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Original Article

The association of dietary approach to stop hypertension (DASH) diet with hospitalization risk in patients with COVID-19

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S U M M A R Y

Background and aim: Given the importance of dietary habits in the immune system, the current study aimed at investigating the association between Dietary Approach to Stop Hypertension (DASH) diet and risk of hospitalization due to COVID-19.
Methods: Dietary data of 141 patients with COVID-19 were collected using 147-item food frequency questionnaire. DASH score in this cross-sectional study was calculated based on eight components, including fruits, vegetables, legumes and nuts and seeds, whole grains, low-fat dairy, red or processed meats, sweetened beverages, and sodium. Multivariable logistic regression models were applied to estimate the OR and 95% CI for hospitalization due to COVID-19 in each tertile of DASH score.
Results: Mean ± SD of DASH score in inpatients (n=74) and outpatients (n= 87) was 22.5 ± 4.57 and 25.34 ± 4.23, respectively. The risk of hospitalization in the highest tertile of DASH score was 81% lower than the lowest tertile (OR=0.19, 95%CI: 0.07–0.55, *P* trend = 0.001 after adjustment for age, sex, BMI, energy intake). Also, more intake of fruits, vegetables and low-fat dairy products and less intake of sodium, red and processed meat were each

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significantly associated with reduced risk of hospitalization due to COVID-19.

Conclusions: Our data provide evidence that adherence to DASH-style diet was associated with lower risk of hospitalization due to COVID-19.

Introduction

One of the global issues that has been emerged in 2019 was Coronavirus disease (COVID-19) that caused severe acute respiratory syndrome (SARS) leading to significant morbidity and mortality in humans [1]. Fever, cough, sore throat, and malaise are considered as the primary symptoms. Other symptoms mainly include gastrointestinal upsets, nausea, vomiting, diarrhea, loss of taste and/or smell, muscle pain [2]. Furthermore, COVID-19 is allied with serious complications such as acute respiratory distress syndrome (ARDS), cardiac insufficiency, sepsis, and multiple organ dysfunctions (MODS) [3]. The burden of mortality and morbidity related to COVID was extraordinary [4]. Recent evidence has shown that the symptoms and complications of the illness may last for weeks or months after recovery in most patients [5], however, attentions are still initially focused on managing the acute symptoms of the disease [6]. On the one hand, comorbidities such as type 2 diabetes, obesity, chronic lung, kidney and liver diseases, hypertension, and cardiovascular diseases are associated with a poor prognosis and an increased risk of death [7,8]. On the other hand, the presence of these diseases predisposes a person to COVID-19 and exacerbates its complications [9].

The key missing link in this relationship may be diet. Healthy dietary patterns may play important roles in the treatment and prevention of COVID-19 due to close association with immunity and inflammation [10,11]. Furthermore, it has been proposed that a balanced diet might improve the immune response to SARS-CoV-2 infection [10]. Moreover, the adoption of a healthy dietary pattern can reduce the risk factors and complications of COVID-19 [11]. Dietary Approaches to Stop Hypertension (DASH) include foods with anti-inflammatory properties that have positive impacts on improving chronic inflammatory processes and preventing metabolic alterations [12]. DASH diet is characterized by consumption of high amounts of fruits, vegetables, legumes, nuts and seeds, whole grains, low-fat dairy, poultry and fish with reduced amounts of processed meats, sweetened beverages, and sodium [13,14]. DASH diet not only effectively reduces blood pressure, but has also been reported to be associated with lower risk of chronic diseases and mortality [15]. Furthermore, previous research has stated the association between DASH and lower biomarkers of lipid peroxidation and higher antioxidant capacity [16]. Low sodium content of DASH diet is associated with a reduced systemic inflammation, which can be attribute to a decreased coagulation level [17].

Comprehending the association between DASH diet and COVID-19 disease can highlight the importance of nutrition in viral and infectious diseases. The aim of the current study was to investigate the relationship of DASH dietary pattern with the COVID-19 related risk of hospitalization.

Method and materials

Participants

A COVID-19 case–control study in 53 inpatients and 88 outpatients was conducted to assess the association of DASH dietary pattern with the COVID-19 related risk of hospitalization. Simple consecutive method was used in order to enroll hospitalized patients from Imam Khomeini referral hospital in Tehran, Iran. Simorgh clinical laboratory was designated to enroll outpatients. Sampling methods has been explained in another article more comprehensively [18]. Briefly, the diagnosis was made based on the results of nasopharyngeal swabs for SARS-CoV-2 RT-PCR and chest computed tomography scans. Patients admitted to the intensive care unit (ICU) or in need of invasive respiratory support were not included in the study. Those who received noninvasive ventilation masks were categorized as the severe group. Patients with COVID-19 infection who were not sick enough to need hospitalization and were treated at home included as the outpatient group. 24 hours after patient assignment, two physicians independently collected clinical characteristics to increase the accuracy of the collected data. This study is related to the project No. IR. NIMAD.REC.1399.041 from national institute for medical research development entitled “Immunological aspects of COVID-19 in selected provinces of Iran”. The flow chart provides a description of the patients recruited and the sample sizes for analysis (Figure 1).

The inclusion criterion was positive PCR COVID-19 test result and the exclusion criteria were diabetes, hypertension, kidney disease, cancer, and cardiovascular diseases and also adherence to special diets over the past year, pregnancy and lactation. The consent form was signed by all patients after explaining them the details about the goals and process of the study. The Ethical Committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.NNFTRI.REC.1399.046) approved the study protocol.

Dietary intake assessment

The 147-item semi-quantitative food frequency questionnaire (FFQ) was used to evaluate dietary intake of patients, the validity and reliability of which have been explained extensively in advance [19].

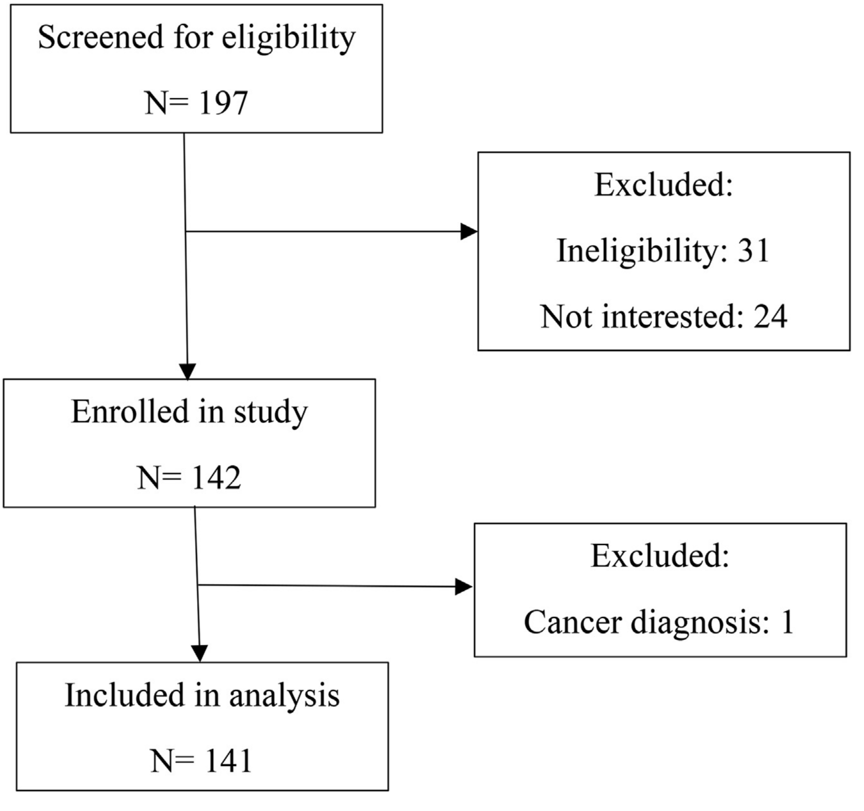

Figure 1. Flowchart of participant recruitment.

The Frequency of consumption of each food items during the past year was gathered via person-to-person interviews by expert nutritionists. The amount of consumed food first converted to grams and then the nutrients and energy contents were calculated by using the United States Department of Agriculture (USDA) food composition table. An Iranian FCT was also used for local food items.

DASH score in this study was calculated based on eight components, including fruits, vegetables, legumes and nuts and seeds, whole grains, low-fat dairy, red or processed meats, sweetened beverages, and sodium [20]. Energy adjustments were carried out for each food component (g/1000). DASH scores had been computed according Fung *et al.* [20]. Briefly, subject's quintile rankings were implemented for whole grains, fruits, vegetables, legumes, nuts and seeds, and low-fat dairy to appoint component scores, e.g. 1 point for the lowest quintile participants and 5 points for the highest. For sodium, red and processed meats and sugar-sweetened beverages, 5 points were assigned for those who received the lowest quintile and consequently 1 point for the highest ones. Then the scores for these eight components were summed up to calculate the DASH score.

Clinical parameters

Measuring weight was conducted by a digital scale with an accuracy of 0.1 kg. Also, mechanical, wall-mounted stadiometer, with an accuracy of 0.1 cm was applied for measuring height. Body mass index was computed as weight (kg) divided by height (m^2). Serum concentrations of neutrophil-to-lymphocyte ratio (NLR), Interlukin-6, C-reactive protein (CRP), white blood cells were measured.

Statistical analysis

Data analyses were carried out using the SPSS software (Statistical Package for the Social Sciences version 20.0; SPSS Inc., Chicago, IL). The level of statistical significance was set at P <0.05. Histogram chart and the Kolmogorov-Smirnov's test were administered in order to monitor the distribution of variables. Classifying the participants was according to tertiles of DASH diet score cutoff points (≤22, 23–26, and ≥27). Baseline characteristics of participants are expressed as mean ± SD or median (25–75 inter-quartile range) for continuous variables, and percentages for categorical variables across tertiles of DASH score. Linear regression was used to examine the trend of continuous variables across tertiles of DASH score, accordingly, P for trend was reported. Logistic regression models were conducted to evaluate the odds ratio (ORs) and 95% confidence intervals

Table 1
Basic characteristics of study participants based on COVID-19 severity.

	In-patients (n= 53)	Out-patients (n= 88)	P-Value
Age, y	50.17 ± 15.45	43.91 ± 15.77	0.024
Male, N (%)	29 (54.7%)	45 (51.7%)	0.433
Weight, kg	78.77 ± 13.45	76.59 ± 11.72	0.313
Height, cm	1.68 ± 0.1	1.69 ± 0.1	0.567
BMI, kg/m^2	27.66 ± 4.57	26.53 ± 3.26	0.089
Dietary intakes			
Energy (Kcal/d)	1542.83 ± 592.03	1920.83 ± 648.07	0.001
Carbohydrate (%)	59.84 ± 8.98	60.44 ± 9.52	0.712
Protein (%)	13.68 ± 2.48	13.43 ± 2.43	0.563
Fat (%)	29.5 ± 8	29.68 ± 7.85	0.899
Biochemical Parameters			
W.B.C (103/μL)	6.34 ± 1.97	6.14 ± 2.24	0.638
Lymphocytes (%)	30.72 ± 10.44	32.62 ± 7.93	0.326
Neutrophils (%)	57.75 ± 11.11	50.09 ± 9.09	0.437
NLR	2.43 ± 2.06	1.95 ± 1.14	0.157
IL-6 (pg/ml)	7.59 ± 15.22	11.38 ± 30.99	0.582
CRP (mg/L)	6.26 ± 7.53	4.96 ± 6.22	0.294
DASH score	22.5 ± 4.57	25.34 ± 4.23	<0.001

Data are presented as mean (SD) for continuous variable and number (percent) for categorical variables.

Table 2
Basic characteristics of study participants based on DASH scores tertile.

DASH score	Tertiles			
	T1 (n= 53)	T2 (n= 47)	T3 (n= 41)	P trend
Age, y	45.05 ± 16.28	45.59 ± 14.83	48.46 ± 16.69	0.561
Male (%)	27 (50.9%)	26 (55.3%)	21 (52.5%)	0.907
BMI, kg/m^2	27.22 ± 3.98	27.63 ± 4.17	25.83 ± 2.97	0.071
Dietary intakes				
Energy (Kcal/d)	1809.99 ± 826.4	1664.07 ± 499.87	1869.81 ± 535.6	0.307
Carbohydrate (%)	58.94 ± 9.74	59.26 ± 8.84	62.97 ± 8.85	0.078
Protein (%)	13.63 ± 2.54	13.79 ± 2.57	13.07 ± 2.15	0.357
Fat (%)	30.36 ± 8.95	30.27 ± 6.91	27.90 ± 7.33	0.257
Biochemical Parameters				
W.B.C (103/μL)	6.08 ± 1.88	5.92 ± 1.76	6.77 ± 2.76	0.230
NLR	2.04 ± 1.1	2.36 ± 2.12	1.91 ± 0.99	0.475
IL-6 (pg/ml)	10.01 ± 17.2	15.47 ± 41.11	4.14 ± 3.61	0.355
CRP (mg/L)	5.66 ± 6.97	6.62 ± 7.43	5.45 ± 6.74	0.145
DASH score	19.60 ± 2.68	25.06 ± 0.84	29.41 ± 2.42	<0.001

Data are presented as mean (SD) for continuous variable and number (percent) for categorical variables.

(CIs) of COVID-related hospitalization risk across tertiles. The first tertile of each score was considered as the reference. The relationship between the DASH scores and the risk of hospitalization caused by COVID-19 were assessed in three models. Potential confounders were included sex, age, BMI, and daily energy intake.

Results

Basic characteristics of study participants based on COVID-19 severity are shown in Table 1. 52.5% of participants in this study were men and 47.5% were women. The mean age of patients was 46.23 ± 15.88 years, but hospitalized patients were older than outpatients (50.17 ± 15.45 vs 43.91 ± 15.77. *P*= 0.024). The mean ± SD of BMI was 26.95 ± 3.83 kg/m^2, and although BMI in hospitalized patients was higher than outpatients, but this difference was not statistically significant. Also, the mean of DASH score of all patients were 23.86 ± 4.4, and in hospitalized patients it was significantly lower than outpatients (*P*<0.001). Although energy intake in hospitalized patients was significantly lower than outpatients, the percentage of macronutrients did not show a statistically significant difference between the two groups. In terms of biochemical parameters there was no significant difference between the two groups.

Table 2 presents basic characteristics of study participants based on DASH scores tertile. As shown in Table 2, there were no significant differences in dietary intakes and biochemical parameters across tertiles of DASH diet scores.

Table 3
95% odds and confidence interval of the relationship between DASH score components with the risk of hospitalization.

	Tertiles			
	T1	T2	T3	P trend
Fruits	1 (ref)	0.75 (0.2–1.93)	0.62 (0.1–1.66)	0.003
Vegetables	1 (ref)	0.63 (0.14–1.91)	0.59 (0.2–1.85)	0.007
Legumes, nuts and seeds	1 (ref)	0.61 (0.25–1.46)	0.43 (0.18–1.02)	0.072
Whole grains	1 (ref)	1.06 (0.45–2.48)	0.79 (0.34–1.81)	0.827
Low fat dairy	1 (ref)	0.94 (0.39–2.27)	0.56 (0.25–1.38)	0.010
Red and processed meats	1 (ref)	1 (0.44–2.26)	3.13 (1.27–7.7)	0.032
Sweet beverages	1 (ref)	1.12 (0.5–2.5)	2.21 (0.92–5.35)	0.488
Sodium	1 (ref)	0.99 (0.42–2.16)	2.3 (0.96–5.53)	0.006

Data are presented as mean (SD) for continuous variable and number (percent) for categorical variables.

Table 4
Odds ratio (95% CI) COVID-19-associated hospitalization risk according to tertiles of DASH scores.

	Tertiles of scores			
	T1	T2	T3	P trend
Mean (IQR)	20 (18, 21)	25 (24, 26)	28 (28, 31)	
Model 1	1 (ref)	0.47 (0.17–1.26)	0.20 (0.08–0.51)	<0.001
Model 2	1 (ref)	0.42 (0.15–1.15)	0.18 (0.06–0.47)	0.001
Model 3	1 (ref)	0.59 (0.2–1.75)	0.19 (0.07–0.55)	0.001

Model 1: Crude.
Model 2: Adjustment for age, sex.
Model 3: Adjustment for age, sex, BMI, energy intake.

The ORs (95% CIs) of the relationship between DASH score components with the risk of hospitalization are presented in Table 3. Higher intake of fruits (*P* trend = 0.003), vegetables (*P* trend = 0.007), and low-fat dairy products (*P* trend = 0.010) was significantly associated with a reduced risk of hospitalization due to COVID-19. Although the risk of hospitalization associated with COVID-19 in second and third tertiles of legumes, nuts and seeds intake was 39% (OR: 0.61, 95%CI: 0.25–1.46) and 57% (OR: 0.43, 95%CI: 0.18–1.02) lower than the first tertile, respectively, but was not statistically significant. While, higher intake of red and processed meats was associated with nearly 3-fold increase in the risk of hospitalization in patients with COVID-19 (*P* trend = 0.032). Regression analysis also showed that sodium intake increased the risk of hospitalization by 2.3 times *P* trend = 0.006).

COVID-19-associated hospitalization risk according to tertiles of DASH scores is shown in Table 4. Higher score of DASH was associated with lower disease-associated hospitalization risk. The risk of hospitalization due to COVID-19 in the second and third tertiles of DASH score, after adjusting for all confounders including age and sex, BMI and energy intake was 41% and 81% lower than the first tertiles, respectively.

Discussion

In this cross-sectional study, higher adherence to DASH-style diet was inversely associated with odds of hospitalization due to COVID-19. Also, greater score of fruits, vegetables and low-fat dairy products and lower score of sodium, red and processed meat were each significantly associated with reduced COVID-19-associated hospitalization risk. Based on our knowledge this is the first study to investigate the relationship between DASH score and risk of hospitalization due to COVID-19.

Findings of the current study are in agreement with previous researches which suggest greater adherence to higher quality healthy diet is associated with beneficial health effects through reducing systemic inflammation as a potential biological mechanism [21,22]. There is a close correlation between immune system with inflammation and oxidative stress. Long-lasting inflammation can lead to a weakened immune system. DASH diet with an anti-inflammatory effects might inhibit an inflammatory response and further consequences such as impaired immune response [23].

DASH pattern is characterized with higher intake of fruits and vegetables, whole grains, legumes, poultry, and less intake of red meat, sodium and sugar. Therefore, the content of calcium, potassium, magnesium and fiber in DASH diet is high [24]. Evidence suggests that these nutrients modulate inflammatory status [25]. On the other hand, less amounts of red and processed meats, refined grains and simple sugar may provide anti-inflammatory benefits [26,27]. This dietary pattern is also rich in bioactive compounds that can inhibit pro-inflammatory pathways and reduce the morbidity and mortality risk of an infectious disease by strengthening the immune response [28]. Furthermore, DASH diet may be considered as including several nutraceuticals that favorably influence health. Nutraceuticals comprise active phytochemicals with medicinal properties such as zinc, vitamins, curcumin, resveratrol, and selenium [29]. In addition to its immune-boosting properties, the nutrient appears to interact with angiotensin-converting enzyme-2 (ACE2) [30]. The effects of these natural compounds in reducing ACE2 activity and consequently treating COVID-19 have been shown in several studies [31,32].

These findings are supported in a meta-analysis of randomized controlled trials which report the beneficial effects of the DASH diet on reducing inflammation [33].

Inflammation is a known component in the pathophysiology of COVID-19 [34]. According to the findings of this study, the higher score of the DASH diet was associated with a reduction in the risk of COVID-19-related hospitalization, which could be due to a reduction in inflammation. Consistently, adherence to plant-based diets or pescatarian diets, as anti-inflammatory diets, has been shown to be associated with a 73% and 59% lower risks of moderate-to-severe COVID-19 severity, respectively [35].

Findings of the present study showed that higher intakes of Legumes, nuts and seeds were associated with a 57% reduction in disease severity, although it was close to a significant level (*P* trend: 0.072). Similarly, a recent study of 158 countries across the world showed that increased beans and legumes intake was significantly associated with lower risk of COVID-19 infection [36]. In the present study, comparing the third tertile of fruit and vegetable intake scores with the first tertile showed a 38% and 41% reduction in disease severity, respectively. One of the possible mechanisms of this effect could be the high fiber content of fruits and vegetables, which as influencer of gut health, strengths the integrity of the intestinal mucosa and reduces gut permeability [37,38]. Also, DASH diet increases short chain fatty acid (SCFA) production by promoting the growth of protective gut microflora, which has positive effects on the immune system [39].

Gut microbiota is not only directly related to the immune system but is also involved in the etiology of respiratory infections [40]. Therefore, since COVID-19 has been shown to be associated with both symptoms of respiratory and gastrointestinal infections [41], modifying the intestinal microbiota by following a healthy diet can reduce the severity of the disease.

In this study, unlike usual case-control studies, outpatients and inpatients were compared and the relationship between DASH dietary pattern and the risk of hospitalization due to COVID-19 was assessed. The main limitation of this study was that we were not able to verify the causal relationship between DASH diet and the infection, due to cross-sectional design of the study. Another important limitation was that we could not adjust all potential confounders. Relatively small study population and the use of FFQ which is inevitably allied with recall bias, were other limitations.

Conclusions

In conclusion, our data provide evidence that adherence to DASH-style diet was associated with lower risk of hospitalization due to COVID-19. Nevertheless, due to the mediocre quality of evidence, it is required to conduct well-designed clinical trials to confirm and generalize these findings.

Statement of authorship

Conceptualization, ZY and AH; Formal analysis, ZY and AZ; Investigation, SS, MS and SK; Methodology, SKA and SRJ; Project administration, ZY and MS; Software, AZ; Validation, TG; Writing – original draft, ZY and AZ; Writing – review & editing, ZY and AH.

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Ethical statements

The Ethical Committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.NNF-TRI.REC.1399.046) approved the study protocol.

Conflict of interest

The authors declare no conflict of interest.

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