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Exploring the link between nutritional status and total antioxidant status in patients with severe asthma: a cross-sectional study

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Abstract

Background and objective This study aimed to assess the nutritional status of individuals with severe asthma and to determine how dietary antioxidant (AO) intake influences the disease prognosis and plasma total antioxidant status (TAS).

Methods The study included 44 patients with severe asthma and 45 healthy participants. Anthropometric measurements, asthma control levels, scores from a validated antioxidant food consumption frequency questionnaire, 3-day food records, and demographic information were gathered from each participant. Blood samples obtained after overnight fasting were analyzed for plasma TAS and total oxidant status (TOS).

Results The mean antioxidant intake measured by the FFQ and food records, as well as plasma TAS levels, were significantly lower in the asthma group compared to the control group ($p < 0.05$). In the asthma group, negative correlations were found between the duration of asthma and both plasma TAS and antioxidant intake from the FFQ and food records, indicating that longer asthma duration was associated with lower antioxidant status ($p < 0.05$). Additionally, a positive correlation was observed between the asthma control level and the antioxidant intake from the FFQ in the case group, suggesting that better asthma control was associated with higher antioxidant intake ($p < 0.05$).

Conclusion Plasma TAS levels in patients with severe asthma were significantly lower than in healthy individuals. Higher dietary antioxidant intake was positively associated with plasma TAS and may contribute to improved asthma control. These findings suggest that increasing dietary antioxidant intake could be beneficial in the management of severe asthma.

Clinical trial number Not applicable.

Highlights

- Patients with severe asthma often exhibit reduced plasma antioxidant levels, which may contribute to the exacerbation of symptoms and increased inflammation.
- Dietary antioxidant intake plays a crucial role in increasing plasma antioxidant levels, which can help reduce oxidative stress and inflammation in conditions like asthma.

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- Adequate intake of antioxidants through nutrition may help reduce oxidative stress, potentially alleviating asthma symptoms and preventing exacerbations.

Keywords Severe asthma, Total antioxidant capacity, Assessment of nutritional status

Introduction

Severe asthma is a type of asthma that is difficult to control, includes chronic symptoms, persistent and recurrent seizures, airway obstruction, and inflammation, and requires continuous short-acting beta-agonists and inhaled corticosteroid treatment. Approximately 3–10% of individuals with asthma are diagnosed with severe asthma [1]. The most prominent pathological finding in asthma is chronic airway inflammation, which in some cases causes permanent structural changes [2]. Inflammatory cells in the respiratory tracts of asthmatic patients are activated by various stimuli, resulting in elevated levels of reactive oxidant products. Activated eosinophils, neutrophils, macrophages, and bronchial epithelial cells produce oxidants that further stimulate inflammatory cells, worsening lung inflammation [3]. Airway inflammation triggers the secretion of various anti-inflammatory and pro-inflammatory markers, such as tumor necrosis factor alpha (TNF-α), interleukin 1 (IL-1), interleukin 6 (IL-6), IL-8, interferon gamma (IFN-γ), transforming growth factor beta (TGF-β) and interleukin 10 (IL-10). The elevation of these markers exacerbates asthma symptoms [4].

Oxidative stress is defined as an increase in reactive oxygen species (ROS) production linked to inflammation and/or a reduction in antioxidant capacity which triggers a chain of events leading to oxidant-induced cellular damage and death. Excessive ROS and its byproducts cause harmful consequences and direct oxidation of biological macromolecules, including proteins, lipids, and nucleic acids, which exacerbates the onset of inflammatory reactions and leads to a number of inflammatory illnesses via activating multiple inflammatory cascades such as nod-like receptor family pyrin domain-containing 3 (NLRP3) inflammasome signaling pathway, nuclear transcription factor-kappa B (NF-κB) signaling pathway, and mitogen-activated protein kinase (MAPK) signaling pathway [5–7].

Antioxidants are known to protect biological membranes against oxidative damage and are potential scavengers of ROS produced as a result of oxidative reactions [8]. The intake of antioxidants protects the structural density of smooth muscle cells in the airway, decreases the production of precursor proteins that cause inflammation [9], improves immunity, provides bronchodilation through prostaglandin-E2 release [10], and decreases airway hypersensitivity to allergens [11].

Overall antioxidant status from the plasma is measured by total antioxidant status (TAS), whereas plasma oxidant levels are measured by total oxidant status in body (TOS). TAS is often linked to the overall body's capacity to counteract oxidative stress, while high TOS levels indicate both increased oxidative stress and oxidative damage [12, 13]. Numerous studies have demonstrated that elevated TOS is a significant byproduct of the inflammatory response in asthma, and it is associated with alterations in both blood and lung antioxidant activity, as well as the development of airway hyperresponsiveness [14].

To effectively manage asthma and reduce risks of exacerbations, airflow limitation, and inflammation, the Global Initiative for Asthma (GINA) report outlines both pharmacologic and nonpharmacologic treatment approaches. Pharmacologic interventions involve specific medications, while nonpharmacologic methods include quitting smoking, exercising, avoiding allergens, and maintaining a healthy diet. A diet rich in fruits and vegetables is recommended for its high antioxidant content [2]. Antioxidant-rich diets, such as the Mediterranean Diet, such as those high in polyphenols, selenium, and vitamins C and E, have been demonstrated to lower inflammation and oxidative stress, two major factors in the pathogenesis of asthma. Furthermore, a diet rich in fruits, vegetables, and omega-3 fatty acids has been linked to higher respiratory function and an enhanced antioxidant status in asthmatic patients. On the other hand, diets rich in processed foods, refined sugars, trans and saturated fats may increase inflammation and oxidative stress, which could make asthma symptoms worse [15]. Given the GINA recommendation, assessing how consuming antioxidant-rich foods, like fruits and vegetables, impacts disease prognosis in individuals with severe asthma and high inflammation levels.

Earlier studies have primarily focused on the common asthma types in adults and children, often evaluating the effects of individual nutrients or general dietary patterns on asthma symptoms and lung function. However, there is a lack of comprehensive study specifically including adults with severe asthma and investigating the relationship between overall dietary antioxidant intake and biomarkers of oxidative stress.

To the best of our knowledge, this is the novel study to emphasize the importance of nutrition status in severe adult asthma patients. This research aims to explore the relationship between dietary antioxidant intake and plasma total antioxidant status, using food consumption records and total antioxidant questionnaires from severe asthma patients, to evaluate the role of nutritional and antioxidant intake in asthma prognosis.

Materials and methods

This cross-sectional study involved patients with severe asthma and healthy volunteers, conducted at Istanbul Süreyyapaşa Chest Diseases and Thoracic Surgery Training and Research Hospital from October 2018 to February 2019 with ethical approval from the Clinical Research Ethics Committee of Marmara University Faculty of Medicine (approval number: 09.2018.680). All participants provided informed consent, adhering to the principles of the Helsinki Declaration.

Participants

The case group was created among the severe asthma patients applying to the polyclinic, those who volunteered and met the inclusion criteria were selected by a random sampling method. The case group was aged 20–69, with no history of chronic diseases or the use of routine/daily medications that could confound the results. Participants in the case group were excluded if they were smokers had other chronic conditions, or were using medications that could affect antioxidant levels or inflammatory responses. The identification of smokers was clarified according to the NHIS Glossary as an adult who has smoked at least 100 cigarettes in his or her lifetime and who smokes now every day or some days is defined as a smoker [16].

The control group comprised healthy individuals without chronic diseases, particularly asthma, and who were non-smokers. Control participants were recruited from hospital staff and the relatives of patients, all of whom volunteered and met the inclusion criteria through a random sampling method. Exclusion criteria for both case and control groups included pregnancy, lactation, chronic diseases, supplement use, or communication difficulties that might hinder participation or understanding of the study protocols.

The G*Power 3.1.9.2 software program was used for calculating the sample size, based on a previous study that reported plasma antioxidant levels in patient with severe asthma. The analysis was based on the plasma antioxidant level difference between groups with an effect size (Cohen's $d = 0.8$), with a 2-tailed type 1 error of 0.05 and a power of 90% showed that to detect a difference in plasma antioxidant levels between patients with severe asthma and healthy controls at least 34 participants per group were required [17]. This study included 44 severe asthma patients and 45 healthy subjects.

Anthropometric measurements

All anthropometric measurements were obtained at the beginning of the study by a specialist, with participants in a fasting state. The patients' heights were measured without shoes, and the waist and hip circumferences were recorded while the patients were wearing light clothes.

The TANITA-DC360 device (Tartı Medical, Istanbul-Turkey, https://www.tarti.com/urunler/profesyonel-vucut-analiz-tartilari/tanita-dc-360-st?%20gad_source=1%26;gclid=Cj0KCQiAyKurBhD5ARIsALamXaGg41R8vELX2QvWllxRb4FM-_wD-hka7w2zVeVeDNchXxoBwS7MMyCOoaArYgEALw_wcB) was used for bioelectrical impedance analysis (BIA). It applies a continuous current to assess body composition. Measurements were taken under standardized conditions, including morning timing, empty bladder, light clothing, and avoidance of food, caffeine, alcohol, dehydration, and strenuous activity before the measurement. Proper posture, skin contact, and electrode placement were ensured. Factors such as menstruation, illness, and hydration status were also considered due to their potential effect on the results [18].

Assessment of dietary intake of the total antioxidant amount

For assessing of dietary antioxidant intake, 3-day food records for 3 months (total 9-day food record) and a validated food frequency questionnaire (FFQ) [13] were gathered from all individuals. The macronutrient, micronutrient, and total antioxidant intake data from the food records and the antioxidant intake from the FFQ were entered into the BeBis software [Ebispro for Windows, Stuttgart-Germany; Turkish Version (BeBiS-8.2)], and the nutrient content was calculated based on the software's database (Bundeslebensmittelschluessel; German Food Code and Nutrient Database-Version 3.01B [http://www.bfr.bund.de/cd/801]). The dietary antioxidant con tent was also calculated by multiplying the amount of a food item by its corresponding TAS value per unit weight from a food TAS database from the study of Carlsen et al. with the database of TAS values including more than 3100 foods [19]. Macro- and micronutrient intake analysis results were also compared with the Nutrition Guideline for Turkey (TUBER) and Recommended Dietary Allowance (RDA) recommendations [20–22]. All the data were evaluated by dietitians.

Assessment of the TAS and TOS status in plasma

To measure TAS and TOS in plasma, venous blood was collected from participants after 8 h of overnight fasting using 10 mL lithium heparin vacuum tubes. The samples were centrifuged at 4400 rpm for 10 min in a cooled centrifuge, and the plasma fractions were stored in Eppendorf tubes at -80 °C until analysis. TAS and TOS were assessed using noncompetitive (sandwich) ELISA kits from SunRed Biological Technology (Human-TAS ELISA, Catalog No: 201-12-7412; Human-TOS ELISA Kit, Catalog No: 201-12-5807; Shanghai, China), following the manufacturer's instructions.

In TAS concentration analysis, antioxidant substances reduced the dark blue-green ABTS

(2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) radical solution to a colorless form, with absorbance changes measured at 660 nm, indicating plasma TAS. For plasma TOS measurements, oxidants in the sample oxidized a ferrous ion chelator complex into ferric ions, which combined with chromogens in an acidic environment to produce a colored complex. The extent of color production directly correlates with the amount of oxidant molecules in the sample, allowing TOS measurement to be measured spectrophotometrically.

Assessment of data for patients with severe asthma

The Asthma Control Test (ACT), a useful tool for assessing asthma symptoms, was first developed by Nathan et al. [23] and the Turkish validation of ACT was done by Uysal et al. [24]. ACT consists of five questions rated 1–5 that assess the degree of influence on daily activities, symptoms during the day and at night, the need for rescue medication, and the person's perception of asthma control. ACT scores of ≥25 points were considered "totally controlled", those between 20 and 24 points were considered "partially controlled", and those ≤19 points were considered "uncontrolled". In addition to ACT, the duration of severe asthma was evaluated.

Statistical analysis

SPSS 20.0 was used for statistical analysis (Inc., Chicago, USA). The Kolmogorov-Smirnov test and histogram graphs were used to assess the normality of the data distribution. For data that were regularly distributed, descriptive statistics were presented as mean and standard deviation. Independent sample t-tests were utilized for normally distributed data, while Mann-Whitney U tests were applied for non-normally distributed data. The chi-square test examined differences in categorical variables between groups. Pearson and Spearman correlation tests compared TAS and TOS data with other quantitative variables. $p<0.05$ was considered statistically significant. Statistically significant results were presented in bold.

Results

The study found that the proportion of female participants was higher in the case group (81.8%) compared to the control group (57.8%) ($p>0.05$). The mean age was 50.41 ± 9.53 years for the case group and 45.98 ± 11.01 years for the control group. The sex distribution and age classifications according to groups are presented in Table 1. In addition to this data, the sleep duration and exercise profile of the case and control groups were assessed. Although the severe asthma patients' mean sleep hours in a day were less than control group (7,2 ± 2,6 and 7,9 ± 3,1 h, respectively) this difference was not significant ($p>0.05$). Parallel to sleep duration, the exercise profile of participants in both case and control group was similar ($p>0.05$). The majority of participants in both the case and control groups (66,4% and 63,2%, respectively) exercised one day or less per week.

The case group had a significantly higher mean BMI than the control group ($p<0.05$). Additionally, weight, fat percentage, fat mass, visceral fat, and BMI were significantly greater in the case group, while body water percentage and body water mass were significantly higher in the control group ($p<0.05$). The fat-free mass (FFM) ratio, FFM, and height were similar between the two groups ($p>0.05$) (Table 2).

Table 1 Demographic data of individuals

		Case Group		Control Group		Total	
		n	**%**	***n***	**%**	***n***	**%**
Sex	Male	8	18.2	19	42.2	27	30.3
	Female	36	81.8	26	57.8	62	69.7
		$x^2=6.084$			$p=0.064$		
Age Classification	20–39	5	11.4	10	22.2	15	16.8
	40–59	31	70.5	27	60.0	58	65.1
	60–69	8	18.2	8	17.8	16	18.0
		$x^2=2.205$			$p=0.698$**		
Working Status	Non-working	23	52.3	6	13.3	33	32.6
	Working	21	47.7	39	86.6	60	67.4
		$x^2=55.301$			$p=0.000$*		
Education Status	Low education (primary education or less)	27	61.4	13	28.9	40	45
	Intermediate education (secondary and high school education)	11	25.0	16	35.6	27	30.3
	Higher education (university degree or postgraduate education)	6	13.6	16	35.6	22	24.7
		$x^2=11.755$			$p=0.019$*		
Total		44	100.0	45	100.0	89	100.0

*Pearson Chi-square. $p<0.05$

**Fisher's Exact Chi-square. $p<0.05$

Table 2 Anthropometric data of individuals

	Case Group ($n=44$)	Control Group ($n=45$)		
	X ± SD	X ± SD	t	*p*
Weight (kg)	83.69 ± 18.66	74.03 ± 13.87	-2.696	**0.007***
Body Fat Percentage (%)	37.03 ± 9.09	31.96 ± 7.54	-2.862	**0.005***
Body Fat Weight (kg)	31.58 ± 12.75	26.27 ± 9.49	-2.007	**0.045***
FFM (%)	51.55 ± 7.41	52.19 ± 7.83	-0.287	0.774
FFM (kg)	48.68 ± 7.67	48.11 ± 9.50	0.332	0.740
BW (%)	44.20 ± 5.53	47.70 ± 4.88	-3.012	**0.003***
BW (kg)	36.15 ± 5.69	39.06 ± 5.60	-2.435	**0.017***
Visceral Fat	10.25 ± 3.85	7.82 ± 2.65	3.241	**0.001***
BMI (kg/m^2)	31.73 ± 7.00	27.89 ± 5.03	3.090	**0.002***

FFM: Fat Free Mass; BW: Body Water; BMI: Body Mass Index

* Independent Sample T-test; $p<0.05$

Asthma attacks were classified according to the ACT as "totally controlled," "partially controlled," or "not controlled." Among the case group, no patients achieved scores indicative of totally controlled (Score = 25); 18 individuals had partially controlled asthma partially controlled (Score = 20–24), while 26 showed no control (Score ≤ 19), over their asthma attacks. The majority of patients in this group relied on reliever inhalers and reported experiencing asthma symptoms and shortness of breath at least once per week (Table 3).

The energy intake, protein amount, protein percentage, and thiamine content were greater in the case group than in the control group, while the amount of fat, fat percentage, carbohydrate amount, cholesterol, vitamin E, niacin, and riboflavin were not significantly different between groups ($p>0.05$). Dietary fiber, vitamin A, and vitamin C intake were significantly greater in the control group than in the case group ($p<0.05$) (Table 4).

In the case group, potassium and calcium intake, as assessed by TUBER, were less than 50% of the recommended levels, with vitamin A, potassium, and calcium also falling below 50% of the RDA. Phosphorus and iron intake were within acceptable ranges according to TUBER, but while iron intake met RDA standards, phosphorus intake did not. Daily dietary fiber intake did not meet the recommended levels set by either TUBER or the RDA. Similarly, potassium intake in the control group was below 50% of the recommended values according to both TUBER and RDA criteria. While fiber and calcium intake were higher in the control group compared to the case group, they still fell short of the standards set by TUBER and RDA (Table 4). Table 5 summarizes the average dietary antioxidant intake (AO), antioxidant intake from the food frequency questionnaire (FFQ-AO), plasma total antioxidant status (TAS), and plasma total oxidant status (TOS). The control group had significantly higher mean dietary-AO levels and lower plasma TOS compared to the case group ($p<0.05$). Statistically significant associations were identified between dietary-AO, FFQ-AO, and plasma-TAS and plasma-TOS. Specifically, plasma-TOS exhibited negative correlations with dietary-AO, FFQ-AO, and plasma-TAS, indicating that higher antioxidant levels were associated with lower oxidative stress. In contrast, positive correlations were observed between dietary-AO, FFQ-AO, and plasma-TAS ($p<0.05$), suggesting that increased antioxidant intake and plasma TAS were positively associated. These results are shown in Table 6.

In patients with severe asthma, a positive correlation was observed between asthma control over the past four weeks and the FFQ-AO score. Conversely, the duration of asthma was negatively correlated with FFQ-AO, dietary-AO, and plasma-TAS ($p<0.05$). A positive correlation was also noted between plasma TOS and the duration of asthma ($p<0.05$). Higher FFQ-AO and plasma-TAS scores were associated with improved asthma management, as reflected in better asthma control stages ($p<0.05$) (Table 7). Plasma-TAS and plasma-TOS can be influenced by dietary intake. In the case group, plasma-TAS positively correlated with the intake of thiamine, riboflavin, vitamin C, magnesium, iron, and zinc, whereas negative correlations were observed with daily intake of protein, carbohydrates, and fat ($p<0.05$). While most micronutrients showed no significant correlation within the case group, the control group demonstrated stronger and more consistent correlations (Table 8). Table 9 presents data on dietary antioxidant intake from specific food subgroups. The severe asthma patient group exhibited a significantly lower intake of orange fruits and green leafy vegetables compared to the control group ($p<0.05$).

Discussion

This research was conducted to reveal the effect of dietary antioxidant intake on plasma-TAS and plasma-TOS in patients with severe asthma. Due to asthma's inflammatory nature, consuming antioxidant-rich foods like fruits, vegetables, and nuts is recommended for better management. Conversely, diets high in fat, sugar, and salt can worsen oxidative stress, leading to increased asthma symptoms and poorer disease outcomes [25].

Asthma pathogenesis is significantly influenced by oxidative stress, which is triggered by persistently activated airway inflammatory cells and results in vascular exudation, smooth muscle contraction, bronchial hyperresponsiveness, excessive mucus production, epithelial cell shedding, and airway dysfunction [26]. Because asthma is such an inflammatory condition, antioxidants are essential for treating severe asthma [27]. Our results revealed significantly lower total dietary antioxidant intake and plasma-TAS in severe asthma patients compared to

Table 3 Asthma control test results for severe asthma patients

Case Group							
		ACT Evaluation					
Asthma Control Test		**Uncontrolled**		**Partially controlled**		**Totally controlled**	
(ACT)		**(Score ≤ 19)**		**(Score = 20–24)**		**(Score = 25)**	
		n	**%**	**n**	**%**	**n**	**%**
1. During the past 4 weeks, how often did your asthma prevent you from getting as much done at work, school or home?	All the time	1	3.8	0	0	0	0
	Most of the time	7	26.9	0	0	0	0
	Some of the time	7	26.9	7	38.9	0	0
	A little of the time	11	42.3	10	55.6	0	0
	None of the time	0	0	1	5.6	0	0
		$x^2 = 7.853$		$p = 0.097$			
2. During the past 4 weeks, how often have you had shortness of breath?	More than once a day	0	0	0	0	0	0
	Once a day	1	3.8	0	0	0	0
	3–6 times a week	7	26.9	0	0	0	0
	1–2 times a week	17	65.4	13	72.2	0	0
	Not at all	1	3.8	5	27.8	0	0
		$x^2 = 10.079$			$p = 0.018$*		
3. During the past 4 weeks, how often did your asthma symptoms (wheezing, coughing, shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning?	4 or more nights a week	3	11.5	0	0	0	0
	2 to 3 nights a week	3	11.5	0	0	0	0
	Once a week	2	7.7	1	5.6	0	0
	Once or twice	15	57.7	5	27.8	0	0
	Not at all	3	11.5	12	66.7	0	0
		$x^2 = 15.801$			$p = 0.003$*		
4. During the past 4 weeks, how often have you used your rescue inhaler or nebulizer medication (such as albuterol)?	3 or more times per day	2	77	0	0	0	0
	1 or 2 times per day	3	11.5	0	0	0	0
	2 or 3 times per week	5	19.2	1	5.6	0	0
	Once a week or less	16	61.5	13	72.2	0	0
	Not at all	0	0	4	22.2	0	0
		$x^2 = 10.882$			$p = 0.028$*		
5. How would you rate your asthma control during the past 4 weeks?	Not controlled at all	1	3.8	0	0	0	0
	Poorly controlled	1	3.8	0	0	0	0
	Somewhat controlled	15	57.7	2	11.1	0	0
	Well controlled	9	34.6	15	83.3	0	0
	Completely controlled	0	0	1	5.6	0	0
		$x^2 = 13.431$			$p = 0.009$*		
Total ACT Score		26	59.1	18	40.9	0	0
Average ACT Total Score		16.81		20.56		0	

*Pearson Chi-square; $p < 0.05$

healthy controls. Previous studies, including a case-control and a cohort, have found that the overall antioxidant status both from plasma and dietary intake of patients with asthma was lower than healthy controls [28, 29]. Consistent with our findings, eating a balanced diet that includes foods high in antioxidants can lower plasma oxidant levels and alleviate symptoms of asthma [30]. It is strongly advised that fruits and vegetables be consumed at high levels due to their synergistic effects and the numerous antioxidant compounds they contain [2, 31].

On the other hand, plasma-TOS serves as an indicator of inflammation in asthma. Our study revealed negative correlations between TOS and dietary-AO, FFQ-AO, and plasma-TAS. Consistent with recent findings showing elevated plasma-TOS and disulfide levels in severe asthma, our research found that individuals with severe asthma exhibited significantly higher plasma-TOS compared to healthy controls [32].

Key antioxidant micronutrients—vitamin C, vitamin A (beta-carotene), iron, and zinc—were all significantly lower in asthma patients according to our results. Vitamin C intake was positively correlated with plasma-TAS and inversely related to plasma-TOS in our study, highlighting its main role in reducing oxidative stress and its link to worsened lung function in parallel with previous studies [33, 34]. Likewise, vitamin A intake was decreased, which is consistent with our lower TAS levels and supports the idea that antioxidant defense may be

Table 4 Food consumption record data of the individuals

Case Group / Control Group								
	Case Group			Control Group				
	X ± SD	Percentage of coverage by TUBER (%)	Percentage of coverage by RDA (%)	X ± SD	Percentage of coverage by TUBER (%)	Percentage of coverage by RDA (%)	t	*p*
Energy (kcal/day)	1930.9 ± 184.38	92.97	101.63	1897.01 ± 159.4	91.33	99.84	-0.530	0.596
Protein (g/day)	111.20 ± 17.46	170.81	241.74	111.07 ± 19.98	170.61	241.46	0.441	0.975
Protein (%)	24.02 ± 3.85	120.10	106.76	23.47 ± 3.81	117.35	104.31	-0.782	0.434
Fat (g/day)	80.55 ± 16.29	115.07	123.92	76.30 ± 14.32	109.00	117.38	-1.265	0.206
Fat (%)	36.89 ± 5.98	122.97	131.75	38.02 ± 6.04	126.73	135.79	-0.957	0.339
Carbohydrate (g/day)	181.03 ± 12.38	139.25	139.25	181.68 ± 18.94	139.75	139.75	-0.509	0.611
Carbohydrate (%)	39.09 ± 2.69	78.18	71.07	38.51 ± 4.31	77.02	70.02	-0.638	0.523
Cholesterol (mg/day)	271.00 ± 91.06	99.45	90.33	299.89 ± 97.69	110.05	99.96	-1.536	0.125
Vitamin A (mcg/day)	399.6± 229.48	57.09	49.95	543.99±260.93	77.71	68.00	-3.014	**0.003***
Vitamin E (mg/day)	17.37 ± 11.12	144.75	115.80	21.85 ± 13.02	182.08	145.67	-1.121	0.262
Niacin (mg/day)	18.04 ± 7.73	269.25	120.27	20.41 ± 9.28	304.63	136.07	-1.347	0.178
Thiamine (mg/day)	1.22 ± 0.38	101.67	101.67	1.20 ± 0.44	100.00	100.00	-0.276	0.782
Riboflavin (mg/day)	1.22 ± 0.30	101.67	101.67	1.35 ± 0.49	112.50	112.50	-0.778	0.437
Vitamin C (mg/day)	113.31 ±71.68	110.55	125.90	185.08±123.75	180.57	205.64	-2.143	**0.032***
Sodium (mg/day)	2301.7±761.15	177.05	100.07	1944.05±510.4	149.54	84.52	-2.168	**0.030***
Potassium (mg/day)	2096.87±475.9	44.61	44.61	2278.07±856.3	48.47	48.47	-0.452	0.651
Calcium (mg/day)	383.36±214.21	40.35	38.34	572.15±257.03	60.23	57.22	-3.302	**0.001***
Magnesium (mg/day)	365.5±108.03	112.46	98.78	358.53±132.11	110.32	96.90	-0.263	0.793
Phosphorus (mg/day)	513.4±135.47	93.35	73.34	782.42±393.88	142.26	111.77	-4.025	**0.000***
Iron (mg/day)	10.86 ± 2.72	98.73	135.75	13.49 ± 3.95	122.64	168.63	-3.092	**0.002***
Zinc (mg/day)	11.49 ± 3.47	100.79	104.45	11.77 ± 3.44	103.25	107.00	-0.542	0.588
Dietary AO (mmol/day)	2.75 ± 1.20	-	-	4.06 ± 2.52	-	-	-2.015	**0.044***
Dietary Fiber (g/day)	16.74 ± 9.37	66.96	66.43	20.74 ± 11.21	82.96	82.30	-2.058	**0.040***

AO: Antioxidant amount

* Independent Sample T-test; $p<0.05$

Table 5 Data on dietary TAS, TAS obtained from the antioxidant food consumption frequency questionnaire, and plasma TAS and TOS levels

	Case Group	Control Group		
	X ± SD	X ± SD	t	*p*
FFQ AO	11.76 ± 7.44	13.81 ± 6.19	-2.265	**0.024***
Plasma TAS (U/ml)	24.72 ± 46.46	114.08 ± 134.63	-3.083	**0.002***
Plasma TOS (U/ml)	22.9 ± 15.88	12.40 ± 8.35	-2.187	**0.029***
Dietary AO	2.75 ± 1.20	4.06 ± 2.52	-2.015	**0.044***

TAS: Total Antioxidant Status; TOS: Total Oxidant Status; Dietary AO: Antioxidant amount from food record; FFQ AO: Antioxidant amount from food frequency questionnaire

* Independent Sample T-test; $p<0.05$

Table 6 Correlation between TAS TOS level of plasma and food intake

		Case Group ($n=44$)		Control Group ($n=45$)	
		Plasma TAS	Plasma TOS	Plasma TAS	Plasma TOS
Dietary AO	r	0.776*	-0.621*	0.919*	-0.812*
	p	0.000	0.000	0.000	0.000
FFQ AO	r	0.409*	-0.251	0.730*	-0.717*
	p	0.006	0.101	0.000	0.000

TAS: Total Antioxidant Status; TOS: Total Oxidant Status; Dietary AO: Antioxidant amount from food record; FFQ AO: Antioxidant amount from food frequency questionnaire

*Spearman correlations; $p<0.05$

compromised by inadequate consumption of foods high in beta-carotene [33, 35]. Regarding minerals, zinc and iron, which support the action of antioxidant enzymes, also showed significant positive associations with TAS, emphasizing the systemic effects of micronutrient insufficiency in severe asthma [36–38].

In addition to micronutrients, we discovered that asthma patients consumed significantly less dietary fiber. The mechanistic function of fiber in regulating immune response and preserving airway integrity was further supported by the correlation between this low intake and elevated inflammation [39, 40].

No significant associations were found between TAS or TOS and general food group intake (grains, dairy, meat, vegetables, fruits), except for dietary fat. We revealed the intake of dietary fat, a macronutrient, which was found to be consumed at higher levels than recommended among

Table 7 Correlation between plasma TAS TOS level and asthma data

Case Group					
Asthma Control Test (ACT)		**FFQ AO**	**Plasma TAS**	**Plasma TOS**	**Dietary AO**
1. During the past 4 weeks, how often did your asthma prevent you from getting as much done at work, school or home?	r	0.268	0.214	-0.106	0.190
	p	0.078	0.162	0.494	0.217
2. During the past 4 weeks, how often have you had shortness of breath?	r	0.256	0.198	-0.078	0.045
	p	0.094	0.198	0.613	0.770
3. During the past 4 weeks, how often did your asthma symptoms (wheezing, coughing, shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning?	r	0.290	0.140	-0.140	-0.056
	p	0.056	0.365	0.363	0.719
4. During the past 4 weeks, how often have you used your rescue inhaler or nebulizer medication (such as albuterol)?	r	0.106	0.071	-0.107	0.117
	p	0.495	0.646	0.488	0.449
5. How would you rate your asthma control during the past 4 weeks?	r	**0.313***	0.251	0.011	0.158
	p	**0.039**	0.100	0.945	0.304
Total ACT Score	r	0.291	0.257	-0.068	0.156
	p	0.055	0.093	0.660	0.312
Duration of having asthma	r	**-0.325****	**-0.628****	**0.634****	**-0,552****
	p	**0.000**	**0.000**	**0.000**	**0.000**

TAS: Total Antioxidant Status; TOS: Total Oxidant Status; Dietary AO: Antioxidant amount from food record; FFQ AO: Antioxidant amount from food frequency questionnaire

*Pearson correlations; $p < 0,05$

**Spearman correlations; $p < 0,05$

asthma patients. Our findings indicated that individuals with asthma ingested more fat than is advised, which could lead to oxidative stress by increasing the levels of saturated fatty acids in the blood, which elevate inflammatory markers and subsequently lower plasma-TAS [41]. High-fat intake is one of the risk factors for obesity, which is associated with increased asthma severity. In our study, the average BMI of severe asthma patients fell within the obesity range. Additionally, in line with the noted higher BMI, our asthma group also showed increased body weight, body fat percentage, and visceral fat. The severity of asthma is further increased by these characteristics, which are strongly linked to oxidative imbalance and systemic inflammation that result in increased plasma-TOS. Our data are consistent with literature suggesting that obesity worsens asthma symptoms and impairs lung function by linking oxidative imbalance to dietary fat intake, adiposity metrics, and BMI [42]. It should be noted that low-grade systemic inflammation in the presence of obesity may be a confounding factor when evaluating the association between dietary antioxidant intake and oxidative stress indicators due to the notable variations in body composition and BMI between groups. It may be challenging to distinguish the effects of dietary antioxidants alone since obesity-related inflammation may have an independent impact on TAS and TOS levels. It can be thought that medical nutrition therapy for asthma will improve body composition and therefore obesity, and will help to control inflammation that increases for various reasons more quickly.

The Asthma Control Test (ACT) is a validated, patient-centered tool known for its reliability, sensitivity, and stability in detecting poorly managed asthma in large populations [43]. Higher plasma-TAS was found to be significantly correlated with high dietary antioxidant intake. Additionally, FFQ-AO showed a strong correlation with ACT scores, indicating that poor asthma management may be linked to reduced antioxidant levels and higher inflammation [44]. Consistent with our findings, a lower plasma malondialdehyde level is associated with improved asthma control [45, 46]. Additionally, low dietary antioxidant intake is linked to poor control of asthma symptoms, according to another study that supports our findings [47]. The duration of asthma affects the inflammatory stage in addition to managing its symptoms. After receiving a long-term diagnosis of severe asthma, our patients found it difficult to manage their symptoms. The longer a patient was diagnosed with severe asthma, the worse their plasma, diet, and FFQ-AO scores were; in contrast, their plasma-TOS were favorably correlated in our study.

A key strength of this study is its novel integration of dietary antioxidant intake with plasma total antioxidant capacity in patients with severe asthma. By assessing the overall antioxidant potential of food, this research provides a comprehensive perspective on the role of dietary antioxidants in asthma prognosis. Furthermore, this study advances existing literature by pioneering an investigation into antioxidant-containing subnutrient groups, offering valuable insights into their potential impact on severe asthma management.

Table 8 Correlation between TAS-TOS levels and nutritional data of case and control group

		Case Group				Control Group			
		FFQ AO	**Plasma TAS**	**Plasma TOS**	**Dietary AO**	**FFQ AO**	**Plasma TAS**	**Plasma TOS**	**Dietary AO**
Energy	r	-0.157	-0.165	-0.097	0.062	-0.113	-0.041	-0.154	-0.060
(kcal/day)	p	0.310	0.284	0.531	0.688	0.462	0.791	0.311	0.697
Protein	r	-0.019	**-0.324***	-0.167	-0.186	**0.534***	**0.579***	**-0.472***	**0.606***
(g/day)	p	0.902	**0.032**	0.278	0.226	**0.000**	**0.000**	**0.001**	**0.000**
Protein	r	0.026	-0.151	-0.127	-0.054	**0.631***	**0.667***	**-0.565***	**0.708***
(%)	p	0.868	0.327	0.411	0.727	**0.000**	**0.000**	**0.000**	**0.000**
Fat	r	-0.030	-0.077	0.092	-0.094	**-0.430***	**-0.480***	**-0.554***	**-0.500***
(g/day)	p	0.847	0.617	0.553	0.543	**0.003**	**0.001**	**0.000**	**0.000**
Fat	r	-0.032	0.023	0.164	0.017	**-0.501***	**-0.594***	**-0.621***	**-0.591***
(%)	p	0.839	0.884	0.286	0.915	**0.000**	**0.000**	**0.000**	**0.000**
Carbohydrate	r	0.117	**-0.302***	-0.213	**-0.316***	0.154	**0.370***	**0.343***	**0.330***
(g/day)	p	0.449	**0.047**	0.166	**0.037**	0.314	**0.012**	**0.021**	**0.027**
Carbohydrate	r	0.089	0.074	-0.137	0.023	0.187	**0.315***	**0.396***	0.293
(%)	p	0.567	0.632	0.376	0.884	0.219	**0.035**	**0.007**	0.051
Fiber	r	0.151	-0.274	-0.141	-0.285	**0.629***	**0.656***	**-0.564***	**0.707***
(g/day)	p	0.328	0.072	0.362	0.060	**0.000**	**0.000**	**0.000**	**0.000**
Cholesterol	r	-0.095	0.219	0.145	0.185	**-0.481***	**-0.600***	**-0.583***	**-0.601***
(mg/day)	p	0.538	0.152	0.348	0.229	**0.001**	**0.000**	**0.000**	**0.000**
Vitamin A (mcg/day)	r	0.172	0.087	-0.201	0.244	**0.628***	**0.660***	**-0.576***	**0.681***
		FFQ AO	**Plasma TAS**	**Plasma TOS**	**Dietary AO**	**FFQ AO**	**Plasma TAS**	**Plasma TOS**	**Dietary AO**
	p	0.263	0.576	0.192	0.111	**0.000**	**0.000**	**0.000**	**0.000**
Vitamin E (mg/day)	r	0.044	0.289	-0.190	**0.338***	**0.463***	**0.577***	**-0.523***	**0.608***
	p	0.775	0.057	0.216	**0.025**	**0.001**	**0.000**	**0.000**	**0.000**
Niacin (mg/day)	r	-0.001	-0.282	-0.147	-0.112	**0.593***	**0.598***	**-0.493***	**0.680***
	p	0.995	0.064	0.342	0.470	**0.000**	**0.000**	**0.001**	**0.000**
Thiamin (mg/day)	r	0.032	**0.309***	-0.180	-0.196	**0.511***	**0.663***	**-0.612***	**0.709***
	p	0.835	**0.041**	0.241	0.203	**0.000**	**0.000**	**0.000**	**0.000**
Riboflavin (mg/day)	r	0.014	**0.356***	-0.255	-0.227	**0.566***	**0.550***	**-0.459***	**0.627***
	p	0.927	**0.018**	0.095	0.138	**0.000**	**0.000**	**0.002**	**0.000**
Vitamin C (mg/day)	r	0.040	**0.435***	**-0.321***	**0.441***	**0.640***	**0.767***	**-0.695***	**0.797***
	p	0.798	**0.003**	**0.034**	**0.003**	**0.000**	**0.000**	**0.000**	**0.000**
Sodium (mg/day)	r	0.066	0.176	0.085	0.041	**-0.400***	**-0.610***	**-0.631***	**-0.570***
	p	0.670	0.252	0.583	0.791	**0.006**	**0.000**	**0.000**	**0.000**
Potassium (mg/day)	r	0.091	-0.125	-0.022	-0.011	**0.530***	**0.553***	**-0.477***	**0.585***
	p	0.559	0.420	0.886	0.945	**0.000**	**0.000**	**0.001**	**0.000**
Magnesium (mg/day)	r	-0.047	**0.384***	-0.228	-0.264	**0.475***	**0.408***	**-0.330***	**0.445****
	p	0.762	**0.010**	0.137	0.084	**0.001**	**0.005**	**0.027**	**0.002**
Iron (mg/day)	r	0.271	**0.301***	-0.162	**0.459***	**0.571***	**0.616***	**-0.553***	**0.626***
	p	0.075	**0.047**	0.293	**0.002**	**0.000**	**0.000**	**0.000**	**0.000**
Zinc (mg/day)	r	0.064	**0.418***	-0.249	0.227	0.263	0.177	0.086	0.238
	p	0.680	**0.005**	0.103	0.138	0.081	0.244	0.575	0.115
Daily fruit consumption	r	0.459	0.175	0.062	-0.073	**0.787***	**0.737***	**-0.744***	**0.746***
		FFQ AO	**Plasma TAS**	**Plasma TOS**	**Dietary AO**	**FFQ AO**	**Plasma TAS**	**Plasma TOS**	**Dietary AO**
	p	0.002	0.257	0.687	0.640	**0.000**	**0.000**	**0.000**	**0.000**
Daily vegetable	r	0.629	-0.046	-0.034	-0.140	**0.806***	**0.649***	**-0.597***	**0.619***
consumption	p	0.000	0.767	0.828	0.363	**0.000**	**0.000**	**0.000**	**0.000**
Daily grain consumption	r	0.345	-0.185	-0.036	-0.245	0.111	-0.093	0.066	-0.044
	p	0.022	0.230	0.815	0.108	0.449	0.543	0.666	0.774
Daily meat and meat	r	0.015	-0.017	-0.043	0.075	**0.479***	**0.433***	**0.425***	**0.452***
products consumption	p	0.925	0.912	0.784	0.630	**0.001**	**0.003**	**0.004**	**0.002**
Daily dairy products	r	0.386	-0.023	-0.062	-0.193	**0.463***	**0.333***	**0.339***	**0.331***
consumption	p	0.010	0.884	0.689	0.209	**0.001**	**0.026**	**0.023**	**0.026**

Table 8 (continued)

		Case Group				Control Group			
Daily fat consumption	r	-0.156	**-0.298**	-0.029	-0.126	**0.558***	**0.551***	**0.644***	**0.529***
	p	0.311	**0.050**	0.853	0.416	**0.000**	**0.000**	**0.000**	**0.000**

TAS: Total Antioxidant Status; TOS: Total Oxidant Status; Dietary AO: Antioxidant amount from food record; FFQ AO: Antioxidant amount from food frequency questionnaire

*Spearman correlations; $p < 0.05$

Table 9 Data of dietary antioxidant consumption from some specific food groups

Antioxidant content (mg)	Case Group	Control Group	U	*p*
Animal foods	0.13±0.57	0,14±0.1	-0.309	0,758
Green leafy vegetables	0.95±0.52	1,33±0.59	**-3.189**	**0,002***
Root vegetables	0.4±0.38	0,56±0.43	-1.881	0,063
Other vegetables	1,38±1.47	1,54±1.46	-0.519	0,605
Orange fruits	1,51±1.69	2,2±1.2	**-2.190**	**0,031***
Red fruits	1,11±1.66	1,5±1.42	-1.182	0,24
Other fruits	1,56±2.01	1,75±1.12	-0.546	0,587

*Mann-Whitney U; $p < 0.05$

However, this study also has some limitations, the relatively small sample size limits the generalizability of the findings to a broader population of asthma patients, which is due to the inclusion of a specific asthma group. Secondly, the cross-sectional nature of the study restricts our ability to infer causal relationships. Future longitudinal studies would be beneficial in examining the directionality and long-term effects of nutritional status on antioxidant status in severe asthma patients. Another limitation of this study is the relatively wide age range of participants. Age-related physiological changes and continuous exposure to oxidative stress may cause antioxidant capacity to fluctuate, which could have affected the outcomes. A more age-homogeneous sample for age-related effects would be useful in future research. For gender distribution, even if that may be evaluated as one of the limitations of this study, this reflects known epidemiological trends in asthma prevalence that the female gender has a higher prevalence than the male gender (9.6% versus 6.3%, respectively) and women are three times more likely than men to be hospitalized for an asthma-related event compared to men [48, 49]. This may be the reason for reaching out to more female patients with severe asthma for this study. Lastly, since the study focused exclusively on severe asthma patients, the findings may not be applicable to individuals with other forms of asthma or those without asthma, suggesting the need for further research across different populations.

Conclusion

The literature and our findings indicate that the both dietary and plasma TAS scores of severe asthma patients are lower than those of healthy individuals. In this study, a high total antioxidant concentration in consumed foods was shown to positively affect the plasma TAS and may be important for the control of asthma. The low frequency and amount of antioxidant-rich food intake in individuals with severe asthma negatively affect the TAS-TOS. In line with these results, both the dietary and plasma TAS-TOS plays an important role in determining asthma severity and symptoms. The results underscore the importance of addressing nutritional factors in asthma management and provide a foundation for future research aimed at exploring potential therapeutic interventions targeting antioxidant pathways in asthma care. Increasing the consumption of antioxidant-rich foods, especially vegetables and fruits, may be recommended to reduce inflammation and inflammation-related symptoms in the pathogenesis of asthma and to improve respiratory function.

Abbreviations

ACT	Asthma Control Test
BMI	Body Mass Index
FFM	Fat-Free Mass
FFQ	Food Frequency Questionnaire
GINA	Global Initiative for Asthma
IL	Interleukin
IFN-γ	Interferon-gamma
RDA	Recommended Dietary Allowance
ROS	Reactive Oxygen Species
TAS	Total Antioxidant Status
TGF-β	Transforming growth factor beta
TNF-α	Tumor Necrosis Factor Alpha
TOS	Total Oxidant Status
TUBER	Nutrition Guideline for Turkey

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Author contributions

Merve Terzi: Conceptualization, Methodology, Formal analysis, Investigation, Resources, Data Curation, Writing - Original Draft, Writing - Review & Editing, Visualizationİsmet Bulut: Conceptualization, Methodology, Resources, SupervisionTuğçe Yakut: Methodology, Resources, Data CurationFatma Esra Güneş: conceptualization, methodology, writing - original draft, writing - review & editing, supervision, project administration.

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Data availability

Data supporting the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

This study was a cross-sectional non-invasive study, and all participants provided writte informed consent, adhering to the principles of the Helsinki Declaration. The Clinical Research Ethics Committee of Marmara University Faculty of Medicine was approved this study (approval number: 09.2018.680).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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