Al-Mustansiriyah Journal of Science
ISSN: 1814-635X (print) 2521-3520 (electronic)

ORIGINAL ARTICLE OPEN ACCESS

The Correlation between Oxidative Stress and Asthma Control Test in Iraqi Asthmatic Patients

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ARTICLE INFO
Received: June 24, 2023
Revised: November 10, 2023
Accepted: November 18, 2023
Published: December 30, 2024

ABSTRACT: ***Background:*** *Asthma is a chronic disease of the airway tract, which can be triggered due to inflammatory and non-inflammatory events. Recently, the prevalence of asthma has reached a significant rate globally. Asthmatic patients have shown significant disturbance in the redox balance, resulting in oxidative stress.* ***Objective:*** *We have aimed to discover the relationship between the severity of asthma and oxidative stress by evaluating several indicators of oxidative stress in asthmatic patients with different degrees of control.* ***Methods:*** *60 diagnosed patients with asthma were enrolled in this study in the overweight category and age range from 18 to 60 years old.* ***Results:*** *The levels of malondialdehyde (MDA), total oxidant status (TOS), and oxidative stress index (OSI) were observed to be significantly higher in asthmatic patients. Moreover, patients with poor asthma control have shown the highest levels of MDA, TOS, and OSI compared to those with good and moderate control of the disease. On the contrary, asthmatic patients have shown significantly lower levels of total antioxidant capacity (TAC) compared to control, where the lowest levels of TAC were observed in poor controlled asthmatic patients compared to those with good and moderate control of the disease. Additionally, a correlation between MDA, TOS, OSI, and the asthma control test (ACT) was observed in an inversely manner, while TAC and ACT were correlated in a positively manner.* ***Conclusions:*** *Oxidative stress has shown significant involvement in the progression of asthma.*

KEYWORDS: *Asthma; Malondialdehyde; TOS; TAC; Oxidative Stress*

INTRODUCTION

Asthma is a chronic disease of the airway tract, which can be triggered due to inflammatory [1] and non-inflammatory events [2]. Asthma is a non-communicable disease that affects individuals worldwide and has severe detrimental consequences on both adolescent and adult health, including significant morbidity and, in severe cases, mortality [3]. In 2020, it was reported that over 300 million individuals globally, including 25 million Americans, suffer from asthma, a varied medical condition. It is the most prevalent chronic ailment of childhood, impacting 6.4 million kids in the USA and children globally. Asthma incidence, severity, and fatalities vary around the world [4]. A record of respiratory problems such as “wheeze, difficulty of breathing, tightness in the chest, and cough those changes across time and magnitude, with fluctuating expiratory airflow limitation” is what is used to identify asthma. The occurrence of several respiratory symptoms, an increase of the symptoms at night, and an aggravation of the symptoms by a viral ailment, physical activity, allergens, weather fluctuations, or smoking are all necessary for the diagnosis of asthma [5].

Asthma triggers local and systematic inflammatory events [6], whereby can cause an advancement of oxidative stress [7]. The latter is a consequence of elevated free radicals/reactive oxygen species (ROS) corresponding to the insufficient capacity of antioxidants to neutralize and detoxify the effects of that species [8], [9]. The toxic effects are seen in the form of oxidative damage to the cellular macromolecules (proteins, nucleic acids, and lipids) [10]. Malondialdehyde (MDA) is one metabolite of the lipid peroxidation process, that is used widely for the detection of oxidative stress by the lipid peroxidation pathway [11], [12]. Because oxidative stress plays a role in the emergence and advancement of a number of clinical disorders, it has been connected to human mortality and morbidity [13]. Several studies have reported a rise of oxidative stress in asthmatic patients, due to elevated ROS, or diminished antioxidants [14]–[16]. In this work, we have attempted to indicate the link between the severity of asthma and oxidative stress by evaluating the serum levels of MDA, total oxidant status (TOS), total antioxidant capacity (TAC), and oxidative stress index (OSI) in people with different control of asthma symptoms.

MATERIALS AND METHODS

Subjects

This work included sixty people who were already diagnosed with asthma from the Specialist Center for Allergy (Al-Rusafa, Baghdad). The asthmatic patients were at an age range between 18 and 60 years old, divided equally to males and females. Moreover, another sixty people were enrolled in the study as healthy controls. All of the participants were informed about the criteria and aims of the study, and they agreed to become a part of the research. The subjects were collected from August 2022 to January 2023.

Methods

The body mass index (BMI) of each participant was calculated by taking weight in kg and height in m^2 as parameters of the mathematical formula [17]. The asthma control test (ACT) value was applied to each asthmatic patient to predict their condition. The ACT was based on five questions directed to the patient, each of which has points from one to five, the sum of all points represents the ACT value of each patient, where 25 points represent good control of asthma, from 20 to 24 point represents moderate control of asthma, and <20 point represents poor control of asthma [18].

This research aimed to establish the amounts of MDA, TOS, TAC, and OSI as oxidative stress markers. All of these were identified using spectrophotometric techniques, except OSI, which was determined via the following calculation:

$$OSI(aribatry\ unit) = \frac{TOS}{TAC} \tag{1}$$

MDA was evaluated according to Stocks and Dormandy [19], where thiobarbituric acid was used as a reagent to react with the MDA present in the serum, giving a colored solution that can be measured at 532 nm. On the other hand, TOS was evaluated by using the Erel method, where its level was assessed relative to hydrogen peroxide standard solution (µmol H_2O_2 Eq/L). TAC level was evaluated according to the Erel method, where its level was assessed relative to vitamin C standard solution (µmol vitamin C Eq/L) [20].

Statistical Analyses

The data collected from the experimental part of the study were analyzed statistically by using the Statistical Package for Social Sciences (SPSS) program version 26.0 to evaluate the mean comparison between asthmatic patients and control using independent sample t-test, and the comparison of means among the asthmatic patients at different ACT categories. Moreover, the correlations were evaluated in asthmatic patients by using Pearson's coefficient.

RESULTS AND DISCUSSION

Table 1 shows the age, BMI, and asthma score test of those who participated in this study. The mean age of patients with asthma (39.68±11.62 years) and the control group (39.23±14.88 years) was comparable, with no statistically significant differences (p>0.05). The BMI of patients with asthma (28.10±4.36 kg.m^{-2}) and the control group (27.83±4.08 kg.m^{-2}) were comparable, with no significant differences (p>0.05).

Table 1. Anthropometric parameters of asthmatic patients and control

Parameters	Control	Asthma patients	*p*-value
Number	60	60	-
Age (year)	39.23±14.88	39.68±11.62	0.885
BMI (kg.m^{-2})	27.83±4.08	28.10±4.36	0.776
ACT	-	15.53±4.44	-

As indicated in Figure 1, the average number of asthma control tests performed for patients with asthma was in the poor controlled asthmatic patients' category (15.53±4.44), owing to the vast majority of poor-controlled asthmatic individuals in the asthma group that was gathered in the present investigation.

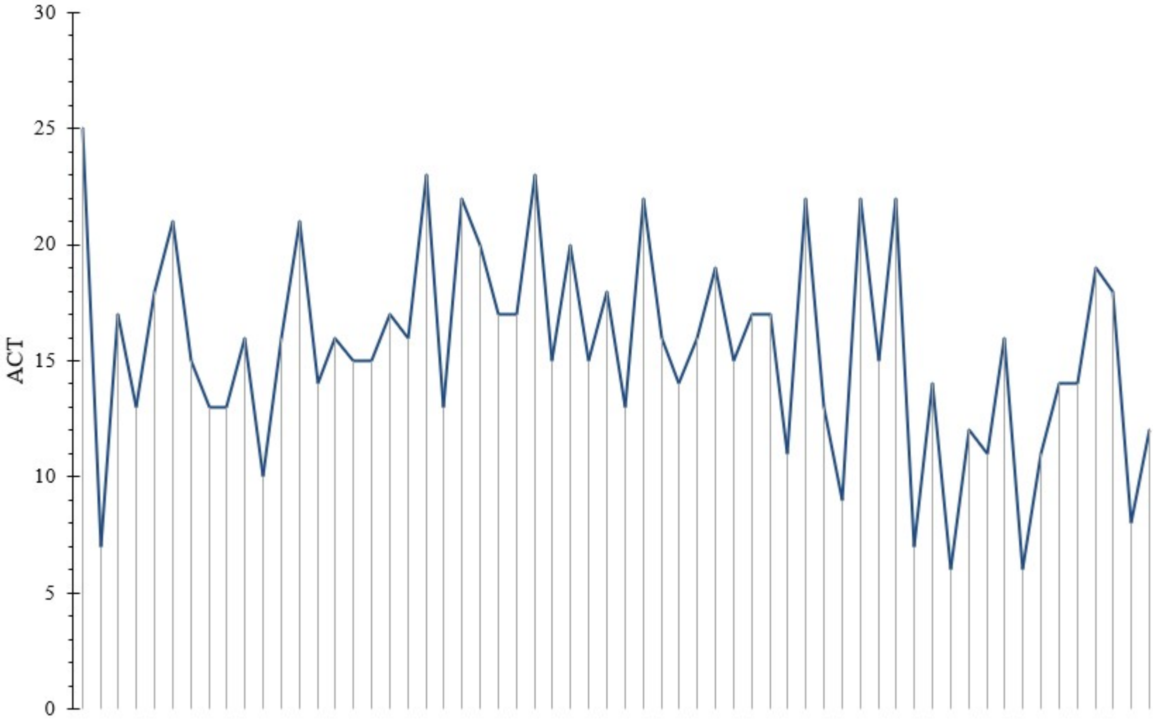

Figure 1. ACT distribution diagram for the Sixty asthmatic individuals included in this research

Table 2 compares the mean age along with BMI of those with asthma based on their ACT classification. Owing to their ACT significance, age differences across people with asthma were insignificant ($p>0.05$). The age of the completely controlled patients was 35.00±0.00 years, 40.73±16.84 years for the well-controlled patients, and 39.54±10.48 years for the poorly controlled patients. Owing to their ACT significance, the variations in BMI across those with asthma were insignificant ($p>0.05$). The BMI of a completely controlled patient was 29.38±0.00 kg.m^{-2}, that of a well-controlled patient was 26.35±3.75 kg.m^{-2}, and that of a poorly controlled patient was 28.47±4.47 kg.m^{-2}.

Table 2. According to the ACT, the age and BMI of individuals with asthma

Parameters	Totally controlled patients	Good controlled patients	Poorly controlled patients	*p*-value
Number	1	11	48	-
Age(year)	35.00±0.00	40.73±16.84	39.54±10.48	0.882
BMI (Kg.m^{-2})	29.38±0.00	26.35±3.75	28.47±4.47	0.338

MDA, TOS, TAC, and OSI values are shown in Table 3 as mean and standard deviation. MDA levels in people with asthma were substantially higher ($p<0.05$) (13.23±3.86 µmol/L) than in controls

(7.75±2.99 µmol/L). TOS levels were considerably higher ($p<0.05$) in asthmatic patients (13.26±5.34 µmol H_2O_2 Eq/L) compared to controls (6.26±2.75 µmol H_2O_2 Eq/L). TAC levels were considerably lower ($p<0.05$) in asthmatic patients (1.13±0.444 µmol Vit C Eq/L) in comparison with controls (1.85±0.44 µmol Vit C Eq/L). The average score of OSI in people with asthma (14.12±8.5) was considerably higher ($p<0.05$) than in controls (3.5±1.5).

Table 3. Spectrum of oxidative stress indicators in asthmatic patients and healthy individuals

Parameters	Control	Asthma patients	*p*-value
MDA (µmol/L)	7.75±2.99	13.23±3.86	<0.001
TOS (µmol H_2O_2 Eq/L)	6.26±2.75	13.26±5.34	<0.001
TAC (µmol Vit C Eq/L)	1.85±0.44	1.13±0.44	<0.001
OSI (arbitrary unit)	3.5±1.5	14.12±8.6	<0.001

In Table 4, the levels of oxidative stress biomarkers in asthmatic patients according to their ACT values are shown. The level of MDA was non-significantly ($p>0.05$) different in asthmatic patients according to their ACT value. The MDA level obtained for totally controlled asthmatic patients was 11.22±0.00 µmol/L, in good controlled patients, was 12.58±3.13 µmol/L, and in poorly controlled patients was 13.42±4.05 µmol/L. The level of TOS was increased significantly ($p<0.05$) in asthmatic patients according to their ACT values. Asthmatic patients with good control have shown the lowest TOS level (7.53±0.00 µmol H_2O_2 Eq/L), whereas the asthmatic patients with good control have shown the middle TOS level (8.01±1.51 µmol H_2O_2 Eq/L), and the asthmatic patients with poor control have shown the highest level of TOS (14.59±5.13 µmol H_2O_2 Eq/L). The level of TAC was increased significantly ($p<0.05$) in asthmatic patients according to their ACT values. Asthmatic patients with good control have shown the highest TAC level (2.15±0.00µmol Vit C Eq/L), where the asthmatic patients with good control have shown the middle TAC level (1.60±0.23 Vit C H_2O_2 Eq/L), and the asthmatic patients with poor control have shown the lowest level of TAC (1.01±0.39 µmol Vit C /L). The level of OSI was increased significantly ($p<0.05$) in asthmatic patients according to their ACT values. Asthmatic patients with good control have shown the highest OSI level (3.05±0.00), where the asthmatic patients with good control have shown the middle OSI level (5.14±1.48), and the asthmatic patients with poor control have shown the lowest level of OSI (16.41±8.10).

Table 4. Oxidative stress indicators of asthmatic patients according to the ACT

Parameters	Totally controlled patients	Good controlled patients	Poor controlled patients	*p*-value
MDA (µmol/L)	11.22±0.00	12.58±3.13	13.42±4.05	0.712
TOS (µmol H_2O_2 Eq/L)	7.53±0.00	8.01±1.51	14.59±5.13	<0.001
TAC (µmol Vit C Eq/L)	2.15±0.00	1.60±0.23	1.01±0.39	<0.001
OSI (arbitrary unit)	3.05±0.00	5.14±1.48	16.41±8.10	<0.001

Sharma *et al.* discovered a substantial rise in blood MDA levels in broncho asthma patients in comparison to individuals in good health. The researchers reported a drop in MDA blood levels in people with asthma two days after the attack, although the level remained greater than in healthy persons [21]. Fatani's study assessed the effects of oxidative stress in individuals with acute and chronic asthma. He found that chronic asthma patients had much greater levels of MDA than those with short-term symptoms and control. TAC and GSH, on the other hand, were lower in chronic asthma individuals, suggesting a change in the redox state associated with asthma [22]. Ahmed *et al.* discovered that asthma patients had significantly larger amounts of blood MDA and carbonyl protein than healthy persons. Furthermore, erythrocytic SOD, GPx, and CAT activities were lowered in asthmatic individuals. Furthermore, MDA levels were substantially greater in severe patients *vs* moderately and mild patients. As a result, damage from oxidation was seen as a component of disease development [23]. Karadogan *et al.* found that allergic asthma patients had significantly higher levels of MDA and carbonyl protein than healthy subjects. Furthermore, they discovered a substantial rise in the concentration of MDA with a drop in ACT value in patients [24]. This is substantially supported by present oxidative stress findings, which point to a significant role of oxidative stress in the pathogenesis of asthma. Abboud *et al.* found that asthmatic patients' blood and salivary MDA levels were significantly higher than in healthy persons. They proposed using salivary MDA levels for assessing the oxidative state of asthmatic children [25]. Özkan *et al.* found a large rise in TOS and a substantial reduction in TAC in asthmatic children in comparison to healthy children [26].

Asthmatic individuals had a substantial positive link between MDA and BMI, whereas TOS levels demonstrated a negative correlation with TAC, a positive correlation with OSI, and a negative correlation with ACT value. Moreover, TAC has shown a negative correlation with the OSI, and positive correlation with the ACT value, whereas the OSI has shown a negative correlation with the ACT value, as shown in Table 5. The negative correlation of ACT with TOS and OSI, and the positive correlation of ACT with TAC represent a significant involvement of oxidative stress in the deterioration of health control in asthma patients.

Table 5. The correlation in asthmatic patients of this study

Parameters	**MDA**		**TOS**		**TAC**		**OSI**	
	r	*p*	r	*p*	r	*p*	r	*p*
MDA	-	-	- 0.052	0.695	- 0.061	0.645	- 0.034	0.795
TOS	- 0.052	0.695	-	-	- 0.434*	0.001	0.840*	0.001
TAC	- 0.061	0.645	- 0.434*	0.001	-	-	- 0.735*	0.001
OSI	- 0.034	0.795	- 0.840*	0.001	- 0.735*	0.001	-	-
Age	0.042	0.752	0.041	0.755	- 0.023	0.863	0.001	0.995
BMI	0.268*	0.038	0.200	0.125	0.008	0.952	0.094	0.474
ACT	0.053	0.686	- 0.441*	0.001	0.552*	0.001	- 0.597*	0.001

* *P*<0

CONCLUSION

The results have indicated a quite relationship between the status of asthmatic patients and oxidative stress, which can be useful in predicting the health condition of patients and to interevent health deterioration through balancing the redox system in asthma patients. This disturbance of oxidative balance can lead to further health deterioration such as cardiovascular and metabolic disorders.

SUPPLEMENTARY MATERIAL

None.

AUTHOR CONTRIBUTIONS

Yousif Nadhim Abbas: Writing—review and editing. Mustafa Taha Mohammed: Conceptualization, methodology, and supervision. Nisred K. Klichkhanov: Investigation and validation.

FUNDING

None.

DATA AVAILABILITY STATEMENT

None.

ACKNOWLEDGMENTS

The Department of Chemistry, College of Science, Mustansiriyah University has been accommodating and unwinding the criteria for this work, therefore the authors of this paper are interested in expressing appreciation for that.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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