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# Dietary phytochemical index associated with cardiovascular risk factor in patients with type 1 diabetes mellitus

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## Abstract

**Background:** Dietary phytochemical index (DPI) is useful and inexpensive method to identify the role of phytochemicals on cardiovascular disease (CVD) risk factors. This study aimed to assess the relationship between DPI and CVD risk factors in patients with type1 diabetes mellitus.

**Methods:** A total of 261 participants aged 18–35 years with T1DM were enrolled in this cross-sectional study to assess the relationship between DPI and CVD risk factors. Anthropometric measurements, blood lipids, glucose, and antioxidant level were measured. Food intakes were determined using a food frequency questionnaire to calculate DPI. Logistic regression was used.

**Results:** The mean age of participants was 25 years. After adjustment for potential confounders, participants in the highest tertile of DPI had 88 % lower chance of hyperglycemia ( $P$  for trend = 0.020), 81 % lower chance of low high-density lipoprotein cholesterol (HDL-C) ( $P$  for trend = 0.030) and 98 % lower chance of high low-density lipoprotein cholesterol to HDL-C ratio ( $P$  for tend = 0.040). There were no relationships between DPI and other CVD risk factors.

**Conclusions:** Although higher intake of phytochemical-rich foods had a beneficial effect on some risk factors of CVD, more studies more studies are warranted to corroborate the present findings.

**Keywords:** Diabetes mellitus, cardiovascular diseases, phytochemicals, adult, hyperglycemia

## Introduction

Diabetes mellitus (DM) is one of the most important cause of death worldwide, especially in developed countries. It is associated with the risk of hypertension (HTN), hypercholesterolemia, and cardiovascular diseases (CVD) [1]. Seven to 12% of patients who suffer from diabetes have type 1 DM (T1DM) [2]. Genetic and environmental triggers including toxins, viral infections, and some dietary factors may affect incidence of T1DM.

Unfortunately, there are currently no preventive measures for the prevention of T1DM, so the reduction of its complications must be focused [2].

Oxidative stress (OS) as an imbalance between oxidants and anti-oxidants in the favor of the oxidants, leading to a disruption of redox signaling and control and/or molecular damage. OS plays an important role in the major diabetic complications, including retinopathy, nephropathy, neuropathy and accelerated coronary artery disease [3]. Insulin deficiency, in turn leads to chronic hyperglycemia and an increase level of lipid and protein peroxidation products, oxidative DNA damage markers, and lower activity of antioxidant enzymes, subsequently [4]. Some evidence showed that antioxidant capacity impairs in

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T1DM due to lower consumption of antioxidant components or lower levels of antioxidant substances [5].

Phytochemicals are mainly found in plant foods such as fruits, vegetables, cereals, soy and tea [6], which is inversely associated with chronic diseases including DM, CVD, and some cancers [7]. The beneficial effects of phytochemicals can be attributed to their antioxidant and anti-inflammatory properties, their effect on cell cycle regulation, hormones, vascular endothelium and immune cells [8]. Dietary phytochemical index (DPI) is a quantitative index defined as percentage of energy intake that are derived from phytochemicals rich foods in order to identify the role of phytochemicals on health [9].

Previous studies investigated the association of DPI with chronic diseases risk factors. Most of these studies conducted on healthy individuals, except of 2 case-control studies on women with breast cancer [10] and individuals with pre-diabetes [11]. The result of these studies showed inverse association between DPI and waist circumference (WC), body mass index (BMI), HTN, glucose intolerance, chance of pre-diabetes, dyslipidemia, and blood biomarkers of OS [11–13].

Few studies investigated the relationship between DPI and health outcomes and none of them were performed in patients with T1DM, who have complex conditions such as impaired glucose and lipid disturbances [14]. We hypothesized that DPI may have a beneficial relationship with the CVD risks; therefore, the aim of this study was to determine the relationship between DPI with CVD risk factors including blood glucose, lipid profile, antioxidant levels, blood pressure and anthropometric measurements in patients with T1DM.

## Materials and methods

### Study design

The present study is part of a cross-sectional study, which investigated the association between dietary patterns with CVD risk factors and OS in patients with T1DM with the approval of Ethics Committee of Tehran University of Medical Sciences (IR.TUMS.REC.1394.1595), and written informed consent was obtained from all the participants. The study was conducted on 273 patients with T1DM from the Iranian diabetes society and Endocrine and Metabolism Research Institute of Tehran University of Medical Sciences in Tehran, Iran. According to the exclusion criteria (individuals who had reported energy intake outside the range of 500–3500 kcal/day in women and 800–4200 kcal/day in men) 261 patients were finally analyzed for the non-biochemical assessments and due to financial limitation, 81 patients recruited for biochemical examination using simple random sampling method. Inclusion criteria were patients who were diagnosed with T1DM for at least six

months, aged between 18 and 35 and hemoglobin A1c (HbA1c)  $\leq$  8%. Participants were excluded if they had BMI  $\geq$  40 kg/m<sup>2</sup>, drugs intake other than insulin to lower blood glucose, diagnosed CVD, cancer, kidney or liver disease, use of contraceptives, hormones and recombinant drugs, thyroid control drugs, taking weight reducing agents, anti-depressants and anti-anxiety drugs, use of any smoking (cigarette, hookah, tobacco pipe) and pregnancy or lactation.

### Demographic and general characteristics

Information about age, sex, duration of DM, educational level, daily insulin dose, type of insulin and dietary supplements intake were collected by questionnaires.

### Dietary intake assessment

Individual's typical dietary intake, during the last year, was evaluated using a semi-quantitative food frequency questionnaire (FFQ) with 147 food items, interviewed by a trained dietitian. The validity and reproducibility of the FFQ were determined previously for fruits, vegetables, and energy intake [15]. In this FFQ, there is a list of food items with a standard serving size that Iranian people commonly consume [16]. Individuals were asked to report their usual frequency and amount of consumption of food items listed by day, week, and month over the previous year. The values listed for each food item were converted to gram using US Department of Agriculture (USDA) serving sizes whenever possible; if this was not possible, household measures were chosen and were then converted to grams. Energy and nutrient contents of food items were obtained from USDA food composition tables (FCTs) because Iranian FCTs are incomplete. The Iranian FCT was used for traditional food items that are not listed in the USDA FCT. Analyzing the energy and nutrients of each food item was done with the Nutritionist IV software version 3.5.1, that modified for Iranian food [17].

DPI is calculated based on the division of energy content of foods rich in phytochemicals on the total daily energy intake  $\times$  100, based on McCarty formula ( $DPI = \frac{\text{Dietary energy derived from phytochemical-rich foods (kcal)}}{\text{Total daily energy intake(kcal)}} \times 100$ ) [9]. To calculate the DPI, all the phytochemical-rich foods including fruits, vegetables (except potatoes), whole grains, legumes, fruit and vegetable juice, soy products, nuts, seeds, olive and olive oil were gathered from the FFQ [13].

### Clinical assessment

The weight was measured by a nutritionist using a digital scale (GAIA 359 PLUS. Jawon Medical Co. Ltd., Gyeongsan, Korea), to the nearest 100 g, with minimal dress

and no shoes. Height was measured to the nearest 0.5 cm with a tape while the patient standing without shoes. The BMI was calculated by dividing the weight (kg) by height (square meter). WC was measured using an elastic tape measuring midpoint between the iliac crest and lowest rib. Blood pressure was measured from the right hand of the participants to the nearest 2 mmHg, after at least 10 min rest, while sitting on a chair with a mercury sphygmomanometer. Overweight and obesity defined as  $BMI = 25-29.9 \text{ kg/m}^2$  and  $BMI \geq 30 \text{ kg/m}^2$ , respectively, central obesity as  $WC \geq 80 \text{ cm}$  in women and  $\geq 94 \text{ cm}$  in men. HTN was defined as blood pressure  $\geq 140/90 \text{ mmHg}$  [18].

### Physical activity assessment

Physical activity of participants, during the previous week, was measured using the short form of International Physical Activity Questionnaire (IPAQ) [19]. The average time that a person would normally spend on different activities each day was asked. Then, to measure the value of metabolic equivalent task (MET)-hour/week, the sum of frequency and duration of activities multiplied by the MET of activity. The reliability and validity of IPAQ was assessed previously [19].

### Laboratory measurements

After a 12–14 h fasting at night, a trained nurse collected 5 mL of venous blood from the participants. Blood samples were collected in 2 separate tubes. One of the tubes was for separating serum and another tube containing ethylenediaminetetraacetic acid was used to separate the plasma. In order to separate the plasma samples from cells, the blood was centrifuged in 3000 rounds for 10 min. Then the remaining blood was washed three times with sodium chloride solution 0.9 g/L. Separation of cell membranes was performed by centrifugation for 5 min at 4 °C. Then hemolytic cells were used to determine the activity of antioxidant enzymes. The serum was separated from the blood by centrifugation for 10 min at 4 °C. After that, all the blood samples were stored at  $-79 \text{ }^\circ\text{C}$ . Blood glucose measurements were performed on the day of the test. This study was conducted with observance of the Declaration of Helsinki and the National Ethical Guidelines in Biomedical Research in Iran.

Measurements of serum glucose and lipids were performed, using Pars Azmoon kit (Pars Azmoon, Tehran, Iran). The measurement of triglyceride (TG) levels was conducted by colorimetric and photometry. Fasting blood glucose (FBG) and total cholesterol (TC) measurement were conducted by enzymatic colorimetric and single point with photometric method. The measurement of total antioxidant capacity (TAC) and activity of glutathione peroxidase (GPx) and superoxide dismutase

(SOD) were measured by commercial kits following the manufacturer's protocol (ZellBio GmbH, Lonsee, Germany). The intra- and inter-assay coefficients of variation for SOD, GPx, and TAC were 5.8 and 7.2%, 3.5 and 4.7%, and 3.4 and 4.2%, respectively. The following formula was used for calculating low-density lipoprotein cholesterol (LDL-C) [37]:  $LDL-C = TC - \text{high-density lipoprotein cholesterol (HDL-C)} - TG/5.0 \text{ (mg/dL)}$ .

Hypertriglyceridemia was defined as serum  $TG \geq 150 \text{ mg/dL}$  (1.7 mmol/L), low HDL-C as serum  $HDL-C < 40 \text{ mg/dL}$  (1.0 mmol/L) for men and  $< 50 \text{ mg/dL}$  (1.3 mmol/L) for women, high LDL-C as serum  $LDL-C \geq 100$  (2.6 mg/dL), hypercholesterolemia as  $TC > 200 \text{ mg/dL}$ , high HbA1c as  $HbA1c \geq 7$ , hyperglycemia as  $FBG \geq 100 \text{ mg/dL}$  and high LDL-C/HDL-C ratio as  $LDL-C/HDL-C > 3$  in women and  $> 3.5$  in men [18, 20, 21].

### Statistical analysis

Statistical analysis was performed using SPSS software for Windows (version 23; SPSS Inc., Chicago, IL, USA; 2015). Individuals who had reported energy intake outside the range of 500–3500 kcal/day in women and 800–4,200 kcal/day in men were excluded from the study [22]. In this order 3 men and 9 women were excluded from the data analysis and the final analysis was done on 261 participants. At first, energy-adjusted DPI was determined by residual method, then according to DPI, participants were categorized into tertiles. Normality of data distribution was tested using graph and Kolmogorov–Smirnov test. Comparison of the general and nutritional characteristics of the participants between the tertiles of energy-adjusted DPI was done using analysis of variance (ANOVA) or  $\chi^2$  test depending on the type of variables. Means  $\pm$  SD of CVD risk factors across tertiles of DPI were compared by ANOVA test for crude model and analysis of covariance for adjusted models which adjusted for age, sex, total energy intake (kcal/day), physical activity (MET/hour/week), BMI ( $\text{kg/m}^2$ ), diabetes duration (year), total daily insulin dose, education and dietary supplement intake. Further adjustment for intake of saturated fatty acids (SFA), mono-unsaturated fatty acids (MUFA), poly-unsaturated fatty acids (PUFA) and trans fatty acids was done for lipids levels. In addition, dietary intake of sodium and potassium was adjusted for systolic blood pressure (SBP) and diastolic blood pressure (DBP). Logistic regression test was used in crude and adjusted model to determine the odds ratio (OR) of cardiovascular risk factors and their 95% confidence interval (CI) in each tertile of DPI, which adjusted for age, sex, total energy intake (kcal/day), physical activity (MET/hour/week), BMI ( $\text{kg/m}^2$ ), diabetes duration (year), total insulin dose (unit/day), education, dietary supplement intake. In all

analyzes, the first tertile of DPI was considered as a reference and OR of the cardiovascular risk factor in the other tertiles was calculated towards it. Furthermore, to determine the overall trends of OR across increasing tertiles of DPI, the median of each tertile was used instead of the number of tertiles. *P* value lower than 0.05 was considered significant.

## Results

### Characteristics of participants across tertiles of DPI

The mean ± SD age of participants was 25 ± 5.4 years and 62.1% of the participants were women. DPI in the first, second and third tertiles of energy-adjusted DPI was < 31.75, 31.75–40.06, and > 40.06, respectively for females and < 27.73, 27.73–36.05, and > 36.05, respectively for males. The characteristics of participants across tertiles of DPI are shown in Table 1. Participants in the lower tertile of DPI were significantly younger (*P* trend = 0.02). Other characteristics including gender, education, short-acting

insulin intake, long-acting insulin intake, dietary supplement intake, daily insulin dose, BMI, weight, WC, diabetes duration, energy intake and physical activity were not significantly different across DPI tertiles (*P* trend > 0.05). The relative contributions of different phytochemical-rich food groups of DPI are shown in Fig. 1. The percentage of daily intake of energy from fruits and vegetables were higher than the other sources of phytochemical rich foods.

### CVD risk factors across tertiles of DPI

Table 2 presents the mean ± SD of CVD risk factors across tertiles of DPI. In the crude model, there was not any significant association between CVD risk factors and DPI (*P* trend > 0.05) (Model 1). After adjustment for age, sex, total energy intake, physical activity, BMI, diabetes duration, insulin dose, education and dietary supplement intake, participants in the higher tertile of DPI had significantly lower LDL-C to HDL-C ratio

**Table 1** Characteristics of participants across tertiles of the sex-specific energy-adjusted DPI in patients with type 1 diabetes

Variables	DPI tertiles				P trend
	T1 (n = 87)	T2 (n = 87)	T3 (n = 87)	Total (n = 261)	
Gender					
Men	33 (33.3)	33 (33.3)	33 (33.3)	99	1.000 <sup>a</sup>
Women	54 (33.3)	54 (33.3)	54 (33.3)	162	
Age (yrs)	24.3 ± 5.1	24.7 ± 5.4	26.0 ± 5.4	25.0 ± 5.4	0.022 <sup>b</sup>
Weight (kg)	66.3 ± 12.3	65.9 ± 11.8	65.5 ± 11.6	65.9 ± 11.8	0.638 <sup>b</sup>
Waist circumference (cm)	86.0 ± 10.2	84.8 ± 10.3	85.7 ± 9.8	85.5 ± 10.1	0.828 <sup>b</sup>
BMI (kg/m <sup>2</sup> )	23.4 ± 3.2	23.5 ± 3.5	23.5 ± 3.1	23.4 ± 3.3	0.857 <sup>b</sup>
Diabetes duration (yrs)	11.2 ± 6.0	12.6 ± 6.6	12.6 ± 6.7	12.1 ± 6.4	0.168 <sup>b</sup>
Insulin dose (unit/day)	48.5 ± 15.4	48.8 ± 16.7	47.0 ± 20.5	48.1 ± 17.6	0.590 <sup>b</sup>
Short-acting insulin intake					
Aspart	18 (34.3)	20 (32.8)	19 (32.8)	57	0.908 <sup>a</sup>
Regular/mix	69 (31.6)	66 (35.1)	66 (33.3)	201	
Long-acting insulin intake					
Glargine/Detemir	18 (31.0)	21 (36.2)	19 (32.8)	58	0.814 <sup>a</sup>
NPH/mix	68 (34.8)	63 (32.4)	66 (32.8)	197	
Dietary supplement intake					
Yes	31 (34.8)	32 (36.0)	26 (29.2)	89	0.564 <sup>a</sup>
No	56 (32.7)	54 (31.6)	61 (35.7)	171	
Education					
Diploma and lower	27 (39.7)	22 (32.4)	19 (27.9)	68	0.382 <sup>a</sup>
Academic	60(31.3)	64 (33.3)	68 (35.4)	192	
Physical activity (MET-hour/week)	26.2 ± 27.5	23.8 ± 26.5	27.3 ± 31.2	25.8 ± 28.4	0.804 <sup>b</sup>
Energy intake (kcal/day)	2287.1 ± 632.9	2476.6 ± 680.3	2368.7 ± 732.4	2377.5 ± 684.9	0.433 <sup>b</sup>
Dietary phytochemical index	23.6 ± 5.0	34.3 ± 3.2	45.8 ± 6.6	34.6 ± 10.4	< 0.001

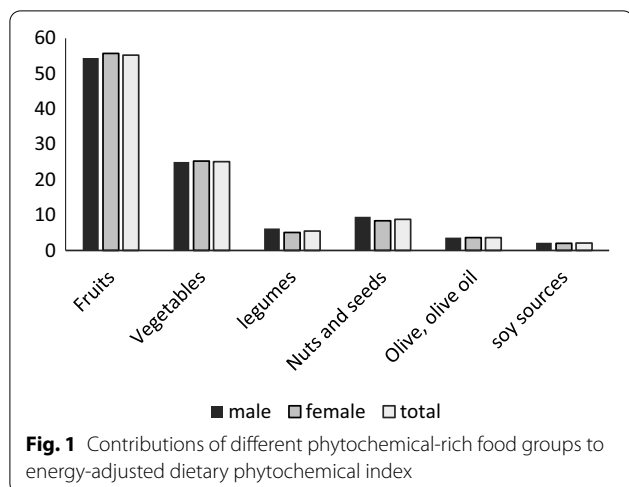
Data are shown as the mean ± SD or number (%)

DPI dietary phytochemical index, BMI body mass index, NPH neutral protamine Hagedorn, no description, MET metabolic equivalent

<sup>a</sup> *P* value is for  $\chi^2$  test, used for categorical data

<sup>b</sup> *P* trend is for analysis of variance test, used to compare continuous variables, calculated by linear regression test





compared with those in the lower tertile ( $P$  trend = 0.03) (Model 2). In addition, after further adjustment for intake of SFA, MUFA, PUFA and trans fatty acids participants in the higher tertile of DPI, had significantly lower LDL-C ( $P$  trend = 0.03) and LDL-C to HDL-C ratio ( $P$  trend = 0.03) compared with those in the lower tertile (Model 3). After further adjustment for dietary intake of sodium and potassium, significant relation was observed between DPI and SBP ( $P$  trend = 0.04) (Model 3) (Fig. 2). No significant association was found between GPx, SOD, TAC and DPI. By increasing the tertiles of DPI, levels of FBG decreased, while TAC increased, however these findings were not statistically significant ( $P$  trend > 0.05).

The OR and 95% CI of CVD risk factors are shown in Table 3. In crude model, no significant association was found between CVD risk factors and DPI ( $P$  trend > 0.05), except for hyperglycemia that compared with participants in the lowest tertile, those in the highest tertile of DPI, had 85% lower chance of hyperglycemia (OR 0.15; 95% CI, 0.03–0.77). After adjustment for age, sex, total energy intake, physical activity, BMI, diabetes duration, total insulin dose, education and dietary supplement intake, compared with participants in the lowest tertile, those in the highest tertile of DPI, had 88% lower chance of hyperglycemia (OR 0.12; 95% CI, 0.02–0.82), 81% lower chance of low HDL-C level (OR 0.19; 95% CI, 0.04–0.86) and 98% lower chance of high LDL-C/HDL-C ratio (OR 0.02; 95% CI, 0.001–0.89). In Fig. 3, the ORs of CVD risk factors across DPI tertiles are presented for statistically significant findings. No relationship was found between DPI and overweight or obesity, central obesity and HTN ( $P$  trend > 0.05). Although the chance of high LDL-C decreased across the DPI tertile in both crude and adjusted model, it was not significant ( $P$  trend > 0.05). All participants had DBP lower than 90 mmHg, so we

were not able to calculate the OR for high DBP. Furthermore, just few participants (7 from 261) had hypertriglyceridemia, so logistic regression was not performed to assess the chance of hypertriglyceridemia. Because of the sparsity of data, wide 95% CI for high SBP was observed (Table 3).

## Discussion

In this cross sectional study, which investigated the relationship between DPI with CVD risk factors in patients with T1DM, we calculated the DPI based on the division of energy content of foods rich in phytochemicals. Our findings indicated that, participants with a higher DPI, had lower chance of high FBG, low HDL-C level, and high LDL-C to HDL-C ratio. Furthermore participants in the higher tertile of DPI had significantly lower LDL-C to HDL-C ratio, LDL-C and SBP compared with those in the lower tertile. Moreover, there were no relationships between DPI and other CVD risk factors.

In line with our findings, a longitudinal study reported significant inverse association between FBG level and DPI at baseline of study but not after 3-years of follow-up [23]. Furthermore, a case-control study has found that participants in the upper quartiles of DPI had lower odds of pre-diabetes [11]. Several studies reported significant association between intake of different phytochemicals and better FBG levels in healthy subjects [24, 25] and patients with type 2 DM [26, 27]. However, some studies have not found significant relationship between FBG level and DPI in healthy individuals [12, 28]. There are several mechanisms that phytochemicals influence carbohydrate metabolism and improve FBG [29], such as inhibition of carbohydrate digestion and intestinal glucose absorption, stimulation of insulin secretion from pancreatic  $\beta$ -cells, stimulation of hepatic glycolysis and glycogenesis, anti-inflammatory and antioxidant properties, effect on intracellular signaling pathway and gene expression [29, 30].

Our study revealed that higher intake of phytochemical rich food is associated with lower mean LDL-C and higher chance of high HDL-C levels. Golzarand et al. [31] observed that after 3 years of follow-up, the levels of TC, TG, HDL-C, and non-high-density lipoprotein cholesterol (non-HDL-C) in the highest quartile of DPI, significantly decreased in healthy men but not in women. Furthermore, our findings about HDL-C is in line with the study of Bahadoran et al. [12] that found higher mean serum HDL-C in the higher DPI tertile in healthy adults. However, in another study no association was reported between HDL-C level and DPI in healthy adults [28]. Different findings might be explained by the discrepancy in

**Table 2** Cardiovascular risk factors across tertiles of the sex-specific energy-adjusted DPI in patients with type 1 diabetes (n = 81)

Variable	DPI tertiles			P value	P trend <sup>c</sup>
	T1 (n = 29)	T2 (n = 25)	T3 (n = 27)		
BMI (kg/m <sup>2</sup> ) <sup>a</sup>					
Model 1	23.4 ± 3.2	23.5 ± 3.5	23.5 ± 3.1	0.983	0.857
Model 2	23.4 ± 3.2	23.5 ± 3.2	23.4 ± 3.2	0.945	0.983
Waist circumference (cm) <sup>a</sup>					
Model 1	86.0 ± 10.2	84.8 ± 10.3	85.7 ± 9.8	0.725	0.828
Model 2	86.0 ± 6.5	84.7 ± 6.5	85.8 ± 6.5	0.422	0.848
Systolic blood pressure (mmhg) <sup>a</sup>					
Model 1	117.3 ± 12.6	110.9 ± 11.5	108.8 ± 14.0	0.308	0.135
Model 2	111.8 ± 11.3	110.8 ± 11.3	109.0 ± 11.4	0.301	0.126
Model 3 <sup>b</sup>	112.6 ± 12.6	110.7 ± 11.2	108.4 ± 12.4	0.144	0.041
Diastolic blood pressure (mmhg) <sup>a</sup>					
Model 1	73.1 ± 6.0	74.0 ± 6.3	73.5 ± 6.7	0.611	0.626
Model 2	73.1 ± 6.5	73.9 ± 6.5	73.6 ± 6.5	0.735	0.633
Model 3 <sup>b</sup>	74.0 ± 7.1	73.8 ± 6.3	72.9 ± 7.0	0.585	0.364
Fasting blood glucose (mg/dL)					
Model 1	175.1 ± 5.9	163.3 ± 5.5	143.0 ± 5.7	0.225	0.112
Model 2	168.7 ± 5.5	167.9 ± 5.5	145.2 ± 5.7	0.421	0.238
HbA1c <sup>a</sup>					
Model 1	7.0 ± 0.8	7.0 ± 0.8	7.0 ± 0.8	0.839	0.571
Model 2	7.0 ± 0.8	7.0 ± 0.8	7.0 ± 0.8	0.966	0.876
Total cholesterol (mg/dL)					
Model 1	171.7 ± 26.8	167.7 ± 37.0	169.8 ± 30.1	0.898	0.819
Model 2	170.1 ± 32.6	171.1 ± 33.4	168.3 ± 32.6	0.941	0.927
Model 3	174.0 ± 30.3	172.2 ± 31.1	163.1 ± 31.4	0.456	0.266
Triglyceride (mg/dL)					
Model 1	81.5 ± 1.6	63.5 ± 1.5	78.5 ± 1.4	0.075	0.703
Model 2	79.8 ± 5.8	61.9 ± 5.4	82.0 ± 5.6	0.038	0.856
Model 3	82.4 ± 5.8	63.5 ± 5.4	77.4 ± 5.7	0.079	0.487
HDL-C (mg/dL)					
Model 1	51.8 ± 9.8	55.1 ± 9.3	53.8 ± 9.4	0.429	0.425
Model 2	50.9 ± 9.4	55.5 ± 9.6	54.4 ± 9.3	0.223	0.232
Model 3	51.8 ± 9.9	55.9 ± 10.2	53.1 ± 10.3	0.203	0.551
LDL-C (mg/dL)					
Model 1	101.9 ± 5.7	92.3 ± 5.3	94.1 ± 5.5	0.344	0.327
Model 2	101.9 ± 5.7	95.9 ± 5.3	91.0 ± 5.5	0.329	0.134
Model 3	104.5 ± 5.7	95.1 ± 5.3	89.1 ± 5.5	0.130	0.033
LDL-C/HDL-C					
Model 1	2.1 ± 0.7	1.8 ± 0.7	1.8 ± 0.5	0.157	0.124
Model 2	2.1 ± 0.6	1.9 ± 0.6	1.7 ± 0.6	0.085	0.027
Model 3	2.1 ± 0.6	1.8 ± 0.6	1.8 ± 0.6	0.137	0.029
Superoxide dismutase activity (IU/mL)					
Model 1	35.2 ± 1.2	34.5 ± 1.1	34.6 ± 1.1	0.871	0.671
Model 2	35.4 ± 5.4	34.2 ± 5.3	34.5 ± 5.3	0.556	0.419
Glutathione peroxidase activity (IU/mL)					
Model 1	144.7 ± 3.4	125.2 ± 3.5	135.2 ± 3.4	0.911	0.835
Model 2	142.6 ± 6.7	126.2 ± 6.6	136.1 ± 6.5	0.906	0.902
Total antioxidant capacity (mmol/L)					
Model 1	362.5 ± 62.0	376.8 ± 65.9	379.9 ± 47.4	0.510	0.274

**Table 2** (continued)

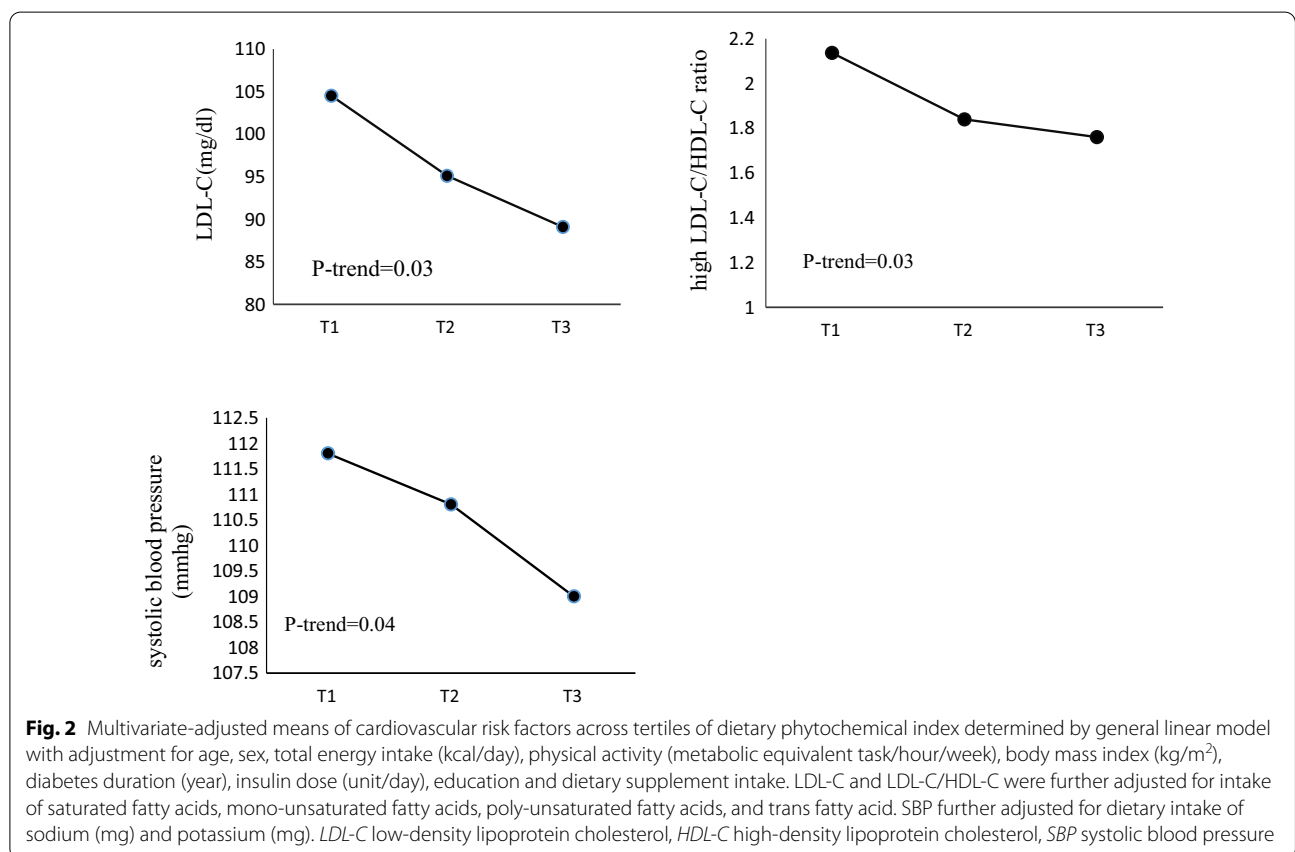
Variable	DPI tertiles			P value	P trend <sup>c</sup>
	T1 (n = 29)	T2 (n = 25)	T3 (n = 27)		
Model 2	357.6 ± 57.0	380.5 ± 59.1	381.5 ± 57.4	0.246	0.132

Data are shown as mean ± SD

Model 1 = crude, analysis of variance test was used. Model 2 = adjusted for age, sex, total energy intake (kcal/day), physical activity (MET/min/week), BMI (kg/m<sup>2</sup>), diabetes duration (year), total daily insulin dose (unit/day), education and dietary supplement intake. Model 3 = adjusted for age, sex, total energy intake (kcal/day), physical activity (MET/min/week), BMI (kg/m<sup>2</sup>), diabetes duration (year), total daily insulin dose (unit/day), education, dietary supplement intake, saturated fatty acid (g/day), mono-unsaturated fatty acid (g/day), poly-unsaturated fatty acid (g/day) and trans fatty acid (g/day), analysis of covariance test was used

DPI dietary phytochemical index, BMI body mass index, HbA1c hemoglobin A1c, LDL-C low-density lipoprotein cholesterol, HDL-C high-density lipoprotein cholesterol, MET metabolic equivalent

<sup>a</sup> T1 = 87, T2 = 87, T3 = 87. <sup>b</sup> Adjusted for age, sex, total energy intake (kcal/day), physical activity (MET/min/week), BMI (kg/m<sup>2</sup>), diabetes duration (year), total daily insulin dose, education, dietary supplement intake, dietary intake of sodium (mg) and potassium (mg). <sup>c</sup> P trend calculated by linear regression



characteristics of participants, study design and study sample size.

Our study showed that higher intake of phytochemical rich food is significantly associated with lower chance of high LDL-C/HDL-C ratio, which is a predictor of CVD risk [32]. There are some studies that investigated the effect of phytochemicals intake on LDL-C/HDL-C ratio. A randomized clinical study on subjects with hypercholesterolemia, showed that intake of insoluble polyphenols

could reduce the LDL-C/HDL-C ratio [33]. Another intervention study indicated that consumption of red wine polyphenols resulted in 7% reduction in LDL-C/HDL-C ratio compared to the baseline values in men who are at high risk of CVD [34]. Phytochemicals may improve lipid profile [35]. One of the best examples of a phytochemical-rich diet is Mediterranean diet. However, adding specific phytochemicals such as phytosterols and proanthocyanidins to Mediterranean diet increased the

**Table 3** Odds ratio and 95% confidence intervals for cardiovascular risk factors across tertiles of sex-specific energy-adjusted DPI in patients with type 1 diabetes

Variable	Models	DPI tertile			P trend <sup>b</sup>
		T1 (n = 29)	T2 (n = 25)	T3 (n = 27)	
Hyperglycemia (> 100 mg/dL)	Model 1	1.0	0.38 (0.06–2.33)	0.15 (0.03–0.77)	0.016
	P value		0.326	0.022	
	Model 2	1.0	0.39 (0.05–3.14)	0.12 (0.02–0.82)	0.020
	P value		0.485	0.031	
Low HDL-C (< 40 mg/dL in men and < 50 mg/dL in women)	Model 1	1.0	0.52 (0.16–1.69)	0.47 (0.14–1.52)	0.195
	P value		0.303	0.274	
	Model 2	1.0	0.24 (0.05–1.09)	0.19 (0.04–0.86)	0.033
	P value		0.064	0.039	
High LDL-C (> 100 mg/dL)	Model 1	1.0	0.60 (0.20–1.80)	0.54 (0.18–1.58)	0.254
	P value		0.487	0.333	
	Model 2	1.0	0.95 (0.26–3.46)	0.40 (0.11–1.44)	0.167
	P value		0.905	0.201	
Hypercholesterolemia (> 200 mg/dL)	Model 1	1.0	2.17 (0.46–10.16)	1.08 (0.20–5.89)	0.928
	P value		0.324	0.998	
	Model 2	1.0	4.59 (0.72–29.28)	1.20 (0.20–7.29)	0.882
	P value		0.114	0.832	
High LDL-C/HDL-C (> 3.5 in men, > 3 in women)	Model 1	1.0	0.33 (0.06–1.83)	0.48 (0.11–2.15)	0.299
	P value		0.222	0.302	
	Model 2	1.0	0.08 (0.004–1.77)	0.02 (0.001–0.89)	0.041
	P value		0.109	0.414	
High HbA1c (> 7%) <sup>a</sup>	Model 1	1.0	1.00 (0.55–1.81)	1.00 (0.55–1.81)	1.000
	P value		1.000	1.000	
	Model 2	1.0	1.10 (0.59–2.03)	1.12 (0.60–2.08)	0.722
	P value		0.898	0.729	
Overweight or obesity (BMI > 24.9 kg/m <sup>2</sup> ) <sup>a</sup>	Model 1	1.0	1.06 (0.55–2.01)	0.79 (0.41–1.55)	0.498
	P value		0.973	0.554	
	Model 2	1.0	1.06 (0.54–2.08)	0.73 (0.37–1.48)	0.383
	P value		0.989	0.458	
Abdominal obesity (waist circumference > 94 cm in men and > 80 cm in women) <sup>a</sup>	Model 1	1.0	0.79 (0.43–1.44)	0.83 (0.45–1.51)	0.542
	P value		0.433	0.501	
	Model 2	1.0	0.49 (0.15–1.61)	0.47 (0.14–1.55)	0.201
	P value		0.210	0.244	
High systolic blood pressure (systolic blood pressure higher than 140 mmHg) <sup>a</sup>	Model 1	1.0	2.02 (0.18–22.73)	4.14 (0.45–37.85)	0.174
	P value		0.658	0.203	
	Model 2		1.59 (0.09–28.31)	4.15 (0.36–48.06)	0.205
	P value		0.887	0.342	

Logistic regression model was used

Model 1 = crude. Model 2 = adjusted for age, sex, total energy intake (kcal/day), physical activity (MET/min/week), BMI (kg/m<sup>2</sup>), diabetes duration (year), total insulin dose (unit/day), education and dietary supplement intake

DPI dietary phytochemical index, LDL-C low-density lipoprotein cholesterol, HDL-C high-density lipoprotein cholesterol, HbA1c hemoglobin A1c, BMI body mass index, MET metabolic equivalent

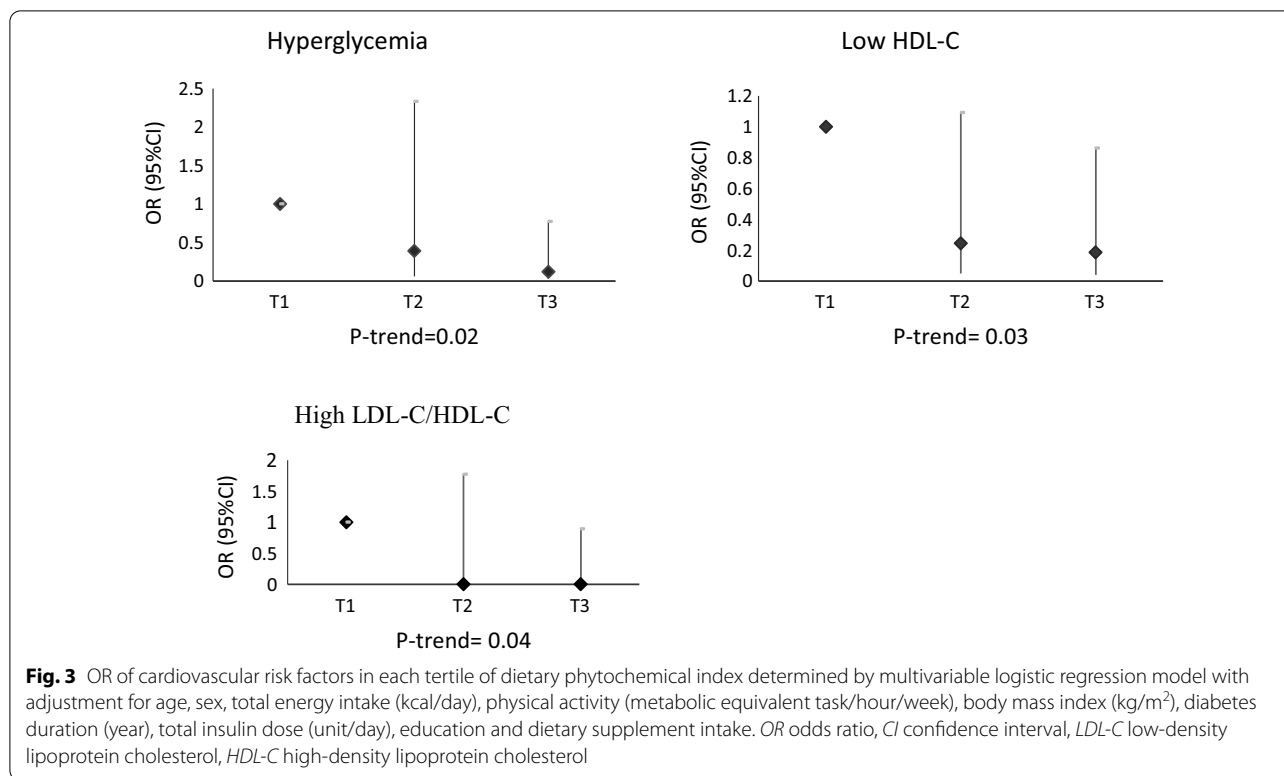
<sup>a</sup> T1 = 87, T2 = 87, T3 = 87

<sup>b</sup> P trend calculated by logistic regression test

effect of diet on decreasing TC, LDL-C, and non-HDL-C and increasing HDL-C compared with Mediterranean diet alone [36]. Peroxisome proliferator-activated

receptors (PPARs) are compounds that play an important role in lipid metabolism. Some phytochemicals as natural PPARs ligands could activate PPARs and affect lipid





metabolism, increase fatty acid uptake, utilization, and catabolism by affecting on fatty acid transport. Furthermore, PPARs lead to lower plasma levels of cholesterol, triacylglycerol and higher HDL-C level [37].

Our findings showed that mean SBP decreased across increasing DPI tertiles, which is similar to the result of a study in healthy participants [12]. However, in logistic regression no association was found between SBP and DPI. On the contrary, some studies reported that participants with higher intake of phytochemical-rich diet had lower risk for occurrence of HTN in 3 years follow-up. However, no significant difference was observed in mean SBP and DBP across DPI quartiles [28]. Previous studies indicated that consumption of phytochemical rich food, such as fruits and vegetables [38], legumes [39] and olive [40], is inversely associated with HTN. Huang et al., reported that consumption of different sources of phytochemicals including soy isoflavones and berries polyphenols significantly reduced SBP but not DBP [41]. However, another study on participants with HTN observed that a combination of isolated phytochemicals and botanical extracts just decreased DBP but not SBP [42]. The dietary approaches to stop hypertension (DASH), which is rich in fruits, vegetables and low-fat dairy foods, reduces blood pressure. DASH diet provides an abundance of phytochemicals that may contribute to blood pressure lowering properties of this type of

diet [43]. OS is an important factor in pathogenesis of HTN, that phytochemicals with antioxidant properties could reduce the risk of HTN. Flavonoids by modulating endothelial nitric oxide synthase activity, could increase endothelial-derived nitric oxide which is a vasodilator factor that enhances endothelial function [44].

In the present study, no association was found between antioxidant biomarkers and DPI. In line with our result, a previous cross-sectional study observed that DPI was not significantly related to total antioxidant status in overweight adults [13]. In a cross-sectional study on healthy adolescents, higher intake of phytochemicals such as retinol,  $\alpha$ -tocopherol, lycopene and the carotenoids was associated with higher serum levels of the mentioned antioxidant compounds, except lycopene [45]. The result of an experimental study showed no significant effect of phytosterol supplementation on plasma TAC in patients with metabolic syndrome [46]. Moreover, flavonoids supplement in patients with T1DM significantly decreased GPx activity, while other parameters of antioxidant capacity such as glutathione, activity of catalase and SOD remained unchanged [47]. These discrepancies could be explained by measuring different antioxidant biomarkers and various phytochemical supplementation.

This study has some limitations. The cross-sectional design is the major limitation of this study, which prevents to observe the cause and effect of the relationship.

The other limitation is inherent limitations of DPI. In this index phytochemical rich food without energy content like spices, green and black tea were not considered. In addition, not considering the type of consumed phytochemicals is another limitation, because two diets with the same DPI but different source of phytochemicals could have different potential benefits. Although the various confounders were carefully controlled, it is possible to miss other residual confounders.

However, the strength of this study is investigating on dietary intake of patients with T1DM who are at high risk of several diabetic complications. Moreover, a validated and reliable FFQ was used which was completed by a trained dietitian.

## Conclusions

In conclusion, the findings of this study demonstrated that higher intake of phytochemical rich food, measured by DPI score was associated with lower chance of some CVD risk factors including dyslipidemia and high FBG in patient with T1DM. More studies more studies are warranted to corroborate the present findings.

## Abbreviations

BMI: body mass index; CI: confidence interval; CVD: cardiovascular disease; DBP: diastolic blood pressure; DPI: dietary phytochemical index; DM: diabetes mellitus; FBG: fasting blood glucose; FCT: food composition tables; FFQ: food frequency questionnaire; GPx: glutathione peroxidase; HbA1c: hemoglobin A1c; HDL-C: high-density lipoprotein cholesterol; HTN: hypertension; IPAQ: international physical activity questionnaire; LDL-C: lipoprotein cholesterol; MET: metabolic equivalent task; MUFA: mono-unsaturated fatty acids; OR: odds ratio; OS: oxidative stress; PUFA: poly-unsaturated fatty acids; SBP: systolic blood pressure; SFA: saturated fatty acids; SOD: superoxide dismutase; T1DM: type 1 diabetes mellitus; TAC: total antioxidant capacity; TG: triglyceride; TC: total cholesterol; USDA: US Department of Agriculture; WC: waist circumference.

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## Authors' contributions

Overall G.S., F.S. and M.Q. supervised the project and approved the final version of the manuscript to be submitted; S.D. and G.S. designed the research; S.D., Z.S., A.B., E.N., and A.R., collected data sampling; S.D., M.A., and M.Q., analyzed and interpreted the data; F.S., A.R., critically reviewed the manuscript; and S.D. and G.S., drafted the initial manuscript. All authors read and approved the final manuscript.

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## Availability of data and materials

All data generated or analyzed during this study are included in this published article.

## Declarations

### Ethics approval and consent to participate

The study was approved by the Ethics Committee of Tehran University of Medical Sciences (IR.TUMS.REC.1394.1595) and written informed consent was obtained from all the participants. This study was conducted with observance of the Declaration of Helsinki and the National Ethical Guidelines in Biomedical Research in Iran.

### Consent for publication

Not applicable.

### Conflict of interests

The authors declare no potential conflicts of interests.

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