The Association Between Dietary Diversity Score and Cardiovascular Risk Factors Among Patients With Pemphigus Vulgaris: A Cross Sectional Study

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ABSTRACT

This study was conducted to evaluate the associations between dietary diversity score (DDS) and cardiovascular risk factors in this population. In this cross-sectional study, 187 patients, aged 18–65 years with pemphigus vulgaris were included. DDS was assessed by a 24-hour dietary recall method. Anthropometric measures and biochemical parameters assessed according to standard protocols. Multivariate linear regression analyses used for detecting any associations between DDS and cardiovascular risk factors. The mean ± standard deviation age and body mass index of studied participants were (46.71 ± 11.49 years) and (27.83 ± 4.39 kg/m²) respectively. Our findings showed that a higher DDS intake was related with higher consumption of vegetables (p = 0.001), dairy products (p < 0.001), cereals (p = 0.002), red and processed meat (p < 0.001), sweets and desserts (p < 0.001). After controlling for confounding variables, the results showed positive associations between DDS and high-density lipoprotein cholesterol (HDL-C, \( \beta = 1.87, 95\% \text{ confidence interval [CI]} = 0.30–3.45, p = 0.02 \)) and total cholesterol (TC) levels (\( \beta = 6.41, 95\% \text{ CI} = 1.62–11.03, p = 0.02 \)). However, there were no associations between DDS and prevalence of obesity and glucose homeostasis. The results of this cross-sectional study showed that DDS might be associated with increased HDL-C and TC. However, further prospective studies are needed to prove these findings.

Keywords: Diet; Pemphigus vulgaris; Cardiovascular risk factors

INTRODUCTION

Pemphigus vulgaris (PV) as the most common form of pemphigus, is a rare life-threatening autoimmune disorder that usually affects skin and mucous membranes [1,2]. It was...
estimated that the incidence rate of PV varies from 0.07–3.2 cases per 100,000 people per year and is about one case per 100,000 population in Iran [3]. Some potential genetic and environmental risk factors for the development of pemphigus disease are certain drugs, viral exposures, physical factors, allergic agents, vaccinations, dietary habits, and psychological stresses [4]. Treatment with corticosteroids and immunosuppressive drugs is the main strategy in the management of pemphigus disease [5]. However, previous evidence showed that long-term treatment with these drugs might increase the risk for diseases such as infections, diabetes mellitus, and osteoporosis [6]. It also suggested that use of corticosteroid drugs in pemphigus patients may detrimentally increases the risk of hypertension, obesity, hyperlipidemia, and insulin resistance—side effects that constitute the criteria for the diagnosis of cardiovascular disease (CVD) [7,8]. Therefore, finding new approaches to overcome the complications of corticosteroids is necessary.

As a modifiable environmental factor, dietary factors play an important role in the development of PV [9-12]. However, there is little evidence about the associations between diet and PV related complications. Accordingly, previous research showed that patients with PV had lower serum selenium, zinc, and copper compared to the healthy people [13]. Other studies also have provided evidence showing an association of PV with low levels of vitamin D compared to healthy subjects which might contribute to worsen the disease [14,15]. Besides, the results of a randomized, double blind, placebo-controlled trial showed that L-carnitine supplementation might have beneficial effects on oxidative markers and lipid profiles in patients with PV [16]. On the other hand, recent nutritional epidemiology shifts toward dietary patterns and dietary indexes are more comprehensive than individual foods and nutrients in the detection of the relationship between dietary intakes and risk of skin and chronic diseases [17,18]. Among these indices, the dietary diversity score (DDS) is of great interest because this priori defined indices assesses the overall quality of diet and the adequacy of nutrient [19,20]. This tool evaluates the diversity within food groups which are usually chosen according to dietary guidelines [21,22]. Previous research has been linked the DDS to several chronic diseases such as cancer and metabolic syndrome [23,24]. However, the latest systematic review and meta-analysis did not show any significant association between the DDS and body mass index (BMI) [25]. Besides, a number of studies have indicated that decreased insulin resistance and abnormal glucose homeostasis [23,26,27], reduced serum triglyceride (TG) level [22,23,26-29], and increased high-density lipoprotein cholesterol (HDL-C) [22,27] are associated with higher dietary diversity. In contrast, other study showed that greater adherence to the DDS was associated with increased total cholesterol (TC) and low-density lipoprotein (LDL) and decreased HDL-C and TG [22].

As mentioned above, there is no sound evidence regarding the associations between the DDS and cardiovascular risk factors. In addition, there is no study investigating the association between the DDS and drug-related corticosteroids complications among patients with PV. Therefore, the present study was conducted to investigate the association between the DDS and some cardiovascular risk factors among PV patients in Iranian populations.

**MATERIALS AND METHODS**

**Study population and design**

This cross-sectional study performed on 187 patients with PV referring to Razi skin Hospital of the Tehran University of Medical Sciences (TUMS). After explaining the goals of the study,
if the patients were willing to participate in the research, they signed written consent forms and were asked to refer to Razi Hospital in the next visit after 12–14 hours of fasting. Inclusion criteria were patient’s satisfaction, age 18–65 years old, diagnosis of PV by a dermatologist based on the European Dermatology Forum Iranian guidelines for rituximab therapy in pemphigus patients (at least one-year disease duration) [30], intake of corticosteroid drugs alone or combine with other drugs (methotrexate, azathioprine, and cellcept). They did not include in the study if they were on dietary regimen and who had total daily energy intakes outside the range of 800–4,200 kcal/d, had cardiovascular or diabetes diseases before PV diagnosis. All steps were performed in accordance with ethical criteria of Tehran University of Medical Sciences (TUMS, ethics code:IR.TUMS.VCR.REC.1397.301). Written informed consent was obtained from all participants.

**Demographic assessment**
Patients completed a questionnaire regarding information about the age, medical condition, disease duration, type and quantity of drugs.

**Anthropometric measurements**
Weight and height were measured according to standardized methods to the nearest 100 g in minimally clothed condition using digital scales and standing position by a tape stadiometer to the nearest 1 mm, respectively. Waist circumference (WC) was assessed to the nearest 0.1 cm at the umbilical level, and hip circumference at the maximal level over light clothing using a non-stretch tape measure. BMI calculated as weight (kg) divided by height in meters squared.

**Biochemical measurements**
All blood tests were done in the morning after 10-hour overnight fasting. Serum glucose level, TG, TC, and HDL-C were measured using commercial kits routinely used in Iran (Pars Azmoon Co., Tehran, Iran). LDL cholesterol (LDL-C) was also calculated by Friedewald formula [31] and serum insulin was measured by electrochemiluminescence immunoassay method (Diagnostic Biochem Canada, Inc., Montreal, Canada). We subtracted the concentration of HDL-C from that TC to determine the non-HDL-C level. Moreover, insulin sensitivity was calculated by the following formulas according to quantitative insulin sensitivity check index (QUICKI = 1/(log(fasting insulin, µU/mL) + log(fasting glucose, mg/dL))) [32], and homeostatic model assessment for insulin resistance (HOMA-IR = (fasting insulin, µm/mL) + (fasting glucose, mg/dL)/405) [33].

**Dietary assessment and DDSs calculation**
Usual dietary intakes of subjects were collected using 24-hour dietary recalls on 2 non-consecutive days (1 workday and one day off). Dietary intakes were gathered with the help of experienced nutritionists. The subjects asked to report all the foods and beverages they consumed during the previous 24 hours. After this, reported dietary intakes converted to grams using Home Scale Guide. Finally, Nutritionist IV software (First Databank, San Bruno, CA, USA) was used to assess the amount of energy and nutrients intake. DDS determined based on the previous research and followed the local and cultural aspects of food grouping [34-36]. Accordingly, the 5 main food groups mentioned in food pyramid including cereals, vegetables, fruits, meats and dairy products were used, which were divided into 23 subgroups. Cereals and their products were classified into 5 subgroups (breads, biscuits, pasta, rice, and barley/bulgur/corn [breakfast cereal]), vegetables into 7 subgroups (tomatoes and their products, starchy vegetables and legumes, yellow and orange vegetables, green leafy vegetables and other vegetables such as eggplant and squash), fruits into 2 subgroups
including citrus, summer vegetables, berries, other fruits and their juices such as apples, bananas, grapes, raisins, etc., dairy products into 3 subgroups (milk, cheese, yogurt, etc.) and meats into 4 subgroups (red meat, chicken, poultry, eggs, fish, etc.). These subgroups were selected in such a way to include diversity of all food items and were adjusted for energy intake. To be considered as a consumer of each food subgroup, one should eat at least a half serving of that item in accordance with the definitions of quantitative food guide pyramid indicators during the 2 days of recall. The final score of dietary diversity is 10, and each of the 5 main groups has a maximum score of 2 out of 10 total score of food diversity. The calculation method of the main groups’ scores shows the percentage of maximum possible score. For example, a person who has consumed at least half of the 4 main subgroups of cereals has a score of (4.5 × 2 = 1.6) in the cereal group. This means that the individual has scored only 1.14 out of 2 points assigned to the main group of cereals. The scores of other main groups is similarly calculated and the total score will be the sum of 5 main groups (5 × 2 = 10).

**Statistical analysis**

After collecting all the samples, the data of the questionnaires were entered into a computer and final analysis was performed on the information related to 187 subjects. Kolmogorov-Smirnov test was used to check the normal of distribution data. Chi-square test were used for comparison of qualitative variables. We used one-way analysis of variance for quantitative variables and Mann-Whitney tests were used if they were not normal. To describe quantitative and qualitative variables, mean (standard deviation or standard error) and frequency report (percentage) were used, respectively. We classified DDS based on mean to 2 groups. Cardiovascular risk factors (dietary intakes of participants across the medians of DDS was assessed using the analysis of covariance (adjusted for age, gender, BMI, energy intake, and anti-diabetic drugs and Lipid-lowering drugs usage). Linear regression was used to investigate the relationship between the DDS and CVD risk factors in crude and adjusted models (adjusted for age, gender, BMI, energy intake, anti-diabetic drugs and Lipid-lowering drugs usage). Spearman was performed to evaluate the correlation between the DDS and cardiovascular biomarkers. Statistical analysis performed using SPSS software version 22 (IBM Corp., Armonk, NY, USA) and p < 0.05 was considered as statistically significant.

**RESULTS**

Sociodemographic characteristics, anthropometric measures, biochemical markers and energy intakes among participants are presented in Table 1. It was showed that the mean of BMI and LDL was higher in female than male (p < 0.05). It also revealed that male participants have higher mean of energy intake (p = 0.005). In addition, these individuals had mean blood glucose (102.70 ± 37.32 mg/dL), TC (185.35 ± 42.72 mg/dL), TG (138.10 ± 102.30 mg/dL), HDL-C and LDL-C, insulin level, HOMA-IR, and QUICKI were 58.68 ± 12.34, 112.63 ± 35.92 mg/dL, 93.17 ± 61.16, 4.79 ± 5.46 and 0.03 ± 0.32, respectively. Moreover, the participants had an average insulin level of 93.17 ± 61.16 microns/mL. The frequency of use of hypoglycemic drugs is 40 (21.4%) and the frequency of fat-lowering drugs is 23 (12.3%). These numbers are different in terms of gender.

General characteristics of participants across the 2 categories of DDS (based on median) presented in Table 2. Statistically significant difference between DDS and total energy intake was seen across the medians of DDS (p ≤ 0.001).
Table 1. Sociodemographic characteristics, anthropometric measures, biochemical markers, and energy intakes among target population

| Variables          | Total (n = 187) | Male (n = 62) | Female (n = 125) | p value |
|--------------------|-----------------|--------------|------------------|---------|
| Age (yr)           | 46.71 ± 11.49   | 46.30 ± 11.42| 46.91 ± 11.56    | 0.730   |
| WC (cm)            | 94.98 ± 11.71   | 93.03 ± 10.36| 95.95 ± 12.26    | 0.100   |
| BMI (kg/m²)        | 27.83 ± 4.39    | 26.86 ± 3.67 | 28.31 ± 4.62     | 0.030   |
| Total energy intake (kcal/d) | 1,945.60 ± 196.27 | 2,002.43 ± 213.98 | 1,917.41 ± 181.23 | 0.005   |
| FBS (mg/dL)        | 102.70 ± 37.35  | 100.19 ± 25.20| 101.95 ± 42.15   | 0.520   |
| TG (mg/dL)         | 138.10 ± 102.30 | 153.20 ± 157.98| 130.60 ± 57.01   | 0.150   |
| TC (mg/dL)         | 185.35 ± 42.72  | 181.28 ± 37.87| 187.39 ± 44.39   | 0.350   |
| HDL-C (mg/dL)      | 58.68 ± 12.34   | 57.45 ± 11.50 | 59.29 ± 12.74    | 0.330   |
| LDL-C (mg/dL)      | 112.63 ± 35.92  | 102.91 ± 39.80| 117.44 ± 32.95   | 0.009   |
| Insulin (miU/L)    | 17.93 ± 16.61   | 20.12 ± 19.40 | 16.85 ± 15.01    | 0.200   |
| HOMA-IR (mg/dL)    | 4.79 ± 5.46     | 5.22 ± 6.53   | 4.57 ± 4.85      | 0.440   |
| QUICKI             | 0.32 ± 0.03     | 0.31 ± 0.02   | 0.32 ± 0.03      | 0.210   |

Data are presented as mean ± standard deviation and number (%). Independent sample t-test or Mann-Whitney U-test were used for comparison of quantitative variables. \(\chi^2\) test or were used for comparison of qualitative variables.

WC, waist circumference; BMI, body mass index; FBS, fasting blood sugar; TG, triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment-insulin resistance; QUICKI, quantitative insulin sensitivity check index.

Table 2. Participants’ characteristics according to different categories of DDS

| Variables                | DDS                   | p value |
|--------------------------|-----------------------|---------|
| ASD                      | Category 1 (n = 94)   | Category 2 (n = 93) |         |
| Age (yr)                 | 46.40 ± 10.25         | 47.02 ± 12.67 | 0.710   |
| BMI (kg/m²)              | 27.54 ± 4.07          | 28.13 ± 4.70 | 0.360   |
| WC (cm)                  | 93.84 ± 12.12         | 96.13 ± 11.23| 0.180   |
| Total energy (kcal/d)    | 1,856.95 ± 136.13     | 2,035.20 ± 207.37| < 0.001 |
| Sex                      |                       | 0.320   |
| Male                     | 28 (29.8)             | 34 (36.6)  |
| Female                   | 66 (70.2)             | 59 (63.4)  |
| Lipid-lowering drug usage|                       | 0.840   |
| Yes                      | 12 (12.8)             | 11 (11.8)  |
| No                       | 82 (87.2)             | 82 (88.2)  |
| Anti-diabetic drugs usage|                       | 0.300   |
| Yes                      | 23 (24.5)             | 17 (18.3)  |
| No                       | 71 (75.5)             | 75 (81.7)  |

Dietary pattern scores are categorized according to the median. Data are presented as mean ± standard deviation or number (%). Independent sample t-test or Mann-Whitney U-test were used for comparison of quantitative variables. \(\chi^2\) test were used for comparison of qualitative variables.

DDS, dietary diversity score; BMI, body mass index; WC, waist circumference.

Table 3 shows participants’ anthropometric measurements and cardiovascular markers across the medians of the DDS in the crude model. We also evaluated the association in 3 model, in the way that model one was adjusted for age and gender, model 2 was adjusted for model 1 plus energy intake (BMI and WC) or energy intake and BMI (fasting blood sugar [FBS], TG, TC, HDL-C, LDL-C, insulin, HOMA-IR, and QUICKI), and model 3 was adjusted for model 2 plus anti-diabetic drugs and lipid-lowering drugs usage. No statistically significant differences were seen in relation of DDS and cardiovascular risk factors (p > 0.05).

Dietary intakes of patients across medians of DDS are displayed in Table 4. It was found that higher DDS was associated with higher consumption of dairy (p < 0.001), grains (p = 0.002), red/processed meats (p < 0.001), and sweets and desserts (p < 0.001).
Table 3. The association of anthropometric measurements and cardiovascular markers across the medians of the DDS

| Variables          | DDS                     | p value* |
|--------------------|-------------------------|----------|
|                    | Low category (n = 94)   | High category (n = 93) |
| **BMI (kg/m²)**    |                         |          |
|                    | Crude                   | 27.54 ± 4.07 | 28.13 ± 4.70 | 0.36 |
|                    | Model 1                 | 27.49 ± 0.45 | 28.17 ± 0.45 | 0.29 |
|                    | Model 2                 | 27.27 ± 0.47 | 28.39 ± 0.48 | 0.11 |
|                    | Model 3                 | 27.25 ± 0.48 | 28.42 ± 0.48 | 0.10 |
| **WC (cm)**        |                         |          |
|                    | Crude                   | 93.84 ± 12.12 | 96.13 ± 11.23 | 0.18 |
|                    | Model 1                 | 93.78 ± 1.19 | 96.19 ± 1.19 | 0.15 |
|                    | Model 2                 | 93.83 ± 1.26 | 96.14 ± 1.27 | 0.22 |
|                    | Model 3                 | 93.99 ± 1.27 | 95.98 ± 1.27 | 0.29 |
| **FBS (mg/dL)**    |                         |          |
|                    | Crude                   | 100.26 ± 30.53 | 105.17 ± 43.20 | 0.37 |
|                    | Model 1                 | 100.24 ± 3.85 | 105.19 ± 3.87 | 0.36 |
|                    | Model 2                 | 101.19 ± 3.93 | 104.23 ± 3.95 | 0.60 |
|                    | Model 3                 | 100.44 ± 3.88 | 105.00 ± 3.91 | 0.43 |
| **TG (mg/dL)**     |                         |          |
|                    | Crude                   | 149.08 ± 132.91 | 127.00 ± 55.26 | 0.14 |
|                    | Model 1                 | 149.84 ± 10.52 | 126.23 ± 10.57 | 0.11 |
|                    | Model 2                 | 149.62 ± 11.17 | 126.45 ± 11.24 | 0.17 |
|                    | Model 3                 | 150.34 ± 11.24 | 125.72 ± 11.30 | 0.14 |
| **TC (mg/dL)**     |                         |          |
|                    | Crude                   | 186.96 ± 46.52 | 183.73 ± 38.68 | 0.60 |
|                    | Model 1                 | 186.80 ± 4.43 | 183.89 ± 4.45 | 0.64 |
|                    | Model 2                 | 180.76 ± 4.58 | 189.99 ± 4.61 | 0.18 |
|                    | Model 3                 | 180.97 ± 4.61 | 189.79 ± 4.64 | 0.20 |
| **HDL-C (mg/dL)**  |                         |          |
|                    | Crude                   | 58.56 ± 9.96 | 58.80 ± 14.41 | 0.89 |
|                    | Model 1                 | 58.52 ± 1.28 | 58.85 ± 1.28 | 0.85 |
|                    | Model 2                 | 57.26 ± 1.34 | 60.11 ± 1.35 | 0.16 |
|                    | Model 3                 | 57.12 ± 1.35 | 60.25 ± 1.35 | 0.12 |
| **LDL-C (mg/dL)**  |                         |          |
|                    | Crude                   | 110.21 ± 37.31 | 115.07 ± 34.48 | 0.35 |
|                    | Model 1                 | 109.67 ± 3.65 | 115.62 ± 3.67 | 0.25 |
|                    | Model 2                 | 107.51 ± 3.88 | 117.80 ± 3.90 | 0.08 |
|                    | Model 3                 | 107.66 ± 3.91 | 117.65 ± 3.93 | 0.09 |
| **Non-HDL-C**      |                         |          |
|                    | Crude                   | 128.43 ± 43.55 | 124.92 ± 36.00 | 0.55 |
|                    | Model 1                 | 128.40 ± 4.14 | 124.92 ± 4.16 | 0.58 |
|                    | Model 2                 | 128.40 ± 4.33 | 124.92 ± 4.35 | 0.32 |
|                    | Model 3                 | 128.40 ± 4.35 | 124.92 ± 4.38 | 0.38 |
| **TC/HDL-C**       |                         |          |
|                    | Crude                   | 3.23 ± 0.83 | 3.25 ± 0.89 | 0.88 |
|                    | Model 1                 | 3.23 ± 0.09 | 3.25 ± 0.09 | 0.88 |
|                    | Model 2                 | 3.23 ± 0.09 | 3.25 ± 0.09 | 0.41 |
|                    | Model 3                 | 3.23 ± 0.09 | 3.25 ± 0.09 | 0.48 |
| **Insulin (µIU/mL)**|                         |          |
|                    | Crude                   | 16.75 ± 16.81 | 19.13 ± 16.41 | 0.33 |
|                    | Model 1                 | 16.86 ± 1.71 | 19.02 ± 1.72 | 0.37 |
|                    | Model 2                 | 17.93 ± 1.75 | 17.94 ± 1.76 | 0.99 |
|                    | Model 3                 | 18.11 ± 1.74 | 17.75 ± 1.75 | 0.89 |
| **HOMA-IR**        |                         |          |
|                    | Crude                   | 4.19 ± 4.25 | 5.39 ± 6.42 | 0.13 |
|                    | Model 1                 | 4.22 ± 0.56 | 5.36 ± 0.56 | 0.15 |
|                    | Model 2                 | 4.61 ± 0.55 | 4.96 ± 0.56 | 0.68 |
|                    | Model 3                 | 4.62 ± 0.55 | 4.96 ± 0.56 | 0.68 |

(continued to the next page)
Table 3. (Continued) The association of anthropometric measurements and cardiovascular markers across the medians of the DDS

| Variables          | DDS          | p value* |
|--------------------|--------------|----------|
|                    | Low category (n = 94) | High category (n = 93) |
| QUICKI             |              |          |
| Crude             | 0.32 ± 0.03  | 0.31 ± 0.02 | 0.02 |
| Model 1           | 0.32 ± 0.00  | 0.31 ± 0.00 | 0.03 |
| Model 2           | 0.32 ± 0.00  | 0.31 ± 0.00 | 0.15 |
| Model 3           | 0.32 ± 0.00  | 0.31 ± 0.00 | 0.17 |

Data are presented as mean ± standard deviation for crude model and mean ± standard error for adjusted models. ANCOVA was applied to assess the relationship among variables.

Crude: Not adjusted for any variables.
Model 1: This model was adjusted for age and gender.
Model 2: This model was adjusted for model 1 plus energy intake (BMI and WC) or energy intake and BMI (FBS, TG, TC, HDL-C, LDL-C, insulin, HOMA-IR, and QUICKI).
Model 3: This model was adjusted for model 2 plus anti-diabetic drugs and Lipid-lowering drugs usage.
DDS, dietary diversity score; BMI, body mass index; WC, waist circumference; FBS, fasting blood sugar; HOMA-IR, homeostasis model assessment-insulin resistance; QUICKI, quantitative insulin sensitivity check index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglyceride; TC, total cholesterol; ANCOVA, analysis of covariance.

*Calculated using t-test for the crude model and ANCOVA in the adjusted models.

Table 4. Dietary intakes of participants across medians of DDS

| Variables                        | DDS          | Category 1 (n = 89) | Category 2 (n = 90) | p value* |
|----------------------------------|--------------|---------------------|---------------------|----------|
| Carbohydrate (g/day)             |              | 267.33 ± 4.18       | 274.80 ± 4.16       | 0.230    |
| Protein (g/day)                  |              | 65.05 ± 1.36        | 64.02 ± 1.35        | 0.610    |
| Total fat (g/day)                |              | 72.70 ± 1.95        | 69.45 ± 1.94        | 0.270    |
| Cholesterol (mg/day)             |              | 188.83 ± 8.67       | 189.06 ± 8.61       | 0.980    |
| Saturated fatty acids (g/day)    |              | 17.19 ± 0.51        | 17.54 ± 0.51        | 0.620    |
| Dietary fiber (g/day)            |              | 16.80 ± 0.39        | 15.90 ± 0.39        | 0.130    |
| Vitamin                          |              |                     |                     |          |
| A (RAE/day)                      |              | 1,066.00 ± 91.22    | 1,121.10 ± 90.66    | 0.680    |
| E (mg/day)                       |              | 20.06 ± 1.02        | 18.72 ± 1.01        | 0.380    |
| K (µg/day)                       |              | 96.86 ± 4.75        | 99.93 ± 4.72        | 0.660    |
| D (µg/day)                       |              | 0.56 ± 0.03         | 0.58 ± 0.03         | 0.670    |
| C (mg/day)                       |              | 104.51 ± 4.93       | 92.70 ± 4.90        | 0.100    |
| B1 (mg/day)                      |              | 1.56 ± 0.03         | 1.63 ± 0.03         | 0.210    |
| B2 (mg/day)                      |              | 1.43 ± 0.06         | 1.41 ± 0.06         | 0.790    |
| B3 (mg/day)                      |              | 17.72 ± 0.38        | 18.26 ± 0.38        | 0.350    |
| B5 (mg/day)                      |              | 4.82 ± 0.12         | 4.79 ± 0.12         | 0.870    |
| B6 (mg/day)                      |              | 1.50 ± 0.04         | 1.48 ± 0.04         | 0.750    |
| B9 (µg/day)                      |              | 341.86 ± 9.57       | 345.23 ± 9.52       | 0.810    |
| B12 (µg/day)                     |              | 5.20 ± 0.61         | 5.11 ± 0.60         | 0.920    |
| Minerals                         |              |                     |                     |          |
| Potassium (mg/day)               |              | 2,544.84 ± 84.69    | 2,562.67 ± 84.17    | 0.880    |
| Calcium (mg/day)                 |              | 668.71 ± 28.24      | 651.19 ± 28.06      | 0.670    |
| Iron (mg/day)                    |              | 13.40 ± 0.37        | 13.60 ± 0.37        | 0.720    |
| Magnesium (mg/day)               |              | 267.41 ± 5.48       | 262.125 ± 5.44      | 0.510    |
| Zinc (mg/day)                    |              | 8.24 ± 0.16         | 8.20 ± 0.15         | 0.860    |
| Phosphorous (mg/day)             |              | 1,084.25 ± 25.36    | 1,076.58 ± 25.21    | 0.830    |
| Sodium (mg/day)                  |              | 1,563.51 ± 102.58   | 1,566.03 ± 101.94   | 0.980    |
| Food groups                      |              |                     |                     |          |
| Fruits (g/day)                   |              | 387.42 ± 31.06      | 464.44 ± 31.24      | 0.100    |
| Vegetables (g/day)               |              | 404.49 ± 28.18      | 520.83 ± 28.35      | 0.006    |
| Dairy (g/day)                    |              | 218.67 ± 19.19      | 354.04 ± 19.31      | < 0.001  |
| Nut/Legumes (g/day)              |              | 40.41 ± 5.09        | 46.99 ± 5.12        | 0.550    |
| Grains (g/day)                   |              | 416.73 ± 12.16      | 472.70 ± 12.24      | 0.002    |
| Fish/Poultry (g/day)             |              | 36.82 ± 4.10        | 43.69 ± 4.12        | 0.260    |
| Red/Processed meats (g/day)      |              | 34.20 ± 3.10        | 56.07 ± 3.12        | < 0.001  |
| Sweets and desserts (g/day)      |              | 51.24 ± 7.15        | 100.10 ± 7.19       | < 0.001  |

Data are presented as mean ± standard error.
DDS, dietary diversity score.
*Analysis of covariance test was used (dietary intakes were adjusted for energy intake).
Crude and adjusted associations between the DDS and cardiovascular risk factors are summarized in Table 5. The results showed that the DDS was positively associated with higher HDL-C ($\beta = 1.87$, 95% confidence interval [CI], 0.30–3.45, $p = 0.02$) and TC ($\beta = 6.41$, 95% CI, 1.62–11.03, $p = 0.02$) after adjusting for potential confounders including age, gender, energy intake and BMI, respectively.

Table 6 shows the possible correlation between the DDS and cardiovascular risk factors in patients with PV. Accordingly, the results showed no significant correlations between the DDS and the risk factors of CVD ($p > 0.05$).

| Variables | Crude | Model 1 | Model 2 | Model 3 |
|-----------|-------|---------|---------|---------|
| BMI (kg/m$^2$) | | | | |
| Crude | 0.09 | 0.15 | 0.31 | 0.34 |
| Model 1 | 0.09 | 0.33 | 0.23 | 0.22 |
| Model 2 | 0.09 | 0.30 | 0.87 | 0.90 |
| Model 3 | 0.09 | 0.30 | 0.87 | 0.90 |
| WC (cm) | | | | |
| Crude | 90.81 | 90.90 | 90.88 | 90.69 |
| Model 1 | 91.00 | 91.10 | 91.20 | 91.30 |
| Model 2 | 91.40 | 91.50 | 91.60 | 91.70 |
| Model 3 | 91.80 | 91.90 | 92.00 | 92.10 |
| FBS (mg/dL) | | | | |
| Crude | -0.03 | -0.03 | -0.03 | -0.03 |
| Model 1 | -0.03 | -0.03 | -0.03 | -0.03 |
| Model 2 | -0.03 | -0.03 | -0.03 | -0.03 |
| Model 3 | -0.03 | -0.03 | -0.03 | -0.03 |
| TG (mg/dL) | | | | |
| Crude | -4.29 | -5.19 | -3.38 | -4.67 |
| Model 1 | -4.29 | -5.19 | -3.38 | -4.67 |
| Model 2 | -4.29 | -5.19 | -3.38 | -4.67 |
| Model 3 | -4.29 | -5.19 | -3.38 | -4.67 |
| TC (mg/dL) | | | | |
| Crude | 0.45 | 0.67 | 6.42 | 6.41 |
| Model 1 | 0.45 | 0.67 | 6.42 | 6.41 |
| Model 2 | 0.45 | 0.67 | 6.42 | 6.41 |
| Model 3 | 0.45 | 0.67 | 6.42 | 6.41 |
| HDL-C (mg/dL) | | | | |
| Crude | 0.49 | 0.56 | 1.75 | 1.87 |
| Model 1 | 0.49 | 0.56 | 1.75 | 1.87 |
| Model 2 | 0.49 | 0.56 | 1.75 | 1.87 |
| Model 3 | 0.49 | 0.56 | 1.75 | 1.87 |
| LDL-C (mg/dL) | | | | |
| Crude | 0.49 | 1.09 | 2.72 | 2.55 |
| Model 1 | 0.49 | 1.09 | 2.72 | 2.55 |
| Model 2 | 0.49 | 1.09 | 2.72 | 2.55 |
| Model 3 | 0.49 | 1.09 | 2.72 | 2.55 |
| Non-HDL-C | | | | |
| Crude | -0.04 | 0.11 | 4.67 | 4.54 |
| Model 1 | -0.04 | 0.11 | 4.67 | 4.54 |
| Model 2 | -0.04 | 0.11 | 4.67 | 4.54 |
| Model 3 | -0.04 | 0.11 | 4.67 | 4.54 |
| TC/HDL-C | | | | |
| Crude | 0.00 | 0.00 | 0.04 | 0.04 |
| Model 1 | 0.00 | 0.00 | 0.04 | 0.04 |
| Model 2 | 0.00 | 0.00 | 0.04 | 0.04 |
| Model 3 | 0.00 | 0.00 | 0.04 | 0.04 |

(continued to the next page)
DISCUSSION

We investigated the relation of DDS and HDL-C and TC levels. However, there was no significant association between DDS and other risk factors of CVD. To the best of our knowledge, this is the first study investigating the association of DDS and CVD risk factors in patients with PV and highlighting the roles of diet in the management of such complications that are resulted mostly from corticosteroid and immunosuppressive drugs consumption.

The results of our study revealed that DDS was significantly associated with higher HDL-C and TC. It is noteworthy that this score was not associated with LDL-C, non-HDL-C, and TC to HDL-C ratio, so it seems that the significant positive association between DDS and TC levels is a function of increased HDL-C and is not related to non-HDL-C cholesterol. In line with our

Table 5. (Continued) Crude and adjusted associations between dietary diversity score and cardiovascular risk factors

| Variables          | Beta   | Confidence interval | p value |
|-------------------|--------|---------------------|---------|
| Insulin (µIU/mL)  |        |                     |         |
| Crude             | 1.39   | −0.43–3.22          | 0.13    |
| Model 1           | 1.28   | −0.56–3.12          | 0.17    |
| Model 2           | 0.71   | −1.31–2.75          | 0.48    |
| Model 3           | 0.73   | −1.31–2.79          | 0.47    |
| HOMA-IR           |        |                     |         |
| Crude             | 0.45   | −0.14–1.05          | 0.13    |
| Model 1           | 0.42   | −0.17–1.03          | 0.16    |
| Model 2           | 0.16   | −0.48–0.81          | 0.60    |
| Model 3           | 0.25   | −0.40–0.90          | 0.44    |
| QUICKI            |        |                     |         |
| Crude             | −0.030 | −0.007–0.000        | 0.08    |
| Model 1           | −0.003 | −0.007–0.000        | 0.10    |
| Model 2           | −0.002 | −0.006–0.002        | 0.32    |
| Model 3           | −0.002 | −0.006–0.002        | 0.26    |

*Calculated using linear regression.

Table 6. Pearson correlation between dietary diversity score and cardio metabolic risk factors among study participant

| Variables          | Correlation coefficient | p value |
|-------------------|-------------------------|---------|
| BMI (kg/m²)       | 0.020                   | 0.69    |
| WC (cm)           | 0.090                   | 0.21    |
| TG (mg/dL)        | −0.050                  | 0.45    |
| TC (mg/dL)        | 0.020                   | 0.85    |
| HDL-C (mg/dL)     | 0.050                   | 0.47    |
| LDL-C (mg/dL)     | 0.010                   | 0.80    |
| Non-HDL-C         | −0.001                  | 0.98    |
| TC/HDL-C          | 0.004                   | 0.95    |
| FBS (mg/dL)       | −0.001                  | 0.98    |
| Insulin (µIU/mL)  | −0.110                  | 0.13    |
| HOMA-IR           | 0.100                   | 0.13    |
| QUICKI            | −0.120                  | 0.08    |

Controlled for age and gender. energy intake (BMI and WC) or energy intake and BMI (FBS, TG, TC, HDL-C, LDL-C, insulin, HOMA-IR, and QUICKI), anti-diabetic drugs and lipid-lowering drugs usage.

BMI, body mass index; WC, waist circumference; FBS, fasting blood sugar; HOMA-IR, homeostasis model assessment-insulin resistance; QUICKI, quantitative insulin sensitivity check index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol.

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In the present research, the DDS was not significantly associated with obesity (both abdominal and general). In accordance with our results, in a meta-analysis on observational studies, Salehi-Abargouei et al. [25] reported that there is no association between the DDS and the chance of overweight/obesity. In fact, the association between the DDS and obesity and obesity indices are based on the case-control and cross-sectional studies and there is no prospective in this context. In addition, the methods for dietary intake assessment were different between the studies. As another limitation for the previous research, it should be noted that the adjustment for potential confounders were varied between the studies. Besides, most of the previous research have used only 5 food groups (grains, fruits, vegetables, dairy products, and meats) for the calculation of the DDS and did not consider dietary fat intake. Based on the recent research, healthy fats (especially plants fats) are of great interest due to their health benefit properties [23,37-39] and considering this food group in the scoring of the DDS can be helpful in the final decision about the association between the DDS and cardiovascular risk factors.

Finally, our results showed that there is no association between the DDS and the indices of glucose homeostasis (FBS, HOMA-IR, QUICKI, and serum insulin) in patients with PV. In contrast, in a cross-sectional study being in the highest quartile of the DDS was associated with higher QUICKI and lower HOMA-IR and serum insulin among subjects with metabolic syndrome. However, the results of this study were based on the crude analysis of the data and it seems this results should be used with cautious [26]. In a case-control study among patients with pre-diabetes, Gholizadeh et al. [27] showed inverse association between the DDS and FBG levels. This finding was also based on a crude analysis without adjusting for potential confounders. Moreover, in a cross-sectional study the risk of abnormal glucose homeostasis decreased with increasing the score of dietary diversity [23]. Alike other cardiovascular risk factors, it seems that there is no sound evidence regarding the associations between the DDS and the indices of glucose homeostasis due to low sample size of the studies, differences in dietary intake assessment and calculation of the DDS. Therefore, further comprehensive prospective and clinical studies are needed to confirm or reject this evidence.

In general, the main mechanisms of the effects of the DDS in improving CVD risk factors is unclear. However, the results of previous studies suggest that DDS is associated with...
increased calcium and vitamin intake as well as decreased intake of fatty acids and cholesterol that may improve the risk factors for chronic diseases [22]. Moreover, the components of dietary diversity, including dairy products [38], fruits and vegetables [40], and whole grains [41] are effective in preventing metabolic syndrome. In addition, fruits and vegetables are important components of dietary diversity and are rich sources of antioxidants, indicating their positive and direct relationship with increasing skeletal muscle strength [42,43].

This study was the first one that investigated the association between the DDS and CVD risk factors in patients with PV. However, our study had some limitations. First, this was a cross-sectional study and we cannot find the causality of the obtained results. Second, our study included low number of participants. Third, although we controlled the results for some potential confounders, however, other confounders (especially physical activity) levels were not taken into account. Forth, it seems that dietary recall could not estimate the overall dietary intakes of the participants because no fish intake reported in our study.

In conclusion, the results of the present study showed that the DDS might be associated with increased HDL-C and TC. However, due to the limitations of the study and inconsistent results of the previous studies more comprehensive prospective studies with larger sample sizes and longer durations taking into account different population is warranted.

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