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Research Report

The difference in the dietary inflammatory index, functional food, and antioxidants intake between COVID -19 patients and healthy persons

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Abstract.
BACKGROUND: The healthy diet is important to maintain immunity against infection. This study aimed to assess and compare the consumption of functional foods, some antioxidants, and dietary inflammatory index between Iranian COVID-19 patients and healthy persons.
METHODS: This case-control study was conducted between 1000 (500 cases and 500 controls) adults aged 18–65years in Iran, that were sampling based on the snowball method and their information was collected electronically. The dietary intake was assessed using the Food Frequency Questionnaire (FFQ).
RESULTS: There was a significant difference ($p = 0.044$) in vitamin D consumption between healthy people and COVID-19 patients. Vitamin E intake in healthy participants was significantly ($p = 0.041$) more than COVID-19 patients. There was a significant difference in Zinc ($p = 0.011$), selenium ($p = 0.021$), and vitamin C ($p = 0.023$) between healthy persons and COVID-19 patients. Healthy participants' consumption of onion (56.5 ± 7.82 g/day), garlic (4.32 ± 0.01 g/day) and oat (6.32 ± 0.71 g/day) was significantly ($p \leq 0.05$) more than COVID-19 patients. With the increase of each unit in the score of the dietary inflammatory index, the risk of COVID-19 incidence increased 1.63 times (OR = 1.63 95%CI: 1.54–1.72). There was an inverse association between the consumption of antioxidants and functional foods with the risk of COVID-19 incidence in the study population ($p \leq 0.05$).

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CONCLUSION: Healthy people consumption of antioxidants and functional foods was more than COVID-19 patients and there was a significant inverse association between the risk of COVID- 19 incidence with the consumption of functional foods and antioxidants. Increasing the dietary inflammatory index score increased the risk of COVID- 19 incidence. There is a need for further clinical trials to confirm the effect of consuming functional foods and antioxidants on the prevention or treatment of COVID-19.

Keywords: COVID-19, antioxidants, functional foods, dietary inflammatory index

1. Introduction

The results of studies have suggested that increased inflammation has an important role in the COVID-19 incidence [1, 2].

Dietary nutrients can affect the immune system through stimulation cells, a manifestation of the gene, and modification of signaling molecules [3, 4]. Many dietary components shape the responses of the body immune like as functional foods and dietary antioxidants that are important factors for the keep the function of the immunity system. These foods expand life quality by prevention of nutrition-related diseases [5–8]. Recent studies [9–11] have suggested that functional foods consumption can improve COVID-19 symptoms, but until now no study has examined these foods consumption impacts on COVID 19 severity of symptoms.

In addition to functional foods, other dietary components can reduce body inflammation levels, like antioxidants. Based on studies results, the antioxidants reduce oxidative stress and serum inflammatory markers. Since COVID -19 disease is also an inflammatory disease [12], the effect of these nutrients on the serum inflammation marker in these patients can be discussed. To date, no study has assessed the intake of functional foods, antioxidants, and dietary inflammation index in COVID -19 patients. Therefore, this study assessed and compared the consumption of functional foods, some antioxidants, and dietary inflammation index between Iranian COVID -19 patients and healthy persons.

2. Methods

This case-control (population base study) study was done between 1000 (500 cases and 500 controls) adults aged 18–65 years old that chosen based on the snowball method and their information was collected electronically. Electronic invitations were sent to people on WhatsApp and they were asked to send this invitation form to their friends and family members. At the beginning of the study, 2540 people participated in this survey through an electronic questionnaire (includes demographic characteristics, history of hypertension, diabetes, hyperlipidemia, COVID- 19 incidence history, and food frequency questionnaire). From all participants, 500 participants had a history of COVID -19 who were diagnosed using a valid laboratory test and have been treated out of the hospital. Then, among the healthy individuals who participated in the initial study 500 healthy individuals were selected by simple sampling. The matching was performed for the control group based on age and sex. All individuals completed a written electronic consent form to participate in the study. This study was approved by the ethics committee of Ardabil University of Medical Sciences and its ethics code is as follows IR.ARUMS.REC.1400.008. This project was financially supported by NIMAD project No.962249.

2.1. Dietary assessment

The nutritional status of study participants was assessed by a food frequency questionnaire (FFQ) with 138 items. In this questionnaire, there is a standard size for each food item, which is designed according to Willett method. The study participants were asked to determine the frequency of their consumption of each food item according to the amount consumed in the previous year. Depending on the type of food consumed, repeated consumption per day, week, or month is asked. Past studies that have used this questionnaire have provided acceptable values of results and a review of the validity of this questionnaire shows that the questionnaire has acceptable validity. Based on the portion size of each food, the amounts consumed from each food item were converted to grams per day, then this information was entered into the Nutritionist IV software and the amounts of all nutrients (vitamin D, vitamin E, vitamin C, vitamin A, Selenium, Zinc) consumed were calculated with this software [13].

2.2. *The Dietary Inflammatory Index (DII):*

Briefly, the DII is a scoring algorithm based on an extensive review of the literature published from 1950 to 2010, linking 1943 articles to a total of forty-five food parameters and including various macronutrients, micronutrients, flavonoids, and food items. These dietary parameters were scored according to whether they increased [1], decreased, or had no effect (0) on six inflammatory biomarkers. An overall food parameter-specific inflammatory effect score was calculated and multiplied by a centered percentile value for each food. This percentile was calculated by first linking the dietary data from a study to the regionally representative world database intake, which was based on actual human consumption in eleven populations from different parts of the world that provided a robust estimate of a mean and standard deviation for each parameter. These values then become the multipliers to express an individual's exposure, relative to the 'standard global mean' as a z-score. This was achieved by subtracting the 'standard global mean' from the amount reported and dividing this value by the standard deviation. To minimize the effect of 'right skewing', this value was then converted to a centered percentile score. The centered percentile score for each food parameter for each individual was multiplied by the respective food parameter effect score that was derived from the literature review to obtain a food parameter-specific DII score for an individual. All of the food parameter-specific DII scores were then summed to create the overall DII score for every participant in the study. The greater the DII score, the more pro-inflammatory the diet, and more negative values represent more anti-inflammatory diets. The DII score could take on values ranging from 7·98 (maximally pro-inflammatory) to 28·87 (maximally anti-inflammatory. Construct validation of the DII was performed using data derived from two different sources of dietary intake information, and serum high-sensitivity CRP as the construct validator [14].

2.3. *Antioxidants consumption*

The food intake data from FFQ were converted to antioxidants intake (vitamin A, vitamin C, vitamin E, vitamin D, zinc, selenium) using the Nutritionist IV software: Based on each food portion size, the amount of food consumed was converted to gram and then these amounts were entered into the Nutritionist IV software and by this software, the amounts of all micronutrients including vitamins and minerals were calculated.

2.4. *Functional foods intake*

The dietary information recorded in the FFQ was used to calculate the intake of some functional foods (oat, garlic, onion, banana, turmeric, green tea). Based on each food portion size, its consumption was changed to grams per day.

2.5. *Statical methods*

For data analysis, the SPSS software version 18 was used. The normality of the variables was assessed by the Kolmogorov-Smirnov test. Independent *T*-test, Chi-square test, and one-way ANOVA were used to compare

Table 1
Demographical characteristics of the participants according to the categories of the DII score by COVID-19

Variables	Healthy people				COVID-19 PATIENTS			
	Q1 N = 120	Q2 N = 298	Q3* N = 82	*P*	Q1 N = 20	Q2 N = 96	Q3* N = 384	*P*
DII mean ± SD	18.9 ± 5.2	19.6 3.8	20.6 4.9	0.041**	19.9 ± 4.5	20.9 ± 5.9	23.8 ± 9.7	0.021**
Age (years) mean ± SD	38.2 ± 4.2	43.1 ± 3.9	45.2 ± 6.1	0.02**	38.4 ± 4.2	42.8 ± 5.8	32.8 ± 9.7	0.042**
Family history of early CHD (%)	100(83.33%)	160(53.69%)	80(97.56%)	0·022#	5(25%)	42(43.75%)	201(52.34%)	0·014#
Hypertension n (%)	35(7%)	160(53.69%)	68(85%)	0·050#	10(50%)	38(39.58%)	220(57.29%)	0·031#
Dyslipidaemia n(%)	65(54.16%)	115(35.59%)	65(79.26%)	0·012#	5(25%)	36(37.5%)	195(50.78%)	0·025#
Diabetes n(%)	55(45.83%)	108(36.24%)	54(65.85%)	0·014#	4(20%)	61(63.54%)	119(30.98%)	0.027#
Marital status n(%)				0·004#				0·043#
Married	72(60%)	66	60		92	91	89	
Widowed	40(33.33%)	27	27		3	3	3	
Single/other	8(6.66%)	7	7		5	6	8	
Educational level n(%)				0,0·001#				0.061#
Primary education or less	53	86	87		22	31	29	
Secondary education	25	11	9		38	39	39	
Any college	22	3	4		40	30	32	

*Highest anti-inflammatory values of the DII.**: Based on one way ANOVA test, #: based on Chi-square test.

parametric and nonparametric/nominal variables between groups. The association between the COVID-19 incidence with consumption of functional foods and antioxidants intake was assessed by the multivariable logistic regression test. In all analyzes, a *p*-value less than 0.05 was considered statistically significant.

3. Results

This case-control study was conducted between 1000 (500 COVID-19 patients and 500 healthy adults) Iranian adults. There was no significant difference in the participants' age between groups of study ($p = 0.07$). The participants mean ± SD of age was 42.1 ± 8·2 years for COVID-19 patients and 42.3 ± 7·9 years for the control group. The mean DII score for the control group was 20.4 ± 3.5 and 22.9 ± 4.1 for the COVID-19 patients)$p = 0.042$). Table-1 reported the participant's demographical characters according to the DII score categories by COVID-19. In both groups, the history of diabetes, cardiovascular disease, and hypertension were significantly ($p \leq 0.05$) higher in those with more DII scores.

Table-2 shows the results of comparing the consumption of antioxidants and functional foods in the two groups of study. There was a significant difference ($p = 0.044$) in vitamin D consumption between healthy people (3.14 ± 0.14 Mg/day) and COVID-19 patients (2.02 ± 0.22 Mg/day). Vitamin E intake of healthy participants (15.25 ± 1.18 mg/day) was significantly ($p = 0.041$) more than COVID-19 patients (13.37 ± 1.32 mg/day). There was a significant difference in Zinc ($p = 0.011$), selenium ($p = 0.021$), and vitamin C ($p = 0.023$) intake between healthy persons and COVID-19 patients. Healthy participants' consumption of onion (56.5 ± 7.82 g/day), garlic (4.32 ± 0.01 g/day) and oat (6.32 ± 0.71 g/day) was significant ($p \leq 0.05$) more than COVID-19 patients.

Table 3 reported the association of COVID-19 incidence with dietary inflammatory index, antioxidants, and functional foods intake. The logistic regression indicated that with each gram increase in oat consumption, the risk of COVID-19 incidence in the study participants decreased by 13% (OR = 0.13 95% CI: 1.33–1.55). Each gram increase in onion consumption reduced the risk of COVID-19 incidence by 97% (OR = 0.97 95 CI%:

Table 2
Dietary consumption in the COVID-19 patients and healthy people

Nutritional intake	COVID-19 Patients Mean ± SD	Healthy persons Mean ± SD	Recommended Dietary Allowance	P*
Antioxidants				
Vitamin C(mg/day)	63.53 ± 2.35	78.3 ± 1.44	75–90	**0.023**
Vitamin A) Mg/day)	702.4 ± 15.44	702.3 ± 13.12	900–700	0.063
Vitamin E(mg/day)	13.37 ± 1.32	15.25 ± 1.18	15	**0.041**
Vitamin D (Mg/day)	2.02 ± 0.22	3.14 ± 0.14	10	**0.044**
Zinc (mg/day)	7.23 ± 0.45	8.1 ± 0.28	11–8	**0.011**
Selenium (Mg/day)	42.21 ± 2.21	51.02 ± 3.1	55	**0.021**
Functional foods (g/day)				
Green Tea (cup/day)	0.51 ± 0.002	0.52 ± 0.005	–	0.054
Oat	6.32 ± 0.71	7.44 ± 0.68	–	**0.024**
Garlic	4.32 ± 0.01	7.91 ± 0.21	–	**0.017**
Onion	56.5 ± 7.82	102.44 ± 10.18	–	**0.038**
Turmeric	2.51 ± 0.001	2.58 ± 0.007	–	0.712
Banana	25.33 ± 4.12	25.31 ± 5.17	–	0.318

*: based on independent *T*-test.

Table 3
The COVID 19-incidence association as dependent variable with dietary inflammatory index, functional foods and antioxidants consumption

Independent variables	OR (95%CI)	P*
Dietary inflammatory index	1.63 (1.54–1.72)	≤ 0.0001
Green tea (cup)	0.001 (0.37–1.17)	0.99
Oat (g/d)	0.13 (1.33–1.55)	≤ 0.0001
Banana (g/d)	0.98 (0.43–1.11)	0.22
Turmeric (g/d)	0.86 (0.51–1.04)	0.194
Onion (g/d)	0.97 (1.14–1.38)	0.003
Vitamin D (mg/d)	0.87 (1.14–1.61)	≤ 0.0001
Vitamin A (mg/d)	0.89(0.97–1.24)	0.065
Vitamin C (mg/d)	0.95(1.10–1.34)	0.04
Selenium (mg/d)	0.91(1.95–2.21)	0.003
Zinc (mg/d)	0.92(1.34–1.82)	0.002

*: Based on multivariable logistic regression.

1.14–1.38). An increase of one unite in Zinc (OR = 0.92 95% CI : 1.34–1.82), Selenium (OR = 0.91 95 CI%: 1.95–2.21), vitamin C (OR = 0.95 95% CI: 1.10–1.34), vitamin E (OR = 0.86 95 CI% : 1.04–1.21) and vitamin D (OR = 0.87 95% CI: 1.14–1.61) consumption also reduced the risk of COVID-19 incidence by 92%, 91%, and 87%, respectively. Increasing each score in the dietary inflammatory index, increased the risk of Covid-19 incidence by 1.63 (OR = 1.63 95%CI: 1.54–1.72).

4. Discussion

This was the first study that assessed the DII, some functional foods, and antioxidant consumption in Iranian COVID-19 patients compared to healthy people. The results showed that the consumption of antioxidants and functional foods in COVID- 19 patients was less than healthy individuals. Also, the score of dietary inflammation index in COVID-19 patients was more than healthy individuals. Also, the dietary inflammation index in COVID-19 patients was more than healthy individuals. The association between vitamin D and the incidence and even severity of COVID-19 has been well established in previous studies [15, 16].

Studies have suggested that a diet with more antioxidants can reduce the serum levels of inflammatory markers in patients and also increase patients' resistance to this viral infection by reducing oxidative stress in the body [17, 18]. Mrityunjaya et al in one study have expressed that a combination of some antioxidants including Zinc, vitamin D, vitamin C, curcumin, cinnamaldehyde, probiotics, selenium, lactoferrin, quercetin, etc, in the form of a food supplement can boost the immune system, prevent virus spread, and decrease the serum inflammation markers [9, 19, 20]. Jothimani et al. [21] in one study indicated that a significant number of COVID-19 patients were zinc deficient. These zinc-deficient patients developed more complications, and the deficiency was associated with a prolonged hospital stay and increased mortality.

In the results of this study, the green tea consumption of healthy people was more than COVID-19 patients, but this difference was not significant. Because green tea is rich in many antioxidants, it can protect the body against oxidative stress caused by the COVID-19 virus [22, 23]. Based on Szulińska et al. study, green tea can reduce the TNF- α, so suppress the body's inflammation [24]. Although no study has examined the effect of green tea consumption in improving or preventing COVID -19, according to the results of previous studies [25–27], it can be predicted that consuming green tea can increase the body's total antioxidant capacity and can prevent the increased serum pro-inflammation side effects in COVID-19 patients.

The onion, garlic, and oat consumption of healthy participants was more than COVID-19 patients. Garlic, oat, and onion are functional foods and according to many studies results, they have many benefits for the body. Pre-clinical data reported that garlic has potential antiviral activity against pathogenic viruses [18, 28, 29]. Functional foods contain phytochemicals that have anti-cancer, anti-bacterial, and anti-inflammatory effects, and their positive effects have been proven in all studies [11, 30, 31]. These foods are "items that modify the battered functions in the body" and increase the immune response and decrease the risk of many diseases. The functional foods and components have immune-boosting properties [32]. These natural compounds do not participate in the direct embarrassment response against COVID-19, but the complete response of immunity in COVID-19 prevention [33]. Micronutrients like vitamin C, D, probiotic foods, flavonoids, carotenoids, and herbs have been reported as functional foods [34].

The results of the present study showed that there is a significant relationship between the intake of vitamin C, vitamin D, vitamin E, and some functional foods such as garlic, onion, and oat with the risk of COVID-19 incidence. By increasing each unit in the amount of consumption of these foods and nutrients, the risks of COVID-19 incidence in the study participants were reduced. However, the risks of COVID-19 incidence in the study population increased with an increasing score of dietary inflammation index. Consistent with the present study result, Moloudi et al. in a study showed that patients with the maximum pro-inflammatory energy-adjusted E-DII score had 7·26 times greater odds of developing COVID-19, as compared to those in tertiles 1 (E-DII T3 v. E-DII T1: OR = 7.26; 95 % CI 2.64 to 9.94, $P < 0.001$). Also, a positive association between E-DII and C-reactive protein (CRP) was observed (BE-DII = 1.37, 95 % CI 0.72, 2.02), such that with each unit increase in E-E-DII, the CRP levels were increased by 1.37 units. Furthermore, a significant association was found between E-DII and the severity of disease (BE-DII = 0.03, 95 % CI 0.01, 0.06. 0.024).

Considering that the increase in inflammatory serum indices in COVID -19 patients is one of the reasons for severe respiratory symptoms, etc.[35], it is necessary to reduce these inflammatory indices in patients using a healthy diet. Studies have shown that an inflammatory diet increases the risk of chronic diseases. Several studies have indicated a converse association between healthy diets and serum indicators of inflammation, as well as a direct association with ‘unhealthy diet [8–14]. Exactly, more consumption of fruits and vegetables decreases the CRP concentration [36]. On the contrary, more red meat consumption increases the serum inflammatory markers [37, 38].

In this study results,

Because the diet’s role in the control and prevention of COVID-19 is important, improving the dietary patterns of people can prevent serious complications of this disease. This study is the first study in Iran that examined the inflammation index of dietary, some antioxidants consumption, and functional food intake in people with a history of COVID 19 incidence. One of the limitations of this study is the use of an electronic questionnaire. In this questionnaire, the accuracy of information is less than a face-to-face interview. We suggest that next future studies complete the information using face-to-face interviews.

5. Conclusion

This study showed that the dietary inflammatory index in COVID -19 patients was 19 more than healthy individuals. The antioxidants and functional foods consumption in healthy people was more than COVID-19 patients and there was a significant inverse association between the risk of COVID- 19 incidence with the consumption of functional foods and antioxidants. Increasing the dietary inflammatory index increased the risk of COVID- 19 incidence. There is a need for further clinical trials to confirm the effect of consuming functional foods and antioxidants on the prevention or treatment of COVID-1.

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Conflict of interest

The authors declare that there is no conflict of interest.

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