		
Other	302 (11.7%)	75 (15.2%)		
Place of residence			8.467	0.004
Urban	2156 (82.6%)	435 (87.9%)		
Rural	455 (17.4%)	60 (12.1%)		
Smoking	734 (28.1%)	174 (35.2%)	9.968	0.002
General obesity	343 (13.1%)	102 (20.6%)	18.914	<0.001
Abdominal obesity	1036 (39.7%)	288 (58.2%)	58.254	<0.001
Daily intake				
Vitamin A (μ gRE)	280.000 (134.000, 500.000)	285.000 (155.000, 435.000)	-0.068	0.946
Thiamine (mg)	0.440 (0.320, 0.640)	0.430 (0.310, 0.560)	-2.254	0.024
Riboflavin (mg)	0.590 (0.420, 0.810)	0.560 (0.420, 0.730)	-2.364	0.018
Vitamin B6 (mg)	0.120 (0.050, 0.220)	0.120 (0.060, 0.210)	-1.022	0.307
Folate (μ g)	27.600 (9.300, 57.800)	32.030 (15.370, 57.700)	-3.222	0.001
Niacin (mg)	7.900 (5.500, 11.600)	7.000 (5.000, 9.400)	-5.262	<0.001
Vitamin C (mg)	45.700 (23.300, 79.500)	40.600 (25.300, 62.800)	-2.573	0.010
Vitamin E (mg)	24.750 (14.950, 41.730)	27.820 (16.390, 42.190)	-1.992	0.046
Note: General obesity, Body mass index (BMI) ≥ 28 Kg/m ² ; Abdominal obesity, male: waist circumference (WC) ≥ 90 cm and female: WC ≥ 85 cm.				

Table 2
Dietary vitamin intakes between diabetes and controls according to gender

Variables	Male				Female			
	Normoglycemia (n=1055)	Diabetes (n=248)	Z value	P value	Normoglycemia (n=1556)	Diabetes (n=247)	Z value	P value
Vitamin A (µgRE)	285.000 (143.000, 522.000)	304.500 (160.250, 454.750)	-0.187	0.852	274.500 (127.250, 484.000)	275.000 (149.000, 407.000)	-0.333	0.739
Thiamine (mg)	0.480 (0.340, 0.710)	0.480 (0.340, 0.600)	-1.392	0.164	0.420 (0.300, 0.590)	0.400 (0.280, 0.500)	-2.788	0.005
Riboflavin (mg)	0.620 (0.450, 0.880)	0.570 (0.453, 0.768)	-1.853	0.064	0.570 (0.400, 0.780)	0.530 (0.400, 0.700)	-2.230	0.026
Vitamin B6 (mg)	0.120 (0.060, 0.240)	0.130 (0.070, 0.210)	-0.055	0.956	0.100 (0.040, 0.210)	0.110 (0.060, 0.190)	-0.924	0.355
Folate (µg)	30.800 (11.300, 64.900)	35.730 (17.765, 57.120)	-1.427	0.154	25.250 (8.200, 54.750)	28.470 (13.800, 58.200)	-2.538	0.011
Niacin (mg)	9.000 (6.200, 13.600)	7.800 (5.648, 10.230)	-4.298	<0.001	7.200 (5.100, 10.500)	6.270 (4.670, 8.300)	-4.515	<0.001
Vitamin C (mg)	45.100 (22.500, 78.700)	41.650 (25.425, 64.875)	-1.047	0.295	46.200 (23.825, 80.075)	38.900 (25.200, 61.400)	-2.540	0.011
Vitamin E (mg)	26.210 (15.850, 44.140)	28.425 (16.055, 43.483)	-0.429	0.668	23.840 (14.535, 40.100)	26.360 (16.620, 40.110)	-2.106	0.035

Regression Analysis

After adjusting for gender, age, educational level, marital status, place of residence, smoking, general obesity and abdominal obesity, the binary logistic regression analysis revealed that participants with diabetes had greater OR for folate intake (OR = 1.002; 95% CI: 1.000-1.004; P = 0.022) and lower OR for niacin intake (OR = 0.965; 95% CI: 0.944-0.986; P = 0.001) than did those with normoglycemia.

In the adjusted regression models stratified by gender, OR for niacin intake for comparing male diabetics with controls were 0.970 (0.945, 0.996), while in the female participants OR for folate and riboflavin intakes were 1.004 (1.001, 1.006) and 0.593 (0.393, 0.893), respectively. The multi-collinearity was checked, and no obvious collinearity was noted.

Table 3
Predictors of diabetes using the binary logistic regression analysis

Variables	OR (95% CI)	P value	Collinearity	
			TOL	VIF
Gender (Female)	0.657 (0.536, 0.805)	<0.001	0.585	1.711
Age (year)	1.037 (1.029, 1.045)	<0.001	0.682	1.467
WC (Abdominal obesity)	1.840 (1.503, 2.252)	<0.001	0.830	1.205
Folate (µg)	1.002 (1.000, 1.004)	0.022	0.660	1.516
Niacin (mg)	0.965 (0.944, 0.986)	0.001	0.419	2.387
Note: OR, Odds ratio; CI, confidence interval; TOL, Tolerance; VIF, Variance Inflation Factor.				

Table 4
Predictors of diabetes according to gender

Variables	Male				Female			
	OR (95% CI)	P value	Collinearity		OR (95% CI)	P value	Collinearity	
			TOL	VIF			TOL	VIF
Age (year)	1.024 (1.013, 1.035)	<0.001	0.707	1.414	1.052 (1.040, 1.064)	<0.001	0.652	1.534
Place of residence (Urban)	0.569 (0.362, 0.895)	0.015	0.786	1.273	-	-	-	-
General obesity	-	-	-	-	1.458 (1.015, 2.096)	0.041	0.855	1.170
Abdominal obesity	1.378 (1.035, 1.834)	0.028	0.850	1.176	2.089 (1.532, 2.848)	<0.001	0.804	1.244
Riboflavin (mg)	-	-	-	-	0.593 (0.393, 0.893)	0.012	0.405	2.469
Folate (µg)	-	-	-	-	1.004 (1.001, 1.006)	0.002	0.626	1.598
Niacin (mg)	0.970 (0.945, 0.996)	0.024	0.426	2.349	-	-	-	-
Note: OR, Odds ratio; CI, confidence interval; TOL, Tolerance; VIF, Variance Inflation Factor.								

Restricted Cubic Spline

Figure 1 and Figure 2 depicted the results of the restricted cubic spline analyses. The odds ratios of diabetes increased with increasing folate intakes until around 36.8 µg and then started to decrease. The ORs of diabetes increased with the increase of niacin intakes until around 6.9 mg, then showed a reduction until 20.2 mg, and then increased thereafter.

Discussion

In the present study, a prevalence of diabetes of 15.9% was reported, suggesting that it was prevalent in Chinese adults. This study also investigated the relationship between the intake of each vitamin with diabetes and found that dietary

folate and vitamin E intakes were significantly higher in diabetic patients than in controls, while dietary thiamine, riboflavin, niacin and vitamin C intakes were significantly lower. After adjusting for potential confounders, subjects with diabetes had a greater odds ratio for dietary folate intake and lower OR for niacin intake in comparison to those without diabetes. In addition, the plots of restricted cubic splines presented an inverted U-shaped association between dietary folate intake and the risk of diabetes. According to gender, there were significant differences in the folate intake for women, and niacin intake for men between the diabetes and normoglycemia groups.

B group vitamins are essential water-soluble nutrients. Folate (vitamin B9) can be found in a wide variety of food, such as vegetables, fruits and nuts ^[25]. Dietary intake of folate was inversely associated with incident diabetes in Korean or Japanese women reported by previous two prospective cohort studies ^[10–11]. Diabetes is an oxidative stress disease, folate deficiency has been linked to oxidative stress in diabetic patients ^[8]. Deficiency of folate has also been reported to severely hamper biosynthesis and secretion of insulin in pancreatic β -cells ^[26]. However, our study showed that people with diabetes had higher dietary folate intakes than the controls. The anti-diabetes drug metformin may cause folate deficiency. In a randomized controlled trial (RCT), after eight weeks of folate supplementation, diabetic men taking metformin showed improved serum total antioxidant capacity ^[27]. Thus, there is a possibility that higher folate intake in diabetics may be due to the reverse causality. The diabetics might have been advised to change their dietary habits during routine examinations.

Niacin (vitamin B3) can be found in meat (especially liver and heart), fish, nuts, and some fruits and vegetables and coffee ^[28]. Niacin is known to lower triglycerides and low-density lipoprotein cholesterol levels while significantly increasing high-density lipoprotein cholesterol levels ^[29]. Few studies have assessed the relationship between dietary niacin intake and diabetes. Inadequate intake of niacin from food may have not been recognized as a problem. The present study indicated that individuals with low niacin intake had a high likelihood of having diabetes. However, a Japanese study concluded that dietary intake of niacin was not associated with a reduced risk of diabetes ^[11]. An RCT study ^[30] showed that the use of niacin for 3 years in subjects with normal baseline glucose levels was associated with an increase in blood glucose levels and the risk of developing impaired fasting glucose. While Sazonov et al. ^[14] reported that niacin has clinically insignificant negative impact on glycaemia. However, further research about the relationship between dietary niacin intake and the risk of diabetes is needed.

Thiamine, also known as vitamin B1, plays a role in various cell functions, such as energy metabolism and the breakdown of sugars and carbon skeletons ^[31]. Riboflavin, also known as vitamin B2, plays a role in tryptophan metabolism, iron absorption, gastrointestinal tract, brain function, mitochondrial function, and other vitamins' metabolism ^[32]. In this study, the dietary intakes of thiamine and riboflavin in diabetic patients were significantly lower than that in the control group. Moreover, riboflavin intake was independently associated with the risk of diabetes in women. Insufficient thiamine level causes inadequate glucose metabolism in mitochondria ^[31]. Taking thiamine for a month has been shown to decrease glucose in diabetics when compared to controls ^[33]. Meanwhile, Md Maroof Alam et al. ^[34] suggested that supplementation with dietary riboflavin might help in the reduction of diabetic complications.

Vitamins C as an antioxidant was found decreased in diabetic patients, possibly due to an increased need to control the excessive oxidative stress caused by abnormal glucose metabolism ^[8]. Plasma vitamin C concentrations have been significantly and inversely associated with glycosylated hemoglobin and fasting and postprandial blood glucose and oxidative stress ^[35–36]. Vitamin E has a very important antioxidant role in the organism and has been found decreased in patients with diabetes ^[37]. However, other studies have shown no association with risk of diabetes or no effect on insulin sensitivity ^[38–39]. Our study showed lower dietary vitamin C and higher vitamin E intakes in diabetic patients. The effect of vitamins C and vitamin E on the risk of diabetes is likely due to its role as an antioxidant.

Several potential limitations warrant mention. First, this study is a cross-sectional design, which does not allow to establish the temporality of cause-effect relationship with certainty. Second, the information of using glucose-lowering drugs or vitamin supplements was not investigated, which may have affected the results. Third, vitamin intake data were obtained through a three-day dietary questionnaire review, which could not accurately reflect an individual's dietary intake due to faulty memory and underreporting. Finally, the study sample was recruited in Bengbu city and was not necessarily representative of all the general populations, which may limit the generalizability of our findings. In spite of this, we have adjusted for some known and proposed potential confounders for reliability in binary logistic regression models and restricted cubic splines analyses, and our findings added to the limited data available on the association of dietary vitamin intakes with the risk of diabetes in Chinese populations.

Conclusions

In conclusion, a dose response relationship between dietary folate and niacin intakes with the odds ratios of diabetes suggest the importance of these kind of vitamins rich diet in the management of diabetes. As vitamin intakes is a simple and feasible indicator of diabetes, increasing B group vitamins intakes among adults may offer promise as a cost-effective strategy to improve diabetes. Larger longitudinal and interventional studies are needed to quantify preventive and therapeutic levels of dietary vitamin intakes, especially the folate and niacin, for control of diabetes in clinical practice.

List Of Abbreviations

OR, Odds ratio

CI, confidence interval

BMI, Body mass index

WC, waist circumference

FPG, fasting plasma glucose

TOL, Tolerance

VIF, Variance Inflation Factor

RCT, Randomized Controlled Trial

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Bengbu medical college. All participants were required to complete the whole survey and sign informed consent.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Author contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Yuhong Jiang, Zhiwen Zhang, Yi Zhu and Yongfei Chai. The first draft of the manuscript was written by Yuhong Jiang and Hong Xie, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Figures

Figure 1

Restricted cubic spline model of the odds ratios of diabetes with dietary folate intake. Adjusted for gender, age, educational level, marital status, place of residence, smoking, general obesity and abdominal obesity. The dashed lines represent the 95% confidence intervals.

Figure 2

Restricted cubic spline model of the odds ratios of diabetes with dietary niacin intake. Adjusted for gender, age, educational level, marital status, place of residence, smoking, general obesity and abdominal obesity. The dashed lines represent the 95% confidence intervals.