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The Relationship between Dietary Inflammatory Index, Pulmonary Functions and Asthma Control in Asthmatics

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ABSTRACT

This cross-sectional study evaluates the relationship of the dietary inflammatory index (DII), a novel tool developed to measure the inflammatory capacity of a diet, with pulmonary functions and asthma control test (ACT) scores in asthmatic individuals.

The study included 120 patients who were diagnosed with asthma for at least one year. The anthropometric measurements, one-day long nutrition uptake records, pulmonary function tests, and ACT scores of the respondents were recorded and compared according to categories of the DII which was calculated from 24- hour recalls.

Forced vital capacity (FVC), forced expiratory volume in one second (FEV_1) and ACT scores decreased with increasing DII tertiles ($p<0.05$). The total energy, carbohydrate, fat, and saturated fat uptake of the participants increased in parallel to DII ($p<0.05$); while vitamin A, C, and E uptakes, on the other hand, decreased as DII increased ($p=0.0001$).

In conclusion, an increase in the inflammatory potential of diet among asthmatics decreases pulmonary functions and asthma control.

Keywords: Asthma; Diet; Inflammation; Pulmonary function

INTRODUCTION

Asthma is a chronic inflammatory disease that is characterized by oversensitivity of the respiratory airways, leading to symptoms such as shortness of breath, wheezing, chest tightness, and coughing episodes.[1]

Inflammatory response plays a significant role in the development and aggravation of the disease, and the levels of inflammatory cytokines such as tumor necrosis factor (TNF)-α, interleukin (IL)-4 and IL-6 that have been found to be higher in asthma patients than in healthy controls.[2] The decreased antioxidant uptake and the consumption of foods with an anti-inflammatory activity that have come with recent changes in nutritional habits have been associated with increased asthma prevalence.[3] In particular, the increased uptake of saturated fats and pro-inflammatory food products such as processed food and decreased uptake of anti-inflammatory nutrients like vitamins A,

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C, E, and omega-3 represent significant examples of such changes.[4]

In addition to changes in nutritional habits, obesity, which develops with increases in body fat, has been frequently associated with asthma.[5] Fat tissue, which is considered a pro-inflammatory substance leading to systemic and local inflammation, enhances the severity of asthma and negatively affects pulmonary function; while abdominal fat tissue is an important source of cytokine production; impairing pulmonary functions in asthmatic individuals by causing increases in TNF-α and C-reactive protein (CRP) levels (Rastogi et al. 2015).[6,7] Obesity develops as a result of both an increased consumption of processed and high-fat foods and an increased calorie uptake and therefore has a negative effect on asthma patients by enhancing inflammatory response in the body.[5,7]

Although it is well documented that nutritional habits affect the inflammatory response, the responsible nutrients or nutrient groups and their level of impact have not been well clarified. For this purpose, Shivappa et al. recently developed the dietary inflammatory index (DII) as a tool for the assessment of the inflammatory potential of a diet. Accordingly, a higher DII score indicates a more pro-inflammatory diet.[8] Previous studies have reported increases in the levels of some inflammatory biomarkers in individuals with increased DII.[9,10] Increasing DII score has also been shown to be associated with increased risk of asthma in a couple of studies in Western countries.[11,12] The present study was carried out to evaluate DII in asthmatics and to uncover the relationship between DII and pulmonary functions and asthma control test (ACT) scores.

PATIENTS AND METHODS

Study Population and Design

This cross-sectional study was carried out in the Pulmonology Department of the Kırşehir Ahi Evran Training and Research Hospital in Kırşehir, Turkey. The study included all participants aged between 20 and 65 years who were referred to the clinics over a two-month period in the spring who had been diagnosed with asthma at least one year earlier and who voluntarily agreed to take part in the study. The diagnosis of asthma was made by a specialist doctor and documented based on the patient's airway hyperresponsiveness history. Pregnant or lactating women were excluded from the study so as to eliminate the potential effects on body weight and changes in nutritional habits.

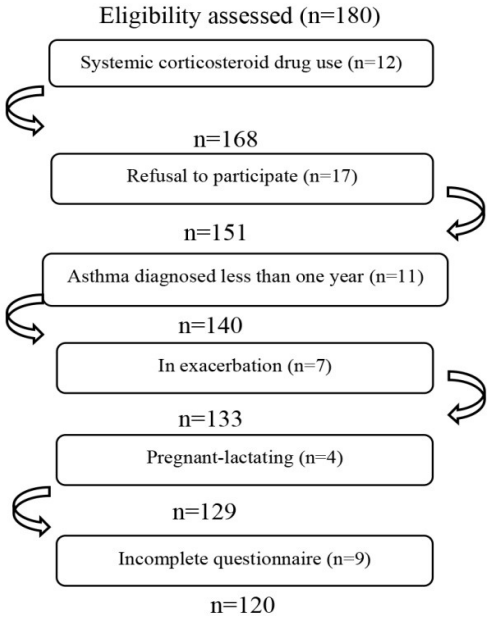

Figure 1. Flowchart of study participants

Patients using systemic corticosteroid medications were also excluded from the study, as these drugs increase food intake and sodium retention.[13] Additionally, participants experiencing asthma exacerbation were also excluded from the study as they were mostly using systemic corticosteroids during these events and experienced greater than the normal decline in pulmonary functions. The study was completed with 120 participants. The necessary permissions were obtained before initiating the study and it was approved by the Ankara University Medical Faculty Science Ethics Committee with approval number 02-43-16. The flowchart of the studied participants is shown in figure 1.

Anthropometric Measurements

Height and weight were measured by standard methods and body mass index (BMI) was calculated. Height was measured; using a height measurement with 0.1 cm accuracy while having no shoes on, in a standing position, looking straight ahead, and putting the shoulders and back of the feet in one direction. Weight was measured with 0.1 kg accuracy; using a scale while having no shoes on, wearing minimum clothing, and after excretion. Waist circumference (WC)was measured; using a steel measuring tape with measurements made halfway between the lower border of the ribs and the iliac crest on a horizontal plane. Hip circumference was measured at the widest point of the buttocks. BMI was calculated by dividing body weight in kilograms by the square of height in meters (kg/m^2), and the classification was made according to the World Health Organization (WHO) data.[14]

Pulmonary Function Tests (PFT)

The PFT measurements of the patients were obtained by a trained and experienced nurse; using a Cosmed Quark Spiro device. Measurements were obtained while the patients were sitting on a flat surface with measurements repeated three times and the best mean values considered. Forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), peak expiratory flow (PEF), and mid-expiratory flow (MEF) values were measured. The patients' age, gender, and height were recorded on the measurement device before the measurements were taken and the values were evaluated after respiratory maneuvers.[15]

Asthma Control Test (ACT)

The ACT consisted of five questions that inquired about the level of influence of asthma symptoms on daily activities and each question was scored on a scale of 1–5. The total score that can be obtained from ACT is in a range of 5–25 with a high score indicating better asthma control.[16] In the present study, ACT was applied to the patients by a specialist physician for the assessment of asthma control.

Assessment of Nutrition Consumption Records

The nutrition consumption records of the participants were recorded retrospectively for one weekday; using the 24-hour recall method. A nutrition photograph catalog was used to determine the measures and amounts during recordings.[17]One day food consumption data provides more realistic results than methods involving longer recording durations (like 3 days record) because some patients may hide their food consumption in the following days due to dietitian control. All consumed nutrients were recorded in detail and the collected data were evaluated; using the Turkey-Specific Nutrition Guide (TOBR) and computer-supported nutrition program.[18]

Dietary Inflammatory Index (DII)

A detailed description of the DII has been previously published.[8] In brief, the literature (approximately 2,000 articles) published between 1950–2010 was reviewed in terms of the relationship between various micronutrients, macronutrients,whole-food items (termed food parameters), and inflammation for the purpose of deriving inflammatory effect scores of the food parameters. At the same time, DII scores calculation included standardized to a world database that contains the means and standard deviations of the food intake parameters from 11 populations around the world. The world mean values for that food parameter was subtracted from the actual intake value for each food parameter and then divided by the world standard deviation to create a z-score. In the next step, the z-scores were converted to proportions which were then centered by doubling the value and subtracting. This value was then multiplied by the inflammatory effect score for each food parameter. These were then summarized across all food parameters to derive the overall DII score. More positive scores indicate pro-inflammatory diets; while negative scores indicate anti-inflammatory diets. The DII was adjusted for energy intake; using the nutrient density method by dividing by an individual's energy-intake and multiplying by

1,000 to obtain the energy-adjusted (E-DII) per 1,000 kcals of intake. In this study, 24 out of 45 food parameters (carbohydrate, protein, total fat, alcohol, fiber, cholesterol, saturated fatty acids (SFA), monounsaturated fatty acids (MUFA), polyunsaturated fatty acids (PUFA), omega-3, omega-6, niacin, thiamine, riboflavin, vitamin B12, vitamin B6, iron. magnesium, zinc, selenium, vitamin A. vitamin C, vitamin E, folic acid, caffeine) were included in the calculation of the DII. The energy was not included as E-DII was adjusted for energy.

Statistical Analysis of Data

The SPSS 22.0 software package was used for the evaluation of the data collected in the study. Descriptive statistics were presented as mean± standard deviation for normally distributed data,

and nominal variables were presented as the number of cases and percentages (%). The DII score was divided into tertiles for all analyses. The study population was divided into three subgroups according to their DII score and analysis of covariance (ANCOVA) was used for testing the differences across DII tertiles, with BMI, age, sex, and education level as covariates.

Pearson correlation test was used to evaluate the association between two continuous quantitative variables. All statistical analyses were performed within a 95.0% confidence interval, and a *p*-value of 0<.05 was considered statistically significant.

RESULTS

The majority of the respondents in all tertiles were women (>75.0%). The mean DII values in tertiles 1, 2 and 3 were -0.79±0.11, 0.74±0.05, and 2.22±0.10, respectively (Table 1).

Table 1. Demographic characteristics of the participants according to tertiles of the DII

	Tertile 1 (n=39)	Tertile 2 (n=39)	Tertile 3 (n=42)	*p*
Age (mean±sd)	41.3±2.1	46.5±1.8	42,8±2,0	0.096
Gender n (%)				
Male	8 (20.5)	6 (15.6)	6 (14,3)	0.729
Female	31 (79.5)	33 (84.6)	36 (85,7)	
Level of education n (%)				
Primary school graduate	14 (35.9)	16 (41.0)	16 (38,1)	0.560
High school graduate	17 (43.6)	21 (53.8)	22 (52,4)	
University graduate+	8 (20.5)	2 (5.1)	4 (9,5)	
Residential area n (%)				
Rural	7 (17.9)	6 (15.3)	7 (16,7)	0.358
Urban	32 (82.1)	33 (84.7)	35 (83,3)	
Smoking n (%)				
Non-smoker/ex-smoker	34 (87.2)	30 (76.9)	35 (83,3)	0.173
Active smoker	5 (12.8)	9 (23.1)	7 (12,7)	
Duration of asthma n (%)				
1–10 years	25 (64.1)	29 (74.4)	34 (81,0)	0.346
10+years	14 (35.9)	10 (25.6)	8 (29,0)	
Comorbidities n (%)				
Diabetes	-	5 (12.8)	4 (9,5)	0.128
Hypertension	1 (2.6)	2 (5.1)	4 (9,5)	
Allergic rhinitis	3 (7.7)	3 (7.7)	3 (7,1)	
Reflux	5 (12.8)	4 (10.2)	5 (11,9)	
DII (mean±sd)	-0.79±0.11	0.74±0.05	2,22±0,10	0.0001**

Data was presented as n (%) or mean±sd.

Tertile 1; ≤0.178 ;tertile 2; 0,178-1,43; tertile 3; ≥1.43. ***p*<0.01.

Table 2. Asthma characteristics and anthropometric measurements of individuals according to DIItertiles

	Tertile 1 (n=39)	Tertile 2 (n=39)	Tertile 3 (n=42)	p^a
FVC	90.6±16.8	90.2±18.5	85.1±17,9	0,038*
FEV_1	88.5±17.8	87.2±22.2	81.6±21,3	0,025*
FEV_1/FVC	102.7±8.0	100.7±13.2	100.3±12,4	0,735
PEF	67.7±22.3	65.9±22.0	61.2±20,0	0,088
MEF_{75}	70.8±23.8	68.8±25.5	62.2±21,8	0,252
MEF_{50}	73.4-±2.2	72.6±33.7	69.±28,3	0,315
MEF_{25}	81.0±27.5	80.2±44.5	77,7±49,5	0,860
MEF_{25-75}	71.0±19.8	72.6±32.8	65,9±28,5	0,227
ACT scor	20.0±3.2	19.2±3.4	19,0±3,3	0,033
BMI (kg/m^2)	27.1±6.8	28.2±7.3	29,4±7,2	0,016*
WC (cm)	83.3±18.0	91.0±17.6	91,2±18,0	0,043*
WHR	0.82±0.9	0.85±0.07	0,86±0,10	0,086

Tertile 1; ≤0,178 ;tertile 2; 0,178-1,43; tertile 3; ≥1,43

FEV_1: Forced expiratory volume in one second, FVC: Forced vital capacity, PEF: Peak expiratory flow, MEF: Mid-expiratory flow, ACT: Asthma control test, BMI: body mass index, WHR: Waist hip ratio. Data were presented as mean±standard deviation. [a]Adjusted for BMI, age, sex, and education level.*p<0.05 **p<0.01.

BMI, WC, and waist to hip ratio (WHR) increased with increasing DII from tertile 1 to tertile 3. The increases in BMI and WC were significant (p<0.05). In terms of pulmonary functions, all values decreased with increasing DII levels, with the decreases in the FVC (p=0.038) and FEV1 (p=0.025) values, in particular, being statistically significant. In parallel with pulmonary functions, the ACT scores also differed between tertiles and decreased with increasing DII values (p=.033) (Table 2).

When the energy and nutrient uptakes of the respondents were evaluated, the total uptake in calories, carbohydrates, fat, and SFA was found to increase in parallel to increases in DII (p<0.05); while the protein, MUFA, and PUFA uptakes were not significantly different between the tertiles. The vitamin A, C, and E uptake significantly decreased with increasing DII from tertile 1 to 3 (p=0.000), and a decrease in the total uptake of vitamins A, C and E lead to an increased DII (Table 3).

Table 3. Energy and macro-micro nutrient uptake of individuals according to DIItertiles

	Tertile 1 (n=39)	Tertile 2 (n=39)	Tertile 3 (n=42)	p^a
Energy (kcal)	1519.1±319.1	1679.0±313.6	1716.7±357.0	0.019*
Carbohydrates (g)	168.7±48.3	170.4±45.4	174.2±47.0	0.038*
Protein (g)	63.9±25.8	61.2±21.1	63.5±17.0	0.080
Total fat (g)	67.9±18.0	78.4±23.0	82.6±22.9	0.040*
SFA (g)	23.1±7.8	26.8±7.3	32.3±8.2	0.036*
MUFA (g)	20.9±9.3	25.7±9.8	25.9±7.8	0.542
PUFA (g)	22.7±10.3	23.8±11.0	24.1±8.1	0.111
Vitamin A (mcg)	1981.3±446.6	1890.4±638.3	742.2±50.0	0.0001**
Vitamin C (mg)	178.3±17.3	98.8±9.6	72.0±7.5	0.0001**
Vitamin E (mg)	24.0±1.2	22.2±1.5	13.4±1.1	0.0001**

Tertile 1; ≤0,178 ;tertile 2; 0,178-1,43; tertile 3; ≥1,43

SFA: Saturated fatty acids, MUFA: Mono-unsaturated fatty acids, PUFA: Poly-unsaturated fatty acids. Data was presented as mean±standard deviation. [a]Adjusted for BMI, age, sex and education level. *p<0.05 **p<0.01.

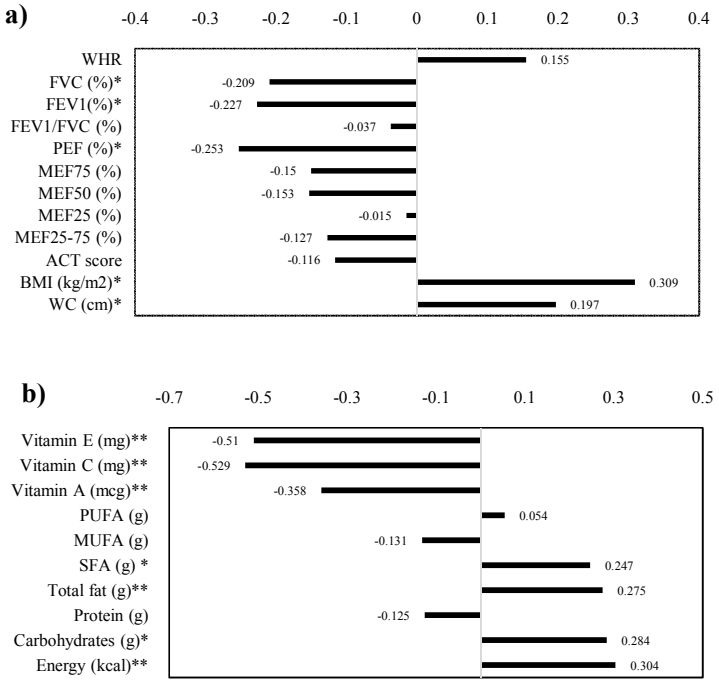

Figure 2. a) Correlation between DII, anthropometric measurements, and asthma characteristics. b) Correlation between DII, energy, and macro-micro nutrient uptake. BMI: Body mass index, WHR: Waist hip ratio, SFA: Saturated fatty acids, MUFA: Mono-unsaturated fatty acids, PUFA: Poly-unsaturated fatty acids, FEV_1: Forced expiratory volume in one second, FVC: Forced vital capacity, PEF: Peak expiratory flow, MEF: Mid-expiratory flow, ACT: Asthma control test. *p<0.05 **p<0.01.

According to the data presented in Figure 2, DII was positively correlated with the anthropometric measurements of BMI (r=0.309) and WC (r=0.197), and negatively correlated with the pulmonary function measurements of FVC (r=-0.209), FEV_1 (r=-0.227), and PEF (r=-0.253) (p<0.05).

The total calorie (r=0.304), carbohydrate (0,284), and fat uptake were positively correlated with DII (p<0.05). On the other hand, the total uptake of vitamin A (r=0.358), vitamin C (r=-0.529), and vitamin E (r=-0.510) were negatively correlated with DII (r=0.275) (p<0.01) (Figure 2).

DISCUSSION

The effects of nutritional habits and some specific nutrients on asthma have been investigated for many years with one of the most important hypotheses suggesting that a diet rich in fruit and vegetables and high anti-inflammatory content such as the Mediterranean diet, provide protection against asthma.[19] Processed foods with high-fat content, on the other hand, have been shown to exacerbate the symptoms of asthma.[4] Previous studies have also indicated that anti-inflammatory nutrients improve asthma control and pulmonary function. Nutrients rich in vitamins A, C, and E, in particular, have been shown to decrease inflammatory response by increasing antioxidant capacity and to improve asthma control as well as pulmonary functions.[20,21,22,23,24] The relationship between DII, as a novel and recent concept reflecting the inflammatory degree of a diet with asthma characteristics, has not been clarified to date. The first study into this topic reported that an increased DII was associated with decreases in FEV_1 and FVC, as measures of pulmonary function (p<0.05).[12] In another study in the US, higher DII (a pro-inflammatory diet) was associated with current wheeze among adults (eg, odds ratio [OR] for quartile 4 vs 1, OR=1.41, 95% confidence interval [CI]=1.17-1.70; p trend<0.01) (Han et al. 2018).Another study similarly reported that increased DII exacerbated dyspnea as a symptom of

impaired respiration and decreased FVC values.[25] In line with the limited number of studies reported in the literature, it was found in the present study that FEV_1, FVC, FEV_1/FVC, PEF, MEF_{75}, MEF_{50}, MEF_{25}, and MEF_{25-75} values decreased with increasing DII, with decreases in FVC and FEV_1 values being more prominent (p<0.05) and negatively correlated with a DII increase. The ACT scores of the patients also decreased with DII increase from tertile 1 to tertile 3 (p<0.05) which may be attributed to the impairment of respiration due to increased inflammatory response and the consequent decrease in asthma control. Previous studies have also reported that increased levels of inflammatory cytokines such as TNF-α, CRP, and IL-6 are associated with decreased asthma control although there have been no previous studies in the literature comparing DII and ACT scores.[26,27]

Obesity itself enhances inflammatory response in asthmatic individuals by causing lipid peroxidation and inflammatory cytokine release through fat tissue; while an increased inflammatory response, on the other hand, enhances bronchial irritability which is a characteristic of asthma by causing airway contractions.[28,29,30]The general opinion on this matter is that an increased BMI aggravates inflammatory response in asthmatic individuals. Previous studies have reported increased blood levels of TNF-α, CRP, and IL-6 with increased BMI in asthmatic individuals.[7,31] In a study by Wood et al. (2015), the DII in asthmatic individuals increased with increasing BMI.[12] Similarly, BMI significantly increased with increasing DII from tertile 1 to tertile 3 in the present study, and both increases were significantly correlated (p<0.05) which is an expected finding.

In addition to BMI, WC, and WHR increase, as markers of abdominal obesity, also impair pulmonary function and asthma control; as increased abdominal fat tissue aggravates the symptoms of inflammatory diseases such as asthma by enhancing the release of inflammatory cytokines.[32,33,34] In a study by Rastogi et al., an increase in the WC of asthmatic individuals was positively correlated with an increase in hs-CRP levels (p<0.01), and other studies monitoring the effects of diet and physical activity on asthma have also reported significant decreases in CRP, TNF-α, IL-6, and IL-10 levels with decreasing WC measurements (p<0.05) (Scott et al. 2011; Freitas et al.2017).[2,35] Similarly, in the present study, DII as an inflammatory marker, increased with increasing WC and WHR measurements, although the increase was more prominent for WC (p<0.05). Based on these findings, one may argue that asthmatics with high WC in the present study more commonly preferred nutrients with high inflammatory content.

Upon the changes in nutritional habits and the change from conventional diets to modern diets, the consumption of high-calorie and high-fat foods such as fast foods has become more common.[36] These foods are intensively processed or fried and increase allergic irritability as well as the symptoms of asthma.[4] In addition, excessively consumed calories and carbohydrates are transformed into fat through triglycerides and cause inflammation through fat tissue.[37] Previous studies have demonstrated that the over-consumption of foods with high SFA and calorie content induce allergic irritability and airway inflammation and is associated with early-onset asthma (Wood et al. 2018; Wood et al. 2017; Sausenthaler et al. 2006).[38,39,40] In the present study, DII increased with increased consumption of calories, carbohydrates, total fat, SFA, and these increases were positively correlated with DII (p<0.05). An increased dietary ratio of omega-6 fatty acids which are rich in a pro-inflammatory substance called arachidonic acid also enhances allergic symptoms.[41] Similarly, DII increased with increasing omega-6 fatty acid-rich PUFA levels in the present study, although the increase was not statistically significant (p>0.05).

One of the most extensively investigated topics related to asthma and nutrition is the effects of antioxidant vitamins.[21] An increased amount of reactive oxygen species in the body enhances the immune response by causing the down-regulation of T-helper1 cells and leads to airway inflammation. Under these circumstances, an insufficient uptake of antioxidant vitamins increases IL-1, IL-6, CRP, and NF-kb levels and enhances inflammatory response in asthmatics.[20] Additionally, the processing of fruit and vegetables in accordance with modern dietary habits decreases the antioxidant and anti-inflammatory capacity of such nutrients.[4] Studies investigating the effects of antioxidant A, C, and E vitamins on asthma have generally reported that insufficient uptake of these vitamins increases the symptoms of asthma and inflammatory response; while the symptoms of asthma and IL-10 levels have been found to decrease in people given supplements containing these vitamins.[22,23,24,42] In line with these results, the Vitamin A, C, and E uptake

in the asthmatics of the present study decreased with increasing DII levels, as a novel marker of dietary inflammation potential.

This study has some limitations. First of all, our results cannot be extrapolated to the overall population as the study was carried out as a single-center and with a relatively small patient sample. Furthermore, we did not analyze the levels of such inflammatory cytokines as CRP, TNF-α, and IL-6, or compare these levels with DII. The number of female subjects was higher than the number of males in this study, although there was no bias in patient selection. The gender difference in the prevalence of asthma is a global fact; being more common in women than men due to the effects of post-pubertal sex hormones.[3]

Despite these limitations, the value of this study is increased through its support of the findings with anthropometric measurements, in addition to pulmonary function test results and ACT scores. The comparisons made between DII, as a new marker reflecting the inflammatory capacity of diet, and the characteristics of asthma, as well as macro-micro nutrients, shed some light on the relationship between asthma and nutrition. This study has also provided clarification on the effect of nutritional habits on asthma control; being the first study to compare DII and ACT scores.

In conclusion, pulmonary function and asthma control decreased with increasing DII in asthmatic patients in the present study; while BMI and WC increased with increasing DII. Accordingly, in addition to weight loss, the increased consumption of foods with high anti-inflammatory content may be helpful in improving the symptoms of asthma as an inflammatory disease and it would hence be appropriate to provide asthmatic individuals with accurate nutritional guidelines in order to ensure a favorable disease course.

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