European Journal of Nutrition (2018) 57:2953–2962
https://doi.org/10.1007/s00394-017-1569-x

ORIGINAL CONTRIBUTION

Fruit and vegetable intake and pre-diabetes: a case–control study

Maryam Safabakhsh[1] · Fariba Koohdani[2] · Fariba Bagheri[1] · Fereydoun Siassi[1] · Farahnaz Khajehnasiri[3] · Gity Sotoudeh[1]

Received: 26 July 2017 / Accepted: 17 October 2017 / Published online: 4 December 2017

Abstract

Purpose Few studies have evaluated the association of fruit and vegetable (FV) intake and pre-diabetes. However, these studies are very limited and incomplete. Therefore, the aim of our study was to compare FV consumption and their subgroups between pre-diabetic and control subjects.

Methods This case–control study included 300 individuals, 150 subjects with normal fasting blood glucose (FBG), and 150 pre-diabetic subjects who were matched for sex and age. We collected the participants' anthropometric and physical activity data and measured their blood glucose level. A 168 items semi-quantitative food frequency questionnaire (FFQ) was used for estimating the FV intake.

Results After adjustment for confounding variables, participants in the lower quartiles of FV and total fruit intake were more likely to experience pre-diabetes compared with those in the higher quartiles (p trend < 0.007). In addition, cruciferous vegetables, other vegetables, and berries were inversely associated with pre-diabetes ($p < 0.05$), although a distinct dose–response relationship was not found. Unexpectedly, higher intake of dark yellow vegetables was significantly associated with a higher chance of pre-diabetes (p trend = 0.006). Other vegetable and fruit subgroups did not show any significant relationship with this disorder.

Conclusion Our findings suggest that higher intake of total FV and total fruits might be associated with lower odds ratio of pre-diabetes.

Keywords Pre-diabetes · Fruits · Vegetables · Case–control · Impaired fasting glucose

Abbreviations

FV	Fruits and vegetables
FBG	Fasting blood glucose
BMI	Body mass index
USDA	United States Department of Agriculture
IFG	Impaired fasting glucose
IGT	Impaired glucose tolerance
ADA	American diabetes association
FFQ	Food frequency questionnaire
OGTT	Oral glucose tolerance test
T2DM	Type 2 diabetes mellitus
WHO	World Health Organization
WC	Waist circumference
IPAQ	International physical activity questionnaire
MET	Metabolic equivalent task
HEI	Healthy eating index
OR	Odds ratio

✉ Fereydoun Siassi
siassif@tums.ac.ir

✉ Gity Sotoudeh
gsotodeh@tums.ac.ir

1 Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences, Hojatdost Street, Naderi Street, Keshavarz Blv., Tehran, Iran

2 Department of Cellular, Molecular Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences, Tehran, Iran

3 Department of Social Medicine, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

Introduction

Obesity, physical inactivity, and imbalanced dietary patterns may increase the prevalence of chronic diseases like type 2 diabetes mellitus (T2DM) [1]. The World Health Organization (WHO) projects that T2DM will affect 552 million cases and will be the seventh leading cause of death in 2030 [2]. Pre-diabetes is a condition that includes impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT). American Diabetes Association (ADA) defines IFG as glucose levels of 100–125 mg/dl and IGT as 2-h glucose levels of 140–199 mg/dl on the 75-g oral glucose tolerance test (OGTT) [3]. Pre-diabetes may lead to T2DM and about 5–10% of people with pre-diabetes will eventually develop T2DM every year [4].

A healthy diet combined with physical activity is crucial to overcome this issue and improve the health status [5]. According to an international recommendation, the daily intake of five servings of fruits and vegetables (FV) in all forms provides a reasonable amount of fiber; vitamins, especially folate, vitamin C, vitamin E, and vitamin B6; carotenoids; minerals, particularly potassium, and magnesium; and certain phytochemicals such as phenolics and flavonoids with antioxidant activity [6, 7]. These compounds decrease the incidence and mortality of many chronic diseases [6]. In addition, the health benefits of FV are attributed to the synergy or interaction of bioactive compounds and nutrients [8].

Although a comprehensive analysis of the epidemiological studies did not show the effect of high consumption of FV on the risk of T2DM [1], a recent meta-analysis showed that higher intake of fruits, especially berries, green leafy vegetables, yellow vegetables, and cruciferous vegetables, was associated with a lower risk of T2DM [9]. It has been suggested that subgroups of fruits and vegetables do not affect the risk of diabetes equally, maybe due to their different contents of fiber, antioxidants, phytochemicals, and other nutrients [9]. Higher consumption of cruciferous vegetables, which are rich in glucosinolates with antioxidant properties, is related to a lower risk of T2DM in cohort studies [10]. Previous cross-sectional and prospective studies showed that intake of green vegetables, rather than total intake of vegetables, may prevent the occurrence of T2DM [11, 12]. It has been suggested that higher intake of green and yellow vegetables leads to higher serum β-carotene levels, which mediates the oxidative stress and improves insulin sensitivity [10, 12]. Furthermore, it has been shown that variety in the fruits consumed is associated with a lower risk of T2DM in a prospective study [11]. Results from three prospective longitudinal cohort studies showed that higher consumption of individual fruits such as the blueberry, grapes, apple, banana, and grapefruit is also associated with a lower risk of T2DM [9]. The prune, peach, plum, apricot, and apple contain chlorogenic acid [13], which decreases glucose absorption in rats [14]. In diabetic rats, citrus pectin improves glucose tolerance [15]. The grapefruit is also a source of naringin [16], which improved glucose tolerance in a study in rats with in vitro and in vivo design [17]. Adversely, results from prospective studies showed that adding cantaloupe to the diet increases the risk, which is justified by its high glycemic index (60–70) [9]. Melons have lower levels of phytochemicals compared to some other fruits [16]. However, its effect on glucose metabolism is not clear. Therefore, it is better to evaluate individual fruits and vegetables or their specific subgroups.

Although most studies have addressed the relationship between FV intake and T2DM, a few studies have evaluated the association of FV intake and pre-diabetes. A cross-sectional study among Framingham offspring suggested that diets rich in fruits, vegetables, whole grains, and low in fat are associated with lower IFG and IGT [18]. Moreover, a cross-sectional study showed that diets rich in vegetables and fruits are inversely associated with IFG in Chinese men [19]. Assessment of the intake of FV has been shown to be useful for existence of oxidative stress and inflammation in pre-diabetic subjects [6].

In comparison with T2DM, pre-diabetes does not present with distinct clinical symptoms, so it can be managed by nutritional interventions [6]. The priority is to prevent pre-diabetes or decrease its prevalence instead of treating T2DM and cardiovascular disease. Although the relationship between the intake of FV and pre-diabetes has been reported in a few studies, the association of specific subgroups of FV and pre-diabetes has not been investigated yet. Therefore, the aim of our study was to determine the relationship between the consumption of FV and their specific subgroups and pre-diabetes.

Methods

Subjects

The subjects were recruited from a diabetes screening center in Shahreza, Iran from May to October 2014. The aim of the study was to determine the relationship between dietary intake and pre-diabetes using a matched case–control study design. The detailed methodology of the study was described previously [3] and is described here in brief. The participants were 300 subjects who attended a diabetes screening center. Overweight or obese individuals who were above 30 years of age, and had a family history of diabetes or at least two symptoms of diabetes (excessive thirst, frequent urination, excessive hyperphagia) were considered at risk of diabetes and were referred to this center.

This study recruited 150 subjects who were diagnosed with pre-diabetes (cases) and 150 healthy subjects with normal FBG (control) at the clinic. We used the frequency matching method and matched the two groups by age and sex. The age frame for matching was as follows: 35–44, 45–54, and 55–65 years. The study criteria for the case group subjects were age 35–65 years, and fasting blood glucose (FBG) 100–125 mg/dl or 2-h OGTT 140–199 mg/dl diagnosed no longer than three months before the interview. The inclusion criteria for the control group were age

35–65 years, and FBG < 100 mg/dl and 2-h OGTT < 140 mg/dl during screening. Subjects with alcohol, drug and any tobacco product use, body mass index (BMI) ≥ 40 kg/m^2, or a special diet during the last year were excluded from the study. Moreover, pregnant or lactating women, and those with heart disease, diabetes, hypertension, dyslipidemia, hepatic or renal impairment, and multiple sclerosis were excluded, as well. The objective and protocol of the study were explained to the participants, and informed consent was obtained from them before the study. The Ethics Committee of Tehran University of Medical Sciences approved the protocol of this case–control study.

Anthropometric and physical activity assessment

During the first interview at the clinic, weight was measured with minimal clothing and without shoes. Standing height was measured without shoes by a Seca stadiometer (Seca 216). All measurements were done by a dietitian. To calculate the BMI, the weight was divided by the square of height (kg/m^2). A flexible measuring tape was used at the midpoint between the lowest rib and the iliac crest to measure waist circumference (WC). The International Physical Activity Questionnaire-short form was used to assess the physical activity of the participants [20]. Inquiries were made regarding vigorous and moderate activity and walking for at least 10 min/day during the previous 7 days. To calculate the activity, the duration and frequency of activity days were multiplied by the metabolic equivalent task (MET) value of the activity. The sum of the scores was calculated as the total physical activity per week.

Laboratory assessment

After an overnight fast, blood samples were drawn for FBG measurement. In addition, the participants underwent a 2-h OGTT. The plasma glucose level was measured at 546 nm using the photometric method (glucose oxidase method) [21].

Dietary assessment

Dietary intake was assessed by a dietitian on the first visit at the clinic. The usual dietary intake during the past year was assessed using a validated semi-quantitative FFQ which included 168 food items [22] (the year before the diagnosis of pre-diabetes for cases and the previous year for controls). The participants were asked to report the frequency of consumption for each food item in terms of daily, weekly, monthly, and yearly. For estimating daily food intake, the information of the FFQ was converted to g/day. The food items were analyzed for their energy and nutrients content using the Nutritionist IV software (First Databank, San Bruno, CA), modified for Iranian foods. The software database drawn from United States Department of Agriculture (USDA) food composition tables [23].

FV was divided into specific groups, including cruciferous vegetables, green leafy vegetables, other vegetables, berries, citrus fruits, and other fruits based on the previous studies [24, 25]. The Healthy Eating Index (HEI-2015) [26] score summarizes the consumption of 13 foods or nutrients, including total fruits, whole fruits, total vegetables, greens and beans, whole grains, dairy products, total protein foods, seafood and plant proteins, fatty acids, refined grains, sodium, added sugars, and saturated fats. Each component was scored on a scale of 0–10. Similar to another study [9], we excluded FV when calculating the HEI score.

Statistical analysis

Data analysis was performed using the SPSS version 16 (SPSS Inc.). The Kolmogorov–Smirnov test was used to evaluate the normality of the data. Data with a non-normal distribution were logarithmically transformed for statistical analyses. The geometric mean (standard error of mean) was calculated for the transformed data. The independent *t* test was used to compare quantitative variables between case and control groups. The mean values of the quantitative variables across the FV quartiles were compared using the ANOVA test. The ANCOVA was used to compare the mean FV intake in the case and control groups after adjusting for potential confounders including BMI, energy intake, and HEI score. Variables with *p* value < 0.05 in ANOVA test were selected for adjustment. In addition, based on evidence from the literature, we selected age and physical activity as potential confounders [27].

Total vegetable and total fruit intakes were mutually adjusted. For each vegetables and fruits subgroups, total fruit and vegetable intakes were adjusted. The relationship between the FV intake and chance of pre-diabetes was analyzed by simple logistic regression. In addition to the unadjusted analysis (Model 1), we used multivariable models to assess the relation between FV intake and pre-diabetes (Model 2). In Model 2, we adjusted for age, BMI, physical activity, energy intake, and HEI. Total vegetable and total fruit intakes were mutually adjusted. For each vegetables and fruits subgroups, total fruit and vegetable intakes were adjusted. Tests for trend were performed by entering the categorical variables as continuous parameters in the models. *P* values less than 0.05 were considered significant.

Results

The characteristics of the participants according to the quartiles of intake of total vegetables and fruits are presented in Tables 1, 2 and 3. Across increasing total FV (Table 1) and total vegetable (Table 2) quartiles, the subjects had lower BMI, WC, FBG and 2-h OGTT. In addition, the subjects had a higher energy intake and, as expected, had a higher HEI score with increasing total FV and total vegetable quartiles. Across increasing total fruit quartiles, the subjects had lower FBG and 2-h OGTT and higher energy intakes and HEI score ($p < 0.05$) (Table 3).

The comparison of FV intake between the case and control groups is shown in Table 4. The intake of total FV, total vegetables, cruciferous vegetables, green leafy vegetables,

Table 1 Characteristic of study participants according to quartiles of total vegetable and fruit intakes

	Quartiles of total vegetable and fruit intakes				
	1 (n = 74)	2 (n = 75)	3 (n = 74)	4 (n = 74)	p trend[a]
g/day (median)	363.1	566.2	771.7	1039.5	
Male (%)	23 (31.1)	28 (37.3)	26 (35.1)	24 (32.4)	0.9
Age (years)	48.1 ± 7.4	47.0 ± 7.6	47.8 ± 8.2	47.5 ± 6.5	0.7
Education (years)	6.8 ± 0.5[b]	6.1 ± 0.6	6.0 ± 0.5	7.6 ± 0.4	0.4
BMI (kg/m^2)	28.9 ± 4.0	28.6 ± 4.1	28.2 ± 3.5	27.2 ± 4.2	0.01
Waist circumference (cm)	94.1 ± 10.0	91.4 ± 11.7	91.6 ± 11.5	88.5 ± 10.3	0.004
Physical activity (MET/h/week)	631.7 ± 136.4[b]	709.7 ± 165.1	683.7 ± 141.6	868.8 ± 141.0	0.1
Dietary supplement use (%)	10 (13.5)	17 (22.7)	10 (13.5)	12 (16.2)	0.9
Energy intake (kcal/day)	2114.7 ± 721.2	2416.0 ± 696.8	2402.1 ± 527.9	2617.7 ± 690.3	< 0.001
Healthy eating index	39.4 ± 5.6	42.4 ± 8.2	46.8 ± 7.7	48.9 ± 7.5	< 0.001
Fasting blood glucose (mg/dl)	100.7 ± 13.1	99.6 ± 14.7	91.5 ± 16.5	90.1 ± 13.3	< 0.001
2-h glucose (mg/dl)	136.8 ± 18.1	134.4 ± 20.4	128.5 ± 17.2	127.2 ± 16.3	< 0.001

Values are means (standard deviations) or percentages unless stated otherwise

Fruits include strawberry, cran berry, blackberry, mulberry, orange, tangerine, sweet lemon, grapefruit, cantaloupe, melon, water melon, pears, apricot, cheery, apple, plum, peach, persimmon, nectarine, green gage, figs, kiwi fruit, pomegranate, date, plum, sour cherry, banana, pineapple, apple juice, cantaloupe juice, grapes, raisin, dry peach, apricot, and fruit juice

Vegetables include white cabbage, red cabbage, broccoli, cauliflower, spinach, lettuce, vegetable greens, carrot, yellow squash, cucumber, tomato, green squash, eggplant, celery, green peas, green beans, garlic, onion, bell peppers, turnip, mushroom, green peppers, olive, and corn

[a]ANOVA

[b]Geometric mean ± SEM

Table 2 Characteristic of study participants according to quartiles of total vegetable intakes

	Quartiles of total vegetable intakes				
	1 (n = 74)	2 (n = 75)	3 (n = 74)	4 (n = 74)	p trend[a]
g/day (median)	253.4	369.7	430.0	480.4	
Male (%)	24 (32.4)	29 (38.7)	22 (29.7)	26 (35.1)	0.9
Age (years)	48.1 ± 7.4	46.7 ± 7.8	48.6 ± 7.4	47.0 ± 7.0	0.7
Education (years)	6.6 ± 0.5[b]	6.9 ± 0.6	5.9 ± 0.5	6.9 ± 0.5	0.6
BMI (kg/m^2)	29.0 ± 4.4	28.3 ± 3.9	28.6 ± 3.7	27.1 ± 4.1	0.007
Waist circumference (cm)	93.4 ± 10.9	92.1 ± 11.9	91.2 ± 10.8	88.91 ± 10.1	0.01
Physical activity (MET/h/week)	595.7 ± 139.0[b]	779.6 ± 161.1	725.3 ± 140.9	789.6 ± 143.6	0.2
Dietary supplement use (%)	10 (13.5)	14 (18.7)	13 (17.6)	12 (16.2)	0.7
Energy intake (kcal/day)	2091.2 ± 734.2	2449.1 ± 667.1	2479.7 ± 652.2	2530.0 ± 600.0	< 0.001
Healthy eating index	39.1 ± 6.0	42.2 ± 6.8	46.5 ± 7.8	49.6 ± 7.9	< 0.001
Fasting blood glucose (mg/dl)	101 ± 13.2	98.9 ± 15.0	93.2 ± 14.6	88.8 ± 14.9	< 0.001
2-h glucose (mg/dl)	136.9 ± 17.1	134.6 ± 21.3	129.5 ± 18.5	125.9 ± 14.3	< 0.001

Values are means (standard deviations) or percentages unless stated otherwise

Total vegetables were defined as in Table 1

[a]ANOVA

[b]Geometric mean ± SEM

Table 3 Characteristic of study participants according to quartiles of total fruit intakes

	Quartiles of total fruit intakes				
	1 ($n=74$)	2 ($n=75$)	3 ($n=75$)	4 ($n=73$)	p trend[a]
g/day (median)	158.5	213.8	263.0	309.0	
Male (%)	23 (31.1)	27 (36.0)	31 (41.3)	20 (27.4)	0.8
Age (years)	47.8 ± 7.3	48.4 ± 7.8	47.2 ± 7.5	47.1 ± 7.0	0.6
Education (years)	6.1 ± 0.6[b]	5.8 ± 0.5	7.4 ± 0.5	7.2 ± 0.4	0.2
BMI (kg/m^2)	28.5 ± 3.9	28.6 ± 4.3	28.2 ± 4.4	27.7 ± 3.7	0.5
Waist circumference (cm)	93.5 ± 10.4	91.9 ± 11.2	91.1 ± 11.6	89.0 ± 10.6	0.09
Physical activity (MET/h/week)	677.5 ± 137.5[b]	605.9 ± 151.6	828.8 ± 148.8	783.9 ± 148.2	0.3
Dietary supplement use (%)	14 (18.9)	9 (12.0)	17 (22.7)	9 (12.3)	0.6
Energy intake (kcal/day)	2161.8 ± 688.9	2365.0 ± 632.6	2421.8 ± 669.7	2605.0 ± 684.3	0.001
Healthy eating index	41.7 ± 7.1	42.7 ± 8.1	46.4 ± 9.2	46.8 ± 7.0	< 0.001
Fasting blood glucose (mg/dl)	98.8 ± 14.5	98.1 ± 15.3	92.6 ± 15.4	92.4 ± 14.4	0.009
2-h glucose (mg/dl)	133.3 ± 17.8	136.2 ± 21.8	128.5 ± 15.8	128.9 ± 16.9	0.02

Total fruits were defined, as shown in Table 1

Values are means (standard deviations) or percentages unless stated otherwise

[a]ANOVA

[b]Geometric mean ± SEM

other vegetables, total fruits, berries, citrus fruits, and other fruits was significantly lower in pre-diabetic subjects as compared to the control group ($p < 0.001$). However, pre-diabetic subjects had a significantly higher intake of dark yellow vegetables ($p < 0.001$). After adjustment for confounding variables, these differences remained significant for total FV, total vegetables, dark yellow vegetables, total fruits, and berries ($p < 0.04$).

The odds ratio (OR) of pre-diabetes across quartiles of FV intake, before and after adjustment for confounding factors, is presented in two different models, as shown in Table 5. Before adjusting the confounders, subjects in the lowest quartile of total FV intake and its all subgroups, except for yellow vegetables, had a higher OR of pre-diabetes compared with those in the highest quartile (p trend < 0.002). After adjusting for the confounders, the participants in the lowest quartile of total FV and total fruits had a higher OR of pre-diabetes compared with those in the highest quartile (p trend < 0.007). Furthermore, compared with the highest quartile, subjects in the lowest quartile of dark yellow vegetables intake had a lower OR of pre-diabetes (p trend = 0.006).

Participants in the second and third quartiles of cruciferous vegetables also had a higher OR compared with those in the highest quartile ($p < 0.04$). In addition, participants in the first quartile of other vegetables ($p = 0.04$) and those in the second quartile of berries ($p = 0.02$) had a higher OR compared with those in the highest quartile ($p < 0.05$). However, a dose–response relationship was not observed after testing pre-diabetes across the quartiles of cruciferous vegetables, other vegetables, and berries.

Discussion

The result of this case–control study showed that higher consumption of total FV and total fruits was significantly associated with lower OR of pre-diabetes. We also found that cruciferous vegetables, other vegetables, and berries might be associated with pre-diabetes, although a distinct dose–response relationship was not found. On the other hand, higher intake of dark yellow vegetables was significantly associated with higher chance of pre-diabetes. Other vegetable and fruit subgroups did not show any significant relationship with pre-diabetes.

Evidence on the relationship between FV consumption and pre-diabetes is very limited and incomplete. Our findings are consistent with the results of other studies suggesting an inverse association between diets rich in FV and IGT. A cross-sectional study showed that high intake of fruits and green leafy vegetables was associated with lower plasma HbA1C levels in individuals not diagnosed with diabetes [28]. Moreover, another cross-sectional study showed that diets rich in fruits, vegetables, seaweed, cereals, and mushrooms beside low intake of alcohol retarded the progression of IFG in Chinese men [19]. Diets rich in fruits, vegetables, and whole grains and low in fat were also associated with lower IFG and IGT in a cross-sectional study on Framingham offspring [18]. However, a cross-sectional study concluded that high intake of fruits and juices may cause glucose metabolism disturbances [29]. Our study showed that pre-diabetes was inversely associated with the intake of total FV and total fruits, and to a lesser extent with cruciferous vegetables, other vegetables, and berries.

Table 4 Fruit and vegetable intakes across controls and pre-diabetic subjects

Daily intake (g)	Controls (n = 150), mean ± SD	Pre-diabetics (n = 147), mean ± SD	p^a	p^b	p^c
Total vegetables and fruits	809.1 ± 297.7	575.9 ± 240.1	< 0.001	< 0.001	< 0.001
Total vegetables	490.5 ± 219.8	341.8.5 ± 153.9	< 0.001	< 0.001	0.03
Cruciferous vegetables	3.53 ± 0.4[d]	2.2 ± 0.3	< 0.001	< 0.001	0.3
Green leafy vegetables	73.0 ± 4.2[d]	45.3 ± 3.2	< 0.001	< 0.001	0.3
Dark yellow vegetables	11.2 ± 2.1[d]	12.6 ± 1.6	0.5	0.8	0.001
Other vegetables	373.7 ± 170.4	260.9 ± 122.8	< 0.001	< 0.001	0.7
Total fruits	281.0 ± 13.6[d]	200.6 ± 11.6	< 0.001	< 0.001	0.001
Berries fruits	2.2 ± 0.2[d]	1.5 ± 1.0	< 0.001	< 0.001	0.02
Citrus fruits	57.6 ± 3.7[d]	42.4 ± 2.7	< 0.001	< 0.001	0.8
Other fruits	214.0 ± 10.8[d]	153.7 ± 9.3	< 0.001	< 0.001	0.1

Values are means (standard deviations) or percentages unless stated otherwise

Total vegetables and fruits were defined, as shown in Table 1

Cruciferous vegetables include white and red cabbage, broccoli, and cauliflower

Green leafy vegetables include spinach, lettuce, and green vegetables such as basil, parsley, cress, leek, spearmint, origany, coriander, and scallion

Dark yellow vegetables include carrot and yellow squash

Other vegetables include cucumber, tomato, zucchini, eggplant, celery, green pea, green bean, garlic, onion, green pepper, turnip, mushroom, olive, and corn

Berries fruits include strawberry, cornel, white mulberry, and black mulberry

Citrus fruits include orange, tangerine, grapefruits, sweet lemon and orange/grapefruit juice. Other fruits include cantaloupe, melon, water melon, pear, apricot, cherry, apple, peach, nectarine, greengage, fig, kiwi fruit, persimmon, pomegranate, date, plum, sour cherry, banana, pineapple, grapes, dry peach and apricot, raisin, and fruit juice

[a]Unadjusted, Student t test

[b]Adjusted for energy intake; ANCOVA test

[c]Adjusted for age, body mass index, physical activity, energy intake and healthy eating index score. Total vegetable and total fruit intakes were mutually adjusted. For each vegetables and fruits subgroups, total fruit and vegetable intakes were adjusted; ANCOVA test

[d]Geometric mean ± SEM

Most of the studies on FV intake and glucose metabolism disturbances have been conducted on T2DM patients [1, 6–11, 15, 18, 19, 28–41]. The results of these studies are inconsistent. Our findings in pre-diabetic subjects are similar to the previous prospective studies on T2DM patients, indicating an inverse association between consumption of cruciferous vegetables [31], total fruits [9, 31, 36] and berries [36] and the risk of T2DM. However, some prospective studies have not found any association between the intake of total FV, fruits, or vegetables separately [11], berries [42], and citrus [11, 43] and the risk of T2DM.

A meta-analysis on prospective studies found no significant association between the risk of T2DM and the intake of total FV, total vegetables, or total fruits [44]. However, a meta-analysis on high-quality prospective studies showed that higher intake of fruits, especially berries, green leafy vegetables, yellow vegetables, and cruciferous vegetables was associated with a lower risk of T2DM [9].

Therefore, the previous studies have not consistently found an inverse association between FV intake and T2DM, but have found it for pre-diabetes. This may reflect that choosing T2DM as an end-point outcome for FV consumption is not sufficient. Since the disease process is long-term and has slow progression, the pre-clinical manifestations of T2D might have lead to changes in diet. Future prospective studies conducted with pre-diabetes as an end-point may clearly indicate the relationship between FV intake and IGT.

We found no significant association between the total vegetable intakes and OR of pre-diabetes. Similar results have been reported for T2DM in the previous meta-analyses [11, 44, 45]. Although other fruits may also be related to glucose metabolism, no significant associations were found between other fruits and chance of pre-diabetes in the present and previous prospective investigations [11, 25].

In the present study, we found an unexpected positive association between the intake of dark yellow vegetables and pre-diabetes. In a Finnish cohort study, the intake of yellow/red vegetables was not associated with a lower incidence of T2DM [36]. However, the results of a meta-analysis on prospective studies showed that higher intake of yellow

Table 5 Odds ratio (95% CI) of pre-diabetes according to quartiles (Q) of fruit and vegetable intakes

Daily intake	Q1		Q2		Q3		Q4	*p* trend*
Total vegetables and fruits								
g/day (median)	363.1		566.2		771.7		1039.5	
Cases of pre-diabetic	52		51		25		19	
Model 1	< 0.001	(3.33–14.08)	6.15	(3.02–12.54)	1.48	(0.73-3.0)	1	< 0.001
p	6.84		< 0.001		0.2			
Model 2	2.47	(0.86–7.15)	5.04	(1.83–13.9)	1.15	(0.44–3.01)	1	0.005
p	0.09		0.002		0.7			
Total vegetables								
g/day (median)	186.5		333.8		461.2		629.4	
Cases of pre-diabetic	53		44		32		18	
Model 1	7.85	(3.77–16.34)	4.56	(2.25–9.24)	2.37	(1.17–4.78)	1	< 0.001
p	< 0.001		< 0.001		0.02			
Model 2	2.33	(0.79–6.81)	1.99	(0.76–5.25)	1.28	(0.49–3.3)	1	0.4
p	0.1		0.1		0.6			
Cruciferous vegetables								
g/day (median)	1		3.5		6		11.7	
Cases of pre-diabetic	36		59		32		20	
Model 1	3.21	(1.57–6.58)	3.35	(1.75–6.42)	2.86	(1.38–5.9)	1	0.001
p	0.001		< 0.001		0.005			
Model 2	1.39	(0.47–4.14)	2.70	(1.07–6.81)	2.99	(1.07–8.38)	1	0.4
p	0.5		0.03		0.03			
Green leafy vegetables								
g/day (median)	23.1		47.6		82.2		129.8	
Cases of pre-diabetic	53		42		32		20	
Model 1	6.81	(3.32-14.0)	3.54	(1.78–7.06)	2.01	(1.01–3.99)	1	< 0.001
p	< 0.001		< 0.001		0.04			
Model 2	1.25	(0.4–3.89)	1.04	(0.38–2.87)	0.69	(0.27–1.76)	1	0.5
p	0.7		0.9		0.4			
Dark yellow vegetables								
g/day (median)	3.5		10.3		19.2		53.5	
Cases of pre-diabetic	34		39		37		37	
Model 1	0.89	(0.47–1.71)	1.08	(0.57–2.06)	0.95	(0.5–1.8)	1	0.9
p	0.7		0.8		0.8			
Model 2	0.16	(0.05–0.52)	0.5	(0.18–1.42)	0.42	(0.15–1.17)	1	0.006
p	0.002		0.1		0.09			
Other vegetables								
g/day (median)	135.8		246.8		353.7		492.4	
Cases of pre-diabetic	51		45		34		17	
Model 1	7.44	(3.58–15.46)	5.03	(2.47–10.25)	2.85	(1.4–5.79)	1	< 0.001
p	< 0.001		< 0.001		0.004			
Model 2	2.78	(1.02–7.62)	2.12	(0.80–5.58)	1.49	(0.58–3.85)	1	0.2
p	0.04		0.1		0.4			
Total fruits								
g/day (median)	123.8		199.8		284.2		452.5	
Cases of pre-diabetic	49		48		28		22	
Model 1	4.54	(2.27–9.1)	4.12	(2.07–8.19)	1.38	(0.7–2.74)	1	< 0.001
p	< 0.001		< 0.001		0.3			
Model 2	3.50	(1.2-10.15)	3.36	(1.28–8.81)	1.54	(0.59–4.01)	1	0.006
p	0.02		0.01		0.3			

Table 5 (continued)

Daily intake	Q1		Q2		Q3		Q4	*p* trend*
Berries fruits								
g/day (median)	1.2		1.7		3.1		5.6	
Cases of pre-diabetic	43		43		40		21	
Model 1	3.44	(1.73–6.82)	3.33	(1.68–6.59)	2.83	(1.43–5.59)	1	0.001
p	< 0.001		0.001		0.003			
Model 2	2.76	(0.93–8.18)	3.38	(1.2–9.52)	2.46	(0.88–6.87)	1	0.06
p	0.06		0.02		0.08			
Citrus fruits								
g/day (median)	22.3		41.7		63.8		106.8	
Cases of pre-diabetic	45		43		37		22	
Model 1	3.67	(1.85–7.26)	3.18	(1.61–6.25)	2.36	(1.2–4.64)	1	< 0.001
p	< 0.001		0.001		0.01			
Model 2	0.87	(0.26–2.94)	1.63	(0.52–5.08)	0.76	(0.28–2.16)	1	0.8
p	0.8		0.3		0.6			
Other fruits								
g/day (median)	96.6		148		219.4		364.8	
Cases of pre-diabetic	51		45		27		24	
Model 1	4.62	(2.31–9.23)	3.12	(1.60–6.11)	1.20	(0.6–2.36)	1	< 0.001
p	< 0.001		0.001		0.6			
Model 2	1.64	(0.42–6.31)	2.04	(0.67–6.28)	0.66	(0.23–1.86)	1	0.1
p	0.4		0.2		0.4			

Model 1: unadjusted

Model 2: adjusted for age, body mass index, physical activity, energy intake, and healthy eating index. Total vegetable and total fruit intakes were mutually adjusted. For each vegetable and fruit subgroup, total fruit and vegetable intakes were adjusted

Fruits and vegetables were defined, as shown in Tables 1 and 4

*Tests for trend were performed by entering the categorical variables as continuous parameters in the models

vegetables was associated with a lower risk of T2DM [9]. We do not have a ready explanation as to why higher intake of dark yellow vegetables is associated with a higher OR of pre-diabetes. However, this may reflect dark yellow vegetables preparation methods such as frying. Frequent fried-food consumption was associated with higher risk of T2DM in cohort studies [46]. In addition, the oils used for frying in Iran have considerable amounts of trans fatty acids [47] which is related to blood glucose disturbances [48].

However, this information was not collected. More research is needed to investigate the association between this type of vegetables and pre-diabetes.

The biological mechanisms behind the inverse association between the FV intake and pre-diabetes are not clear. However, FV are rich sources of folate, potassium, magnesium, vitamin K, antioxidants such as vitamin C, E, carotenoids, and flavonoids, which are related to lower risk of T2DM [49]. Cruciferous vegetables have a high content of glucosinolates which have antioxidant properties and are related to a lower risk of T2DM in the prospective studies [10]. Berries are rich in anthocyanins which was inversely related to glucose disturbances in a cohort study [40]. Lower dietary magnesium intake has been linked to higher risk of T2DM or glucose intolerance in a cohort study [50]. In an observational study, higher dietary vitamin K intake was related to greater insulin sensitivity and better glycemic status in adults [51]. Folate, due to its antioxidant properties [52], together with vitamin C and carotenoids, can suppress oxidative stress which is involved in the onset of chronic diseases like T2DM [53]. Furthermore, FV are rich sources of fiber which can protect against diabetes by reducing adiposity and postprandial glycaemia. In addition, fiber increases insulin sensitivity [54]. Diets rich in FV can also improve the feeling of fullness and consequently may decrease the intake of energy-dense foods and lower the risk of obesity, which is a risk factor for pre-diabetes and T2DM [55, 56].

The result of the Comprehensive Study on Household Food Consumption Patterns and Nutritional Status of I.R. Iran during 2001–2003 showed that the mean intake of fruits and vegetables was 229.3 and 142.5 g/day, respectively [57].

Compared to these figures at a national level, the subjects in the present study consumed much more fruits and vegetables. The reason may be the place of the study (Shahreza), which has plenty of gardens and fruit trees.

Selecting the subjects who were diagnosed within the past 3 months was one of the strengths of the current study, which minimized the possible effect of diagnosis on the dietary report.

However, since participants were aware of their pre-diabetes diagnosis, they may report their dietary intake differently than the controls. Furthermore, in our statistical analysis, instead of adjusting only for a few dietary factors, we adjusted for overall quality of diet. We found that the inverse association between total FV and total fruits and chance of pre-diabetes persisted after adjustment for HEI. It appears that eating more FV is related to lower OR of pre-diabetes, regardless of the quality of diet. However, our study had some limitations. First, response errors are possible in the FFQ. In addition, the evaluation of reliability and validity of the FFQ used in our study was performed in a different population. Second, like all case–control studies, no cause and effect relationship could be determined between the FV intake and pre-diabetes. Third, although we adjusted for many confounding variables, residual confounding remains a possible concern for our results, together with potential unmeasured confounders. Fourth, the findings of the study might not be generalized to other populations. Regardless of these limitations, this study is among a few studies to examine the relationship between the FV intake and chance of pre-diabetes.

In conclusion, we investigated the relationship between the intake of FV and their specific subgroups and pre-diabetes. We found that higher consumption of total FV, total fruits, cruciferous vegetables, other vegetables, and berries might be associated with a lower OR of pre-diabetes. However, some parts of the results should be interpreted with caution due to the lack of a dose–response relationship. Further studies are needed to confirm these findings.

Acknowledgements This research project was supported by Tehran University of Medical Sciences (TUMS) (Grant No. 93-454-76).

Compliance with ethical standards

Conflict of interest None.

References

1. Boeing H, Bechthold A, Bub A et al (2012) Critical review: vegetables and fruit in the prevention of chronic diseases. Eur J Nutr 51(6):637–663
2. World Health Organization (2016) Global reports on diabetes. World Health Organization, Switzerland. http://www.who.int/mediacentre/factsheets/fs312/en/. Accessed July 2017
3. American Diabetes Association (2014) Standards of medical care in diabetes. Diabetes Care 37(Suppl 1):S14–80
4. Tabák G, Herder Ch, Rathmann W, Brunner E, Kivimäki M (2012) Prediabetes: a high-risk state for developing diabetes. Lancet 379(9833):2279–2290
5. World Health Organization (2004) Global strategy on diet, physical activity and health. World Health Organization, Geneva. http://www.who.int/dietphysicalactivity/en. Accessed 1 Aug 2017
6. Folchetti LD, Monfort-Pires M, de Barros CR, Martini LA, Ferreira SRG (2014) Association of fruits and vegetables consumption and related-vitamins with inflammatory and oxidative stress markers in prediabetic individuals. Diabetol Metab Syndr 6:22
7. Yao B, Fang H, Xu W et al (2014) Dietary fiber intake and risk of type 2 diabetes: a dose–response analysis of prospective studies. Eur J Epidemiol 29(2):79–88
8. Liu RH (2013) Health-promoting components of fruits and vegetables in the diet. Adv Nutr 4(3):384s–392s
9. Muraki I, Imamura F, Manson J et al (2013) Fruit consumption and risk of type 2 diabetes: results from three prospective longitudinal cohort studies. BMJ 347:f5001
10. Wang PY, Fang JC, Gao ZH, Zhang C, Xie SY (2016) Higher intake of fruits, vegetables or their fiber reduces the risk of type 2 diabetes: a meta-analysis. J Diabetes Investig 7(1):56–69
11. Cooper AJ, Forouhi NG, Ye Z et al (2012) Fruit and vegetable intake and type 2 diabetes: EPIC-InterAct prospective study and meta-analysis. Eur J Clin Nutr 66(10):1082–1092
12. Higuchi K, Saito I, Maruyama K et al (2015) Associations of serum beta-carotene and retinol concentrations with insulin resistance: the Toon Health Study. Nutrition 31(7–8):975–80
13. Dragovic UV, Levaj B, Mrkic V, Bursac D, Boras M (2007) The content of polyphenols and carotenoids in three apricot cultivars depending on stage of maturity and geographical region. Food Chem 102(3):966–975
14. Tunnicliffe JM, Eller LK, Reimer RA, Hittel DS, Shearer J (2011) Chlorogenic acid differentially affects postprandial glucose and glucose-dependent insulinotropic polypeptide response in rats. Appl Physiol Nutr Metab 36(5):650–659
15. Liu Y, Dong M, Yang Z, Pan S (2016) Anti-diabetic effect of citrus pectin in diabetic rats and potential mechanism via PI3K/Akt signaling pathway. Int J Biol Macromol 89:484–488
16. US Department of Agriculture, Agricultural Research Service (2013) USDA database for the flavonoid content of selected foods, release 3.1. Nutrient Data Laboratory. http://www.ars.usda.gov/Services/docs.htm?docid=6231. Accessed May 2014
17. Parmar HS, Jain P, Chauhan DS et al (2012) DPP-IV inhibitory potential of naringin: an in silico, in vitro and in vivo study. Diabetes Res Clin Pract 97(1):105–111
18. Liu E, McKeown NM, Newby PK et al (2009) Cross-sectional association of dietary patterns with insulin-resistant phenotypes among adults without diabetes in the Framingham Offspring Study. Br J Nutr 102(4):576–583
19. Zhang M, Zhu Y, Li P et al (2015) Associations between dietary patterns and impaired fasting glucose in Chinese Men: a cross-sectional study. Nutrients 7(9):8072–8089
20. IPAQ (2005) Guidelines for data processing and analysis of the international physical activity questionnaire (IPAQ)—short and long forms. IPAQ Research Committee. https://epi.grants.cancer.gov/paq/q026.html. Accessed 8 July 2016
21. Sandip B, Bankar MV, Bule RS, Singhal LA (2009) Glucose oxidase—an overview. Biotechnol Adv 27(4):489–501
22. Esmaillzadeh A, Mirmiran P, Azizi F (2005) Whole-grain intake and the prevalence of hypertriglyceridemic waist phenotype in Tehranian adults. Am J Clin Nutr 81(1):55–63
23. United States Department of Agricultural (USDA) (2015) National nutrient database for standard reference. https://ndb.nal.usda.gov/ndb/. Accessed May 2016

24. Liu S, Manson JE, Lee IM et al (2000) Fruit and vegetable intake and risk of cardiovascular disease: the Women's Health Study. Am J Clin Nutr 72(4):922–928
25. Liu S, Serdula M, Janket SJ et al (2004) A prospective study of fruit and vegetable intake and the risk of type 2 diabetes in women. Diabetes Care 27(12):2993–2996
26. National Cancer Institute (2015) Developing the Healthy Eating Index. https://epi.grants.cancer.gov/hei/. Accessed 29 Aug 2017
27. Nooyens AC, Bueno-de-Mesquita HB, van Boxtel MP, van Gelder BM, Verhagen H, Verschuren WM (2011) Fruit and vegetable intake and cognitive decline in middle-aged men and women: the Doetinchem Cohort Study. Br J Nutr 106(5):752–761
28. Sargeant LA, Khaw KT, Bingham S et al (2001) Fruit and vegetable intake and population glycosylated haemoglobin levels: the EPIC-Norfolk Study. Eur J Clin Nutr 55(5):342–348
29. Sartorelli DS, Freire RD, Ferreira SR, Cardoso MA (2005) Dietary fiber and glucose tolerance in Japanese Brazilians. Diabetes Care 28(9):2240–2242
30. Barbagallo M, Dominguez LJ (2015) Magnesium and type 2 diabetes. World J Diabetes 6(10):1152–1157
31. Bazzano LA, Li TY, Joshipura KJ, Hu FB (2008) Intake of fruit, vegetables, and fruit juices and risk of diabetes in women. Diabetes Care 31(7):1311–1317
32. Broekmans WM, Klopping-Ketelaars IA, Schuurman CR et al (2000) Fruits and vegetables increase plasma carotenoids and vitamins and decrease homocysteine in humans. J Nutr 130(6):1578–1583
33. Esposito K, Giugliano D (2011) Increased consumption of green leafy vegetables, but not fruit, vegetables or fruit and vegetables combined, is associated with reduced incidence of type 2 diabetes. Evid Based Med 16(1):27–28
34. Gemen R, de Vries JF, Slavin JL (2011) Relationship between molecular structure of cereal dietary fiber and health effects: focus on glucose/insulin response and gut health. Nutr Rev 69(1):22–33
35. Liese AD, Roach AK, Sparks KC, Marquart L, D'Agostino RB, Mayer-Davis EJ (2003) Whole-grain intake and insulin sensitivity: the Insulin Resistance Atherosclerosis Study. Am J Clin Nutr 78(5):965–971
36. Montonen J, Jarvinen R, Heliovaara M, Reunanen A, Aromaa A, Knekt P (2005) Food consumption and the incidence of type II diabetes mellitus. Eur J Clin Nutr 59(3):441–448
37. Ong KW, Hsu A, Tan BK (2012) Chlorogenic acid stimulates glucose transport in skeletal muscle via AMPK activation: a contributor to the beneficial effects of coffee on diabetes. PLoS One 7(3):e32718
38. Sartorelli DS, Franco LJ, Gimeno SG, Ferreira SR, Cardoso MA (2009) Dietary fructose, fruits, fruit juices and glucose tolerance status in Japanese–Brazilians. Nutr Metab Cardiovasc Dis 19(2):77–83
39. Takahashi K, Kamada C, Yoshimura H et al (2012) Effects of total and green vegetable intakes on glycated hemoglobin A1c and triglycerides in elderly patients with type 2 diabetes mellitus: the Japanese Elderly Intervention Trial. Geriatr Gerontol Int 12(Suppl 1):50–58
40. Wedick NM, Pan AN, Cassidy A et al (2012) Dietary flavonoid intakes and risk of type 2 diabetes in US men and women. Am J Clin Nutr 95(4):925–933
41. Zino S, Skeaff M, Williams S, Mann J (1997) Randomised controlled trial of effect of fruit and vegetable consumption on plasma concentrations of lipids and antioxidants. BMJ 314(7097):1787–1791
42. Nettleton JA, Harnack LJ, Scrafford CG, Mink PJ, Barraj LM, Jacobs DR (2006) Dietary flavonoids and flavonoid-rich foods are not associated with risk of type 2 diabetes in postmenopausal women. J Nutr 136(12):3039–3045
43. Kurotani K, Nanri A, Goto A et al (2013) Vegetable and fruit intake and risk of type 2 diabetes: Japan Public Health Center-based Prospective Study. Br J Nutr 109(4):709–717
44. Carter P, Gray LJ, Troughton J, Khunti K, Davies MJ (2010) Fruit and vegetable intake and incidence of type 2 diabetes mellitus: systematic review and meta-analysis. BMJ 341:c4229
45. Hamer M, Chida Y (2007) Intake of fruit, vegetables, and antioxidants and risk of type 2 diabetes: systematic review and meta-analysis. J Hypertens 25(12):2361–2369
46. Cahill LE, Pan A, Chiuve SE et al (2014) Fried-food consumption and risk of type 2 diabetes and coronary artery disease: a prospective study in 2 cohorts of US women and men. Am J Clin Nutr 100(2):667–675
47. Hajimahmoodi M, Arami S, Nosrati M et al (2013) Trans fatty acid content of iranian edible oils. Food Nutr Sci 4(11):1167–1174
48. Guess N, Perreault L, Kerege A, Strauss A, Bergman BC (2016) Dietary fatty acids differentially associate with fasting versus 2-hour glucose homeostasis: implications for the management of subtypes of prediabetes. PLoS One 11(3):e0150148
49. Harding AH, Wareham NJ, Bingham SA et al (2008) Plasma vitamin C level, fruit and vegetable consumption, and the risk of new-onset type 2 diabetes mellitus: the European prospective investigation of cancer—Norfolk prospective study. Arch Intern Med 168(14):1493–1499
50. Kao WH, Folsom AR, Nieto FJ, Mo JP, Watson RL, Brancati FL (1999) Serum and dietary magnesium and the risk for type 2 diabetes mellitus: the Atherosclerosis Risk in Communities Study. Arch Intern Med 159(18):2151–2159
51. Yoshida M, Booth SL, Meigs JB, Saltzman E, Jacques PF (2008) Phylloquinone intake, insulin sensitivity, and glycemic status in men and women. Am J Clin Nutr 88(1):210–215
52. Parker SE, Yazdy MM, Tinker SC, Mitchell AA, Werler MM (2013) The impact of folic acid intake on the association between diabetes, obesity, and spina bifida. Am J Obstet Gynecol 209(3):239.e1–239.e8
53. Suarez A, Pulido N, Casla A, Casanova B, Arrieta FJ, Rovira A (1995) Impaired tyrosine–kinase activity of muscle insulin receptors from hypomagnesaemic rats. Diabetologia 38(11):1262–1270
54. Lee NK, Sowa H, Hinoi E et al (2007) Endocrine regulation of energy metabolism by the skeleton. Cell 130(3):456–469
55. Lattimer JM, Haub MD (2010) Effects of dietary fiber and its components on metabolic health. Nutrients 2(12):1266–1289
56. Liu S, Willett WC, Manson JE, Hu FB, Rosner B, Colditz G (2003) Relation between changes in intakes of dietary fiber and grain products and changes in weight and development of obesity among middle-aged women. Am J Clin Nutr 78(5):920–927
57. Abdollahi M, Mohammadi-Nasrabadi F, Houshiarrad A, Ghaffarpur M, Ghodsi D, Kalantari N (2014) Socio-economic differences in dietary intakes: the comprehensive study on household food consumption patterns and nutritional status of I.R. Iran. Nutr Food Sci Res 1(1):19–26