Original Article

# Association between dietary pattern and the risk of type 2 diabetes mellitus in Zhejiang Province, China: A case-control study

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**Background and Objectives:** Diet is a modifiable risk factor of T2DM with the potential to improve the patients' quality of life. The diet–diabetes relationship has received considerable attention in past decades. This study describes dietary intake of nutrients in a matched case-control study of adults with and without T2DM. **Methods and Study Design:** Dietary nutrient intake was evaluated by semi-quantitative FFQ and biochemical indexes were studied in enrolled 207 participants with T2DM (diabetes group) and 215 healthy participants (control group). The t-test of two independent-sample and chi-square test were used to compare data by age and other characters. Exploratory factor analysis was used for dietary pattern analysis. Logistic regression analysis were used to test the effect of different dietary patterns and dietary intakes on the risk of T2DM. **Results:** The blood glucose, triglyceride and low-density lipoprotein cholesterol levels were significantly higher in the diabetes group ($p<0.05$). Three major dietary patterns were identified, "High-salt and high-fat", "Traditional Chinese" and "Western" dietary patterns. With or without adjustment, highest quintile of high-salt and high-fat dietary pattern showed a significantly higher risk of T2DM than the lowest quintile. (OR=2.08, 95%CI: 1.24, 3.49, OR=1.70, 95%CI: 0.98, 2.54, OR=1.67, 95%CI: 0.97, 2.51). **Conclusions:** Individuals with a high-fat and high-salt dietary pattern had an increased risk of T2DM. These findings offered further insights into the dietary structure of T2DM patients. These findings put nutrition education at the center for T2DM patient management. Further follow-up study is needed to assess the dynamic changes of nutrient-metabolism association.

**Key Words: nutrient intake, type 2 diabetes mellitus, case-control study, nutrition education, life quality**

## INTRODUCTION

Diabetes mellitus affects 285 million adults worldwide (global prevalence: 6.4%) and costs the international health care system 367 billion USD annually.[1] It is also one of the most significant emerging public health problems in Asian countries. According to a 1994 study, the incidence of type 2 diabetes mellitus (T2DM) in China was the lowest in the world (0.72%).[2] However, with the increasing economic prosperity, T2DM was estimated to affect 9.7% (92.4 million) of the Chinese population in 2010.[3]

The diet–diabetes relationship has received considerable scientific attention over the past decades. High caloric intake increases the risk of T2DM by increasing body weight and decreasing insulin sensitivity.[4] Refined carbohydrates, especially those containing high fructose, may increase the risk of T2DM by increasing insulin resistance.[5] International evidence has identified that some dietary items, such as whole-grain rich foods, cereal fiber, legumes, and green leafy vegetables, play a protective role against chronic conditions including T2DM.[6-8] The nutritional composition (i.e., fiber, vitamins and minerals) of protective foods may decrease the risk of T2DM by reducing inflammation while improving glucose metabolism, endothelial function, and insulin sensitivity.[9]

Diabetes educators should have a clear understanding of the differences of diet choice between non-T2DM individuals and T2DM patients. The aim of this study is to provide a detailed description of dietary patterns or different dietary intake between age-, gender-, Body mass index (BMI)- and social class-matched and the risk of T2MD in Zhejiang Province, China.

## METHODS

### *Study design and participants*

This research was approved by the medical ethics committee of Sir Run Run Shaw Hospital. This case-control study was conducted from February 2014 to February 2015 at Sir Run Run Shaw Hospital in Hangzhou, Zhe-

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jiang Province, China. A total of 207 individuals diagnosed with T2DM treated by the endocrinology and metabolism departments of the hospital at the outpatient clinic were enrolled. The following details were recorded for each participant: social demographic characteristics (including gender, age, body mass index, and waist circumference), lifestyle behaviors, diabetic history, lipid profile, blood pressure, and kidney function. All medical tests were performed on the same day. Participants who met the following criteria were enrolled in the study: (a) age <70-year and (b) a diagnosis of T2DM according to the World Health Organization criteria.10 Patients with the following characteristics were excluded from this study: BMI (<19 kg/m$^2$); heavy cigarette smoking (>20 cigarettes/day),[11] heavy alcohol consumption (>1000 mL of beers or equivalent drinks per day),[12] and heavy consumption of caffeinated beverages (>5 cups of brewed tea or equivalent drinks per day).[13]

Control subjects (n=215) were selected from individuals without T2DM undergoing routine annual medical checkups and a series of biochemical tests, including blood glucose, insulin sensitivity, and beta-cell function, at the Sir Run Run Shaw Hospital outpatient clinic during the same time period. We matched the age, gender, and residence area of the diabetes and control groups. Those who had a past medical history or family history of diabetes mellitus were not included in the control group (see Figure 1).

### *Variable measurements*

Specialist nurses collected baseline information from patients when first diagnosed with T2DM. Each patient received a clinical examination and met with a dietitian. At follow-ups, Patients were asked to report back a simple questionnaire that called quantitative food frequency questionnaire (FFQ) and had blood drawn for laboratory tests.

### Assessment of dietary intake

Dietary intake was evaluated by using a 143-item (9 food groups with 20 categories) semi-quantitative FFQ. The FFQ was based on the food frequency questionnaire used in the 2010 China National Nutrition and Health Survey (CNNHS). The food group including grains, vegetables, beans and their products, mushrooms, algae, fruits and products, nuts, meat and eggs, preserved foods, dairy products, beverages, other pastry snacks, condiments.[14] Participants were required to recall the frequency of each food item over the past year and the estimated portion size, using local weight units (1 Liang = 50 g) or natural units (cups) Intakes of food were converted into g/d and used in the following analysis.

### Laboratory examination

Blood samples (5-6mL) were collected by a vein puncture method from all the participants in the morning, following a 12-hour fasting. Serum concentrations of glucose, hemoglobin A1c (HbAlc), triacylglycerols (TG), total cholesterol (TC), and high-density lipoprotein cholesterol (HDL-C) were measured on an SynchronLX[20] analyzer (Beckman Coulter Inc., CA, USA) using the appropriate reagents. Low-density lipoprotein cholesterol (LDL-C) was calculated using the formula, which is reliable in the absence of severe hyperlipidemia: TC – HDL-C – (TG / 2.2).

### *Statistical analyses*

The data were analyzed using SAS9.2 and SPSS17.0 software (SPSS Inc., Chicago, Il, USA). Normality distribution of the quantitative data was measured using the Kolmogorov-Smirnov test, and nonparametric tests were used because the data was not normally distributed. To

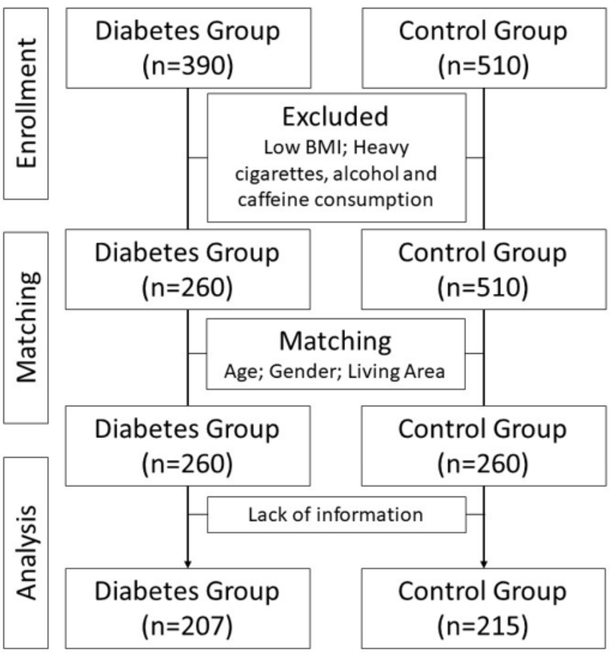


**Figure 1.** Enrollment and Matching. Reasons for exclusion included low body mass index (BMI) (<19 kg/m$^2$); heavy cigarette smoking (>20 cigarettes/day), heavy alcohol consumption (>1000mL of beers or equivalent drinks per day), heavy consumption of caffeinated beverages (>5 cups of brewed tea or equivalent drinks per day), unmatched epidemiological characters and loss of follow-up.

compare the case and control groups, an independent t-test and the Mann-Whitney U test were employed for continuous variables and categorical variables, respectively. Exploratory factor analysis was used for dietary pattern analysis, and each food frequency was converted into the number of intakes per week. Considering that low intake of food may affect the assumptions of factor analysis and produce incorrect factor estimates, it is appropriate to use Kaiser sampling Measurement method. Finally, 24 foods or food types were identified from 100 foods to enter factor analysis. Factor extraction principal component analysis method, in order to make each factor more clear and professional, Varimax rotation of the initial factor load matrix, Kaiser-Meyer-Olkin and Bartlett spherical test before analysis, suggesting whether it is suitable for factor analysis. Combining lithotripsy, characteristic roots, rationality of food combination, and variance contribution rate to determine the main dietary pattern. After obtaining the standard factor scores, the factor score model expressed by the original index is converted, and the factor scores of the individual dietary patterns are calculated by the regression method. Only foods with a factor loading ≥|0.40| were included in this study. Dietary patterns and dietary intake were divided into five groups by using quintile and in accordance with dietary pattern scores, with the lowest quintile as a reference. Logistic regression analysis were used to test the effect of different dietary patterns and dietary intakes on the risk of T2DM, with adjustment for age, sex, education level, per capita income, marital status, residence place, smoking status (current or no smoke), alcohol consumption (current or no drink), total energy and fat intake confounding factors.[15] Hypothesis test has a test level of 0.05.

## RESULTS

### *Study population demographics*

The median age of participants in the case group was 60.21 y, and that in the control group was 55.90 y. Age was converted from a continuous variable to an ordinal categorical variable with an interval of 10 years, according to the standard of the2002 Chinese National Health Survey. According to the FFQ investigation of nutrient intake, the energy, fat and fat supply in the case group were significantly higher than those in the control group ($p$<0.001), no significant differences were found in other nutrients and energy supply. A chi-square test showed no significant differences in gender, marriage status, residence area, economic status, or smoking behavior between the case and the control groups (see Table 1).

### *Biochemical parameters of cases and controls*

The biochemical parameters of the participants are shown in Table 2. No significant difference was observed in gender between the case and control groups. Compared with the control group, the age, plasma glucose levels, HbAlc, TG, and LDL-C levels were significantly higher in the case group. The plasma levels of uric acid (UA), TC and HDL-C were significantly lower in the case group than in the control group

### *Dietary patterns and characteristics*

According to the factor analysis results, three main factors were extracted, and their characteristic roots were 19.79, 10.03, and 5.60, respectively, and the contribution rate of variance was 35.42%. According to the type of food in the factor load, the food pattern is named after the food type to which the factor with the highest absolute value of the factor load belongs. Three major dietary patterns were identified by factor analysis: "high-salt and high-fat" pattern, which is characterized by a high frequency of high intakes of salted meats or bacon, salted foods, fats and oils, and refined grains and their products; the "traditional Chinese" pattern, which is characterized by high intakes of wholegrains and related products, vegetables and fruit, beans and their products; the "Western" pattern. The main feature is high intakes of raw meat, aquatic product and milk and its product. The factor-loading matrices for these dietary patterns are shown in Table 3.

### *Relationship between 3 dietary patterns and T2DM*

Unadjustment for confounding factor, fifth quintile of high-salt and high-fat dietary pattern had a significant higher T2DM risk than the lowest quintile of high-salt and high-fat dietary pattern (OR=2.08, 95%CI: 1.24, 3.49), While after adjusted for age, marital status, education, economic status, smoking, alcohol consumption in model 1shown fifth quintile of high-salt and high-fat dietary pattern had a significant higher T2DM risk than the lowest quintile of high-salt and high-fat dietary pattern again (OR=1.70, 95%CI: 0.98, 2.54), However, there were no significant differences for the effect of the quintiles of the traditional Chinese and Western dietary pattern on the risk of T2DM. Three effects of the quintiles of the different dietary pattern on the risk of diabetes are presented in Table 4.

## DISCUSSION

In the present matched case-control study, we assessed the association between nutrient intake and blood glucose and lipid metabolism in Zhejiang Province China with and without T2DM, and found more the intake of high-fat and high-salt dietary pattern, more the increased risk in T2DM, T2DM has a widespread harmful effect on patients in terms of health condition and life quality. One case control study showed that Chinese with T2DM had an increased risk of hyperglycemia and coronary heart disease and a similar risk of high blood pressure, abnormal lipids, diabetic nephropathy and stroke.[16] Risk factors for diabetes vary. Fortunately, some of them are within patients' control to change through the modification of lifestyles. Diet is one of the modifiable risk factors for T2DM that requires much attention in China, where the eating habit is shifting towards fat-and-protein rich foods. Therefore, we carried out this study of the dietary structure of Zhejiang Province, China with and without T2DM to further assess and compare their nutrient intake.

Increasing evidence suggested that high intake of Western and high-fat and high-salt dietary patterns were associated with incremental risk of T2DM,[17] while it was not observed in our study. No significant association could be due to the reverse causality. Study participants with a risk of T2DM might have been advised to reduce their food and sugar intake, thereby changing dietary hab-

**Table 1.** Demographics of study participants

| Characteristic | Cases (n=207) | Controls (n=215) | $\chi^2/t$ | *p*-value |
|---|---|---|---|---|
| Age (years) | | | | |
| Median (intervals of quartile) | 60.2 (19.5) | 55.9 (29.3) | | |
| Age (year), n (%) | | | | |
| ≤45 | 77 (19.7) | 135 (34.4) | | |
| 46~ | 71 (18.2) | 55 (14.0) | | |
| 56~ | 111 (28.5) | 98 (25.0) | | |
| 66~ | 99 (25.4) | 63 (16.1) | | |
| ≥76 | 32 (8.2) | 41 (10.5) | 6.50 | 0.117 |
| Nutrients intake | | | | |
| Energy (kcal) | 2. 14*$10^3$±320 | 1.95*$10^3$±216 | 15.8 | <0.001 |
| Protein (g) | 79.0±11.8 | 76.5±11.5 | 1.67 | 0.164 |
| % Total energy | 14.80±0.88 | 14.88±1.56 | 1.74 | 0.657 |
| Carbohydrate (g) | 258.9±43.7 | 249.7±35.8 | 2.41 | 0.111 |
| % Total energy | 48.2±1.48 | 47.1±4.36 | 1.83 | 0.524 |
| Fat (g) | 87.8±11.5 | 73.4±10.5 | 11.0 | <0.001 |
| % Total energy | 37.0±0.94 | 33.91±3.2 | 4.11 | <0.001 |
| Gender, n (%) | | | | |
| Males | 143 (36.7) | 160 (41.2) | | |
| Females | 247 (63.3) | 233 (59.3) | 2.94 | 0.087 |
| BMI (kg/$m^2$) | 23.6 (2.91) | 21.6 (2.84) | 3.15 | 0.052 |
| Marital status, n (%) | | | | |
| Married | 327 (83.9) | 315 (80.2) | | |
| Unmarried | 47(16.2) | 51 (13.0) | 2.48 | 0.115 |
| Present residence†, n (%) | | | | |
| Resident | 374 (96.0) | 366 (93.1) | | |
| Migrant | 16 (4.10) | 27 (6.87) | 0.30 | 0.590 |
| Education status, n (%) | | | | |
| Primary school or below | 139 (35.6) | 81 (20.6) | | |
| Middle school | 191(49.0) | 210 (53.4) | | |
| College | 44 (11.3) | 75 (19.1) | 24.18 | <0.001 |
| Economic status (yuan/person/year), n (%) | | | | |
| Low (≤19999) | 141 (36.2) | 161 (41.0) | | |
| Medium (20000-34999) | 174 (44.6) | 151 (38.4) | | |
| High (≥35000) | 58 (14.9) | 63 (16.0) | 3.15 | 0.207 |
| Cigarette smoking‡, n (%) | | | | |
| Current smokers | 51 (13.1) | 65 (16.5) | | |
| Non-smokers | 335 (86.9) | 323 (82.8) | 1.90 | 0.191 |
| Alcohol intake, n (%) | | | | |
| Current drinkers | 121 (31.0) | 94 (23.9) | | |
| Non-drinkers | 268 (68.7) | 299 (76.1) | 5.07 | 0.024 |

†Usually residing in an area for 6 months or more.
‡Smoking 1 or less than 20 cigarettes per day for a period of 6 months or more consuming alcohol at least once per day, or ≤the equivalent of 5 beers per day

**Table 2.** Biochemical parameters in case and control groups†

| Parameters | Control (n=215) | Case (n=207) | *p* |
|---|---|---|---|
| Age (year) | 60.2 (19.5) | 55.9 (29.4) | <0.001 |
| Glucose (mmol/L) | 5.08 (4.79, 5.42) | 10.31 (7.76, 13.80) | <0.001 |
| HbAlc (%) | 4.96 (3.94,5.98) | 7.18 (6.12, 8.24) | 0.004 |
| UA (μmol/L) | 310 (261, 357) | 278 (233, 351) | 0.008 |
| TG (mmol/L) | 1.33 (0.97, 1.91) | 1.54 (1.07, 2.19) | 0.011 |
| TC (mmol/L) | 5.09 (4.59, 5.77) | 4.78 (4.03, 5.61) | <0.001 |
| HDL-C (mmol/L) | 1.52 (1.21, 1.80) | 1.16 (1.02, 1.40) | <0.001 |
| LDL-C (mmol/L) | 2.54 (2.05, 2.94) | 2.87 (2.19, 3.41) | <0.001 |

HbAlc: hemoglobin A1c; UA: uric acid; TG: triglyceride; TC: total cholesterol; HDL-C: high density lipoprotein-cholesterol; LDL-C: low density lipoprotein-cholesterol.
†Data were expressed as percentages; other data were expressed as median.

**Table 3.** Rotated factor loading matrix for the four dietary patterns among among 422 subjects

| Food groups | Dietary patterns | | |
|---|---|---|---|
| | High-salt and high-fat | Traditional Chinese | Western |
| Refined grains and their products | 0.581 | — | — |
| Whole grain and related products | — | 0.764 | — |
| Vegetables and fruits | — | 0.650 | — |
| Raw meats | | — | 0.561 |
| Salted meat/bacon | | | 0.640 |
| Salted food | 0.560 | — | — |
| Aquatic products | — | — | 0.757 |
| Milk and its product | — | — | 0.463 |
| Beans and their products | — | 0.476 | — |
| Fats and oils | 0.564 | — | — |

The food items were considered to be strongly associated with the dietary pattern that factor load absolute values were more than 0.4.

**Table 4.** The odds ratio of diabetes according to quintiles of different dietary pattern among 422 subjects

| Dietary pattern | Quintiles† | OR (95%CI) | | |
|---|---|---|---|---|
| | | Model 1‡ | Model 2§ | Model 3¶ |
| High-salt and high-fat | Q1 | 1 | 1 | 1 |
| | Q3 | 1.55 (0.89, 2.63) | 0.87 (0.41, 1.85) | 0.89 (0.41, 1.92) |
| | Q5 | 2.08 (1.24, 3.49)* | 1.70 (0.98, 2.54)* | 1.67 (0.97, 2.51) |
| Traditional Chinese | Q1 | 1 | 1 | 1 |
| | Q3 | 0.73 (0.45, 1.18) | 1.03 (0.51, 2.08) | 1.04 (0.50, 2.14) |
| | Q5 | 0.84 (0.52, 1.34) | 1.26 (0.64, 2.47) | 1.20 (0.60, 2.41) |
| Western | Q1 | 1 | 1 | 1 |
| | Q3 | 1.74 (1.04, 2.90) | 1.56 (0.74, 3.27) | 1.49 (0.70, 3.19) |
| | Q5 | 1.56 (0.92, 2.63) | 1.83 (0.87, 3.86) | 1.63 (0.75, 3.51) |

OR: odds ratio; CI: confidence interval.

†Q1, Q2, Q3: according to dietary patterns and dietary intake were divided into five groups, Q1, <20% (reference level, OR=1.00), Q2, 20%–80%, Q3, 80%–100%; *$p<0.05$.

‡Model 1: unadjusted;

§Model 2: adjusted for age, marital status, education, economic status, smoking, alcohol consumption;

¶Model 3: adjusted for age, marital status, education, economic status, smoking, alcohol consumption, total energy and fat intake

its. This possibility cannot be excluded in a cross-sectional study. In addition, crucial reasons are study participant size and more the number of study participants, the more accurate results will be. The study participants are restricted to 422 Chinese population at Sir Run Run Shaw Hospital in Hangzhou, Zhejiang Province, China. Thus, regional differences can influence the result, which may not be consistent with previous numerous studies.

Considerable studies indicated that dietary carbohydrate may influence postprandial blood glucose and consequently, insulin secretion. The glycemic index (GI) is a tool that allows for the quantification of the postprandial blood glucose response to dietary carbohydrate from foods.[18] The consumption of high-GI foods, such as those rich in refined dietary carbohydrate (just presented in high-fat and high-salt dietary pattern), induces a rapid increase in blood glucose concentration and thus a high demand for pancreatic insulin production. Excessive consumption of foods with a high GI would thus be expected to elevate the demand for insulin, which could ultimately lead to exhaustion of pancreatic β-cells and the development of T2DM.[19] Evidence from epidemiological investigation also suggested that the refining process had changed the composition and thus the quality of carbohydrates.[20] The association between high intakes of refined cereal and the risk of T2DM could have the following mechanisms. On the one hand, high intakes of processed carbohydrate food could cause expansion of adipose tissue, increased glucose utilisation, lipoproteinase activity, making the body in chronic low grade inflammation state.[21] On the other hand, high intakes of refined grain could strikingly increase the levels of inflammatory factors such as tumor necrosis factor alpha, interleukin 6, interleukin 10, interleukin and transforming growth factor beta in adipose tissue[22] and those inflammatory states and inflammatory factors may be a key component in the pathogenesis of T2DM. Whole grains usually contain low-saturated fatty acids, high-dietary fiber, vitamins (especially B vitamins), minerals and a wide range of phytochemicals, which are associated with increased intestinal probiotics and improved healthy outcome. Research showed that the imbalance of these probiotics might have an important effect on the pathogenesis of cardiovascular disease.[23] Furthermore, loss of the outer bran layer and stratification of the endosperm allow the finished product to be digested by human digestive enzymes faster than whole grains.[24] As such, refined carbohydrates could contribute to a rapid increasing in blood glucose and insulin levels compared to whole grain products, while high-insulin stimulates insulin-like growth factor IGF-1 through growth stimulation, promote vascular smooth muscle cell proliferation and increase the risk of diabetes.[25]

Our research has limitations, which affects the interpretation of the results. First and foremost, different dietary intakes were estimated by using a semi-quantitative food frequency questionnaire, so recall bias seems to be inevitable and estimation of food intake seem to be inaccurate.

Second, although the case groups were all from newly diagnosed diabetes, we did not know whether they had a hyperglycemia before diagnose, which affect study participants dietary habits, like they might have been advised to reduce their food and sugar intake. Third, the present study was a case-control investigation and causality was difficult to be identified in a case-control study. Thus, our results still need to be confirmed in a prospective cohort study.

### *Conclusions*

In summary, this case-control study provides a detailed picture of how self-reported food intake differs between individuals with T2DM attending a hospital-based diabetes service compared with similar adults without diabetes. We found that, individuals consumed more the intake of high-fat and high-salt dietary pattern, more the increased risk in T2DM, These findings offer insights into the dietary structure intake of T2DM patients and put nutrition education at focus for those patients. The effects of dietary habits can take a long time to develop. Therefore measures to improve the dietary structure of T2DM patients are needed with a follow-up study to dynamically assess their nutrient-metabolism association.

## AUTHOR DISCLOSURES

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