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Original Article

Role of oxidative stress and serum lipid levels in stable chronic obstructive pulmonary disease

Ummugulsum Can [a,*], Fatma Humeyra Yerlikaya [b], Sebnem Yosunkaya [c]

[a] *Department of Biochemistry, Konya Education and Research Hospital, Konya, Turkey*
[b] *Department of Biochemistry, Meram Faculty of Medicine, University of Necmettin Erbakan, Konya, Turkey*
[c] *Department of Chest Diseases, Meram Faculty of Medicine, University of Necmettin Erbakan, Konya, Turkey*

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Abstract

Background: Chronic obstructive pulmonary disease (COPD) has been associated with increased oxidative stress or reduced antioxidant resources. The main goal of this study was to evaluate the levels of serum ischemia-modified albumin (IMA), oxidized low-density lipoprotein (ox-LDL), total oxidant status (TOS), and total antioxidant status in patients with stable COPD, compared with a control group.
Methods: This study was performed on 51 patients with stable COPD (42 men and 9 women; mean age 56.92 ± 3.0 years) and 45 healthy control participants (32 men and 13 women; 54.8 ± 3.8 years). The levels of serum lipids, IMA, total antioxidant status, TOS, and ox-LDL were measured in all participants.
Results: The levels of serum IMA, ox-LDL, and TOS were significantly higher in patients with COPD than those in control individuals. There was no difference between the levels of serum total antioxidant status, triglycerides, total cholesterol, and low-density lipoprotein cholesterol (LDL-C) of patients with COPD and those of control individuals. Serum high-density lipoprotein cholesterol levels were significantly lower in patients with COPD than in control individuals.
Conclusion: Our study indicated that serum IMA, ox-LDL, and TOS may be increased as a result of chronic hypoxia, inflammation, and oxidative stress in patients with severe and very severe stable COPD. Our findings also revealed that IMA is higher in patients with Global Initiative for Chronic Obstructive Lung Disease Stages II, III, and IV, while TOS and ox-LDL are higher in patients with Global Initiative for Chronic Obstructive Lung Disease Stage IV. Measurements of serum IMA, TOS, and ox-LDL levels may be useful markers in the evaluation of stable COPD.

Keywords: chronic obstructive pulmonary disease; ischemia-modified albumin; oxidative stress; oxidized low-density lipoprotein; total oxidant status

1. Introduction

Chronic obstructive pulmonary disease (COPD) is a preventable and treatable disease characterized by generally progressive and not completely reversible airflow limitation that is associated with an abnormal inflammatory response of the lungs to noxious particles or gases.[1,2]

Oxidative stress is related to an imbalance between the increased production of reactive oxygen species (ROS) and reactive nitrogen species (RNS), and reduced antioxidant capacity.[3,4] The pathogenesis in COPD includes disturbed oxidant–antioxidant and proteinase–antiproteinase balances.[5] Lungs are continuously subject to oxidants, arising either endogenously by metabolic reactions (e.g., from mitochondrial electron transport during respiration or activation of phagocytes) or exogenously from air pollutants or cigarette

Conflicts of interest: The authors declare that there are no conflicts of interest related to the subject matter or materials discussed in this article.

* Corresponding author. Dr. Ummugulsum Can, Konya Eğitim Araştırma Hastanesi, Hacışaban Mahallesi, Yeni Meram Caddesi, 74 Karatay, Konya, Turkey.
E-mail address: cangulsum@yahoo.com (U. Can).

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smoke.[4,6] Air pollutant-generated lung inflammation is characterized by the activation of inflammatory cells, including neutrophils, alveolar macrophages, monocytes, and epithelial and endothelial cells, releasing ROS and RNS, which can increase inflammation and tissue damage.[2,7] It has been observed that ROS may damage proteins, DNA, and lipids, and may cause lung injuries.[1] Furthermore, ROS and RNS can act on proteins to cause nitration and oxidation of peptides, bond cleavage, or amino acid side chain modifications. The levels of nitrated proteins (fibrinogen, transferrin, plasminogen, and ceruloplasmin) are increased in smokers.[3,6,7]

The amino terminal end (N-terminal) of albumin molecules is connected to transitional metals such as cobalt, copper, and nickel.[8] Under acute ischemic conditions, the N terminus of albumin is changed, possibly as a result of hypoxia, acidosis, or free-radical injury. The metal-binding capacity of albumin is then reduced. Ischemia-modified albumin (IMA) is increased in most patients with cardiac ischemia, liver cirrhosis, acute infections, advanced cancers, brain ischemia (stroke), and end-stage renal disease.[9]

Oxidized low-density lipoprotein (ox-LDL) is generated during oxidative stress and increases the production of ROS.[10] It accumulates in macrophages and other cell types at the site of chronic inflammation.[10,11] Additionally, ox-LDL can induce atherosclerotic plaque formation and progression, matrix degradation, endothelial cell apoptosis, and the secretion of matrix metalloproteinases, mediating the degradation of protein components of the extracellular matrix and of basement membranes in target cells.[10,12]

There exists an excessively abundant number of ROS radicals, such as superoxide anion, hydroxyl, alkyl, alkoxyl, peroxyl, and semiquinone radicals, and RNS radicals, such as nitric oxide and nitrogen dioxide, which include phenols and quinines. However, separately measuring different oxidant species is time consuming, costly, and impractical, and because their oxidant effects are additive, evaluation of total oxidant status (TOS) is therefore more practical.[13] In our study, TOS was measured in relation to the cumulative oxidative effects of various oxidants. Total antioxidant status (TAS) was also measured to evaluate the efficiency of all antioxidants, such as superoxide dismutase, glutathione peroxidase, glutathione reductase, and catalase, as well as nonenzyme antioxidant molecules including glutathione, uric acid, melatonin, vitamins A, C, and E, ferritin, transferrin, and ceruloplasmin.

The aim of our study was to evaluate pulmonary oxidative stress parameters such as IMA, TOS, and ox-LDL in patients with stable COPD and in a control group. However, more recent studies have failed to find a significant relationship between plasma oxidant and antioxidant capacities, and pulmonary function in patients with COPD. To the best of our knowledge, there are no studies evaluating the relationship between serum IMA and COPD. The aim of our study was to investigate whether IMA and ox-LDL levels are related to the pathogenesis of COPD. IMA and ox-LDL levels were also evaluated in patients and control groups in order to define the level of pulmonary oxidative stress.

2. Methods

2.1. Participants

This study was performed on 51 COPD patients (42 men and 9 women), aged 35−75 years (mean 56.92 ± 3.0 years), and 45 healthy control individuals (32 men and 13 women), aged 35−75 years (mean 54.8 ± 3.8 years). Patients with stable COPD who were admitted to the outpatient clinic of Meram Medical School of Necmettin Erbakan University in Konya, Turkey, between November 2012 and September 2013 were included in the study. A diagnosis of COPD was established based on the medical history and spirometric data [forced expiratory volume in 1 second (FEV1)/forced vital capacity (FVC) ratio <0.7] of patients. All patients with COPD had at least Global Initiative for Chronic Obstructive Lung Disease (GOLD) Stages II, III, and IV of COPD. Control individuals with normal spirometry and no infectious or inflammatory diseases were matched with patients in terms of age, sex, body mass index (BMI), and smoking history (pack-years). Control individuals were volunteers recruited from the hospital staff. Healthy control participants were fully examined by a chest physician and excluded if they had lung impairment, cardiovascular diseases, diabetes mellitus (DM) or other diseases, or a history of use of any medicine and vitamins for the prior 3 months.

Those with no exacerbations due to any reason in the prior 8 weeks; no changes in respiratory medication on a standard treatment regimen consisting of inhaled corticosteroids, N-acetylcysteine (NAC), and beta adrenergic agonists; and the absence of infection were included in the study, who constituted the patient group. Patients with COPD were current smokers or exsmokers with at least 10 pack-years. Those with malignant disease, systemic inflammatory disease, chronic gastrointestinal disease, another lung disease, hypertension, cardiovascular disease, and COPD exacerbations, such as an increase in cough, sputum production, and worsening of dyspnea or sputum purulence within the prior 8 weeks, and those treated with oral corticosteroids or any medication apart from COPD maintenance therapy or immunosuppressors for any reason within the prior 3 months were excluded. The study was approved by the local ethics committee (no. 2012/70). All participants were informed about the design, and written consents were obtained.

2.2. Body composition

BMI was calculated as weight divided by the square of the height (kg/m^2).

2.3. Pulmonary function testing

The stages of COPD were determined using GOLD criteria 2012[14]: GOLD II (moderate), FEV1/FVC <70%, FEV1 <80% and ≥50%; GOLD III (severe), FEV1/FVC <70%, FEV1 <50% and ≥30%; and GOLD IV (very severe): FEV1/FVC <70%, FEV1 <30%. FEV1, FVC, FEV1/FVC

were measured according to the American Thoracic Society criteria. FEV1 was measured 20 minutes after the administration of 400 μg of albuterol through a metered-dose inhaler. Spirometry was performed using a Sensor Medics VMax 22 Respiratory Analyzer (SensorMedics Corporation, Yorba Linda, CA, USA). According to the GOLD criteria, the severity of COPD was as follows: 19 patients were in GOLD Stage II, 17 in GOLD Stage III, and 15 in GOLD Stage IV.

2.4. Laboratory methods

Blood samples were obtained from stable-phase COPD patients and healthy control participants. Fasting peripheral blood was collected in empty vacuum tubes after overnight fasting (8 hours) and serum samples were obtained after suitable centrifugation. The samples were stored frozen at −80°C until the day of analysis of serum IMA, TAS, TOS, and ox-LDL levels. Thereafter, serum triglycerides, total cholesterol (total-C), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) levels were measured immediately.

Arterial oxygen and carbon dioxide tensions (pO_2 and pCO_2) were analyzed using a blood gas analyzer. For arterial blood gas analysis, blood was drawn from the brachial artery using a dedicated preheparinized blood sampler, while the patients were breathing room air, and studied with a blood gas analyzer (ABL 700 series; Radiometer, Copenhagen, Denmark).

2.5. Biochemical analyses

2.5.1. Measurement of TAS

We determined serum TAS level using an automated measurement method based on the bleaching of the characteristic color of a more stable 2,2′-azino-bis(3-ethylbenzthiazoline 6-sulfonic acid) radical cation by antioxidants.[15] The results were expressed in mmol Trolox equivalents/L.

2.5.2. Measurement of TOS

Serum TOS level was determined using a novel automated measurement method.[16] Oxidants present in the sample oxidize the ferrous ion-o-dianisidine complex to ferric ion. The oxidation reaction is enhanced by glycerol molecules, abundantly present in the reaction medium. The ferric ion makes a colored complex with xylenol orange in an acidic medium. The color intensity, which can be measured spectrophotometrically, is related to the total amount of oxidant molecules present in the sample. The assay is calibrated with hydrogen peroxide, and the results are expressed in terms of micromolar hydrogen peroxide (H_2O_2) equivalents per liter (μmol H_2O_2 equiv./L).

2.5.3. Measurement of IMA levels

The IMA level was measured using a colorimetric assay based on the measurement of unbound cobalt after incubation with patients' serum, developed by Bar-Or et al.[17] Increased amounts of IMA result in reduced cobalt binding, consequently increasing the levels of residual unbound cobalt available for the formation of complexes with a chromogen [dithiothreitol (DDT)], which can be measured photometrically. The procedure was as follows: 50 μL of 0.1% cobalt chloride was added to 200 μL of serum, gently mixed, and held for 10 minutes for adequate cobalt−albumin binding. Fifty microliters of DTT, at a concentration of 1.5 mg/mL, was added as a colorizing agent, and the reaction was stopped 2 minutes later by adding 1.0 mL of 0.9% sodium chloride. The colored product was measured at 470 nm, compared with a serum-cobalt blank without DTT, and reported in absorbance units.

In our study, adjusted IMA was calculated as follows: (individual serum albumin concentration/median serum albumin concentration of the population) × IMA value in absorbance units. This formula was applied to correct IMA values for serum albumin, and the median serum albumin concentration of each group was used separately.[18]

2.5.4. Measurement of ox-LDL levels

Analysis of ox-LDL was performed on serum samples using the Mercodia ox-LDL enzyme-linked immunosorbent assay kit (Mercodia AB, Uppsala, Sweden), in accordance with the manufacturer's guidelines. Absorbance was measured at 450 nm on an ELx800 Absorbance Microplate Reader (BioTek Instruments, Inc., Winooski, VT, USA). This assay employs a quantitative sandwich enzyme immunoassay technique that measures ox-LDL, with the resulting concentration values reported in mU/L.

2.5.5. Measurement of albumin, triglyceride, total-C, HDL-C, and LDL-C levels

Serum albumin, triglycerides, total-C, HDL-C, and LDL-C levels were measured using commercially available kits, based on routine methods, on the Architect C 8000 System (Abbott Laboratories, Abbott Park, IL, USA).

2.6. Statistical analysis

All the data are expressed as mean ± standard deviation. Statistical analyses were performed using SPSS version 16.0 (SPSS Inc., Chicago, IL, USA). To compare the ratio of categorical variables, we used the Chi-square test [sex (female/male) and smoking status]. Normality of the variables was evaluated using the one-sample Kolmogorov−Smirnov test. Normal distributions of variables were examined using the independent samples t test, and non-normally distributed variables were examined using the Mann−Whitney U test. Groups of data were compared with an analysis of variance followed by Tukey's multiple comparison tests. A multivariate analysis was used to compare mean levels of serum TAS, TOS, IMA, and ox-LDL concentrations between patients with GOLD Stages II, III, and IV and control participants. Differences were considered significant at a probability level of $p < 0.05$.

3. Results

Fifty-one (32 smokers and 19 nonsmokers) stable COPD patients and 45 (25 smokers and 20 nonsmokers) healthy control individuals were studied. Clinical and demographic characteristics of COPD patients and healthy individuals are presented in Table 1. Smoking history, smoking status, age, sex, and BMI were similar between groups.

Biochemical parameter levels in COPD patients with GOLD stages and the controls are shown in Table 3. Serum IMA levels of COPD patients were significantly higher than those of the control participants ($p = 0.001$). Patients with GOLD Stages II, III, and IV had significantly higher IMA levels than those of control individuals ($p = 0.004$, $p = 0.001$, and $p = 0.001$, respectively) (Table 3). There was a significant difference of serum IMA levels between GOLD Stages II, III, and IV in patients ($p = 0.001$) (Table 3). Serum TOS levels of patients with COPD were significantly higher than those of control individuals ($p = 0.042$) (Table 2). Patients with GOLD Stage IV had significantly higher serum TOS levels, compared with those of control individuals ($p = 0.042$) (Table 3). A significant difference of serum TOS levels was also detected between GOLD Stages II, III, and IV in patients ($p = 0.045$) (Table 3).

There was no difference between serum TAS levels of COPD patients and control individuals ($p = 0.137$) (Table 2). Serum ox-LDL levels of COPD patients were significantly higher than those of control participants ($p = 0.034$) (Table 2). Patients with GOLD Stage IV had significantly higher ox-LDL levels than those of control individuals ($p = 0.033$) (Table 3). There was no difference between serum triglycerides, total-C, and LDL-C levels of COPD patients and control individuals ($p = 0.429$, $p = 0.197$, and $p = 0.398$, respectively) (Table 2). Serum HDL-C levels of COPD patients were significantly lower, compared with those of control individuals ($p = 0.001$) (Table 2). Patients with GOLD Stages III and IV had significantly lower HDL-C levels than control individuals ($p = 0.040$ and $p = 0.035$, respectively) (Table 3). There was a significant difference between serum HDL-C levels of patients with GOLD Stages II, III, and IV ($p = 0.010$) (Table 3). No difference was observed between serum ox-LDL, TAS, serum triglycerides, total-C, and LDL-C levels of patients with GOLD Stages II, III, and IV ($p = 0.053$, $p = 0.137$, $p = 0.789$, $p = 0.437$, and $p = 0.758$, respectively) (Table 3).

In multivariate analysis, when comparing patients with GOLD Stages II, III, and IV with control individuals, a significant difference was found with respect to IMA levels ($p = 0.001$, $p = 0.001$, and $p = 0.001$, respectively). Patients with GOLD Stages II, III, and IV showed a significant difference with respect to ox-LDL levels, compared to control individuals ($p = 0.516$, $p = 0.165$, and $p = 0.002$, respectively). Given TAS and TOS levels in patients with GOLD Stages II, III, and IV, we also found a significant difference from those of the control individuals ($p = 0.224$, $p = 0.119$, and $p = 0.040$; and $p = 0.283$, $p = 0.807$, and $p = 0.008$, respectively).

Table 1
Clinical and demographic characteristics of patient and control groups.

	Control individuals $n = 45$	Stable COPD patients $n = 51$	p
Age (y)	54.8 ± 3.8	56.92 ± 3.0	0.084
Sex (male/female)	32/13	42/9	0.144
BMI (kg/m^2)	27.53 ± 3.4	28.76 ± 2.9	0.082
Disease duration (y)	—	14.88 ± 9.0	
Smoking history (pack-year)	37.85 ± 11.56	38.45 ± 17.14	0.852
Smoking status (smoker/nonsmoker)	25/20	32/19	0.220
FEV1 (%)	94.1 ± 2.3	43.97 ± 16.8	0.001
FEV1/FVC (%)	85 ± 0.8	61.73 ± 9.5	0.001
Arterial pO2 (mmHg)	92.4 ± 1.2	64.25 ± 15.3	0.001
Arterial pCO2 (mmHg)	41.3 ± 0.6	44.14 ± 8.8	0.001
GOLD Stage II		$n = 19$	
GOLD Stage III		$n = 17$	
GOLD Stage IV		$n = 15$	

All values (except GOLD stage, sex and smoking status) are mean ± standard deviations.
BMI = body mass index; COPD = chronic obstructive pulmonary disease; FEV1 = forced expiratory volume in 1 second; FVC = forced vital capacity; GOLD = Global Initiative for Chronic Obstructive Lung Disease.

Table 2
Serum and plasma biomarkers of patients and control individuals.

	Control individuals $n = 45$	Stable COPD patients $n = 51$	p
IMA (ABSU)	0.62 ± 0.26	0.98 ± 0.25	0.001
Adjusted IMA (ABSU)	0.62 ± 0.25	0.94 ± 0.31	0.001
TOS (μmol H_2O_2 equiv./L)	4.53 ± 3.81	6.51 ± 4.85	0.042
TAS (mmol Trolox equiv./L)	1.53 ± 0.14	1.59 ± 0.20	0.132
Ox-LDL (mU/L)	4.51 ± 2.05	5.91 ± 3.61	0.034
Triglycerides (mg/dL)	124.62 ± 46.32	133.39 ± 47.22	0.429
Total-C (mg/dL)	192.64 ± 33.82	181.50 ± 39.72	0.197
HDL-C (mg/dL)	44.19 ± 10.14	36.49 ± 9.60	0.001
LDL-C (mg/dL)	121.34 ± 29.43	115.16 ± 32.86	0.398

All values are mean ± standard deviation.
ABSU = absorbance units; COPD = chronic obstructive pulmonary disease; equiv. = equivalent; HDL-C = high-density lipoprotein cholesterol; IMA = ischemia modified albumin; LDL-C = low-density lipoprotein cholesterol; Ox-LDL = oxidized low-density lipoprotein; TAS = total antioxidant status; TOS = total oxidant status; Total-C = total cholesterol.

4. Discussion

Serum IMA, ox-LDL, and TOS levels were found to be elevated in patients with COPD, compared to control individuals. Serum IMA levels were significantly increased in patients with GOLD Stages II, III, and IV, compared with those of control individuals, while levels of ox-LDL and TOS were significantly increased in patients with GOLD Stage IV compared to control individuals. Additionally, a significant difference was found between serum IMA, TOS, and HDL-C levels detected in GOLD Stages II, III, and IV. To the best of our knowledge, this is the first study to examine the

Table 3
Serum and plasma biomarkers in GOLD stages of patients and control individuals.

	Control group $n = 45$	COPD patients GOLD Stage II $n = 19$	COPD patients GOLD Stage III $n = 17$	COPD patients GOLD Stage IV $n = 15$	p
IMA	0.62 ± 0.3	0.94 ± 0.4*	0.96 ± 0.2***	1.01 ± 0.2***	0.001
TOS	4.53 ± 3.8	4.99 ± 2.3	6.49 ± 4.8	8.48 ± 6.4**	0.045
TAS	1.53 ± 0.1	1.62 ± 0.3	1.62 ± 0.2	1.64 ± 0.2	0.137
Ox-LDL	4.51 ± 2.0	4.99 ± 3.0	5.57 ± 3.0	6.91 ± 4.4****	0.053
Triglycerides	124.62 ± 46.3	139.46 ± 45.4	133.00 ± 43.0	126.73 ± 57.3	0.789
Total-C	192.64 ± 33.8	178.69 ± 42.5	189.50 ± 32.9	174.64 ± 45.9	0.437
HDL-C	44.19 ± 10.1	38.55 ± 11.6	35.84 ± 8.9******	35.45 ± 9.0*****	0.010
LDL-C	121.34 ± 29.4	114.86 ± 30.8	119.16 ± 33.1	110.42 ± 37.2	0.758

All values are mean ± standard deviation.
*$p = 0.004$, compared with control group for IMA.
**$p = 0.042$, compared with control group for TOS.
***$p = 0.001$, compared with control group for IMA.
****$p = 0.033$, compared with control group for Ox-LDL.
*****$p = 0.035$, compared with control group for HDL-C.
******$p = 0.040$, compared with control group for HDL-C.
COPD = chronic obstructive pulmonary disease; GOLD = Global Initiative for Chronic Obstructive Lung Disease; HDL-C = high-density lipoprotein cholesterol; IMA = ischemia modified albumin; LDL-C = low-density lipoprotein cholesterol; Ox-LDL = oxidized low-density lipoprotein; TAS = total antioxidant status; TOS = total oxidant status; Total-C = total cholesterol.

correlations between serum IMA levels in COPD patients and indicators of lung function, inflammation, and oxidative stress.

Serum albumin is a major antioxidant for the respiratory tract[19] because the N-terminal region of albumin eliminates free oxygen radicals and binds transition metals such as cobalt, copper, and nickel.[20] The elevation of IMA is directly associated with free radicals generated during ischemia.[20] IMA levels are elevated in cardiac ischemia, cerebrovascular occlusion, pulmonary ischemia, gastrointestinal ischemia, and muscle ischemia.[8,19,20]

Hypoxia was demonstrated to impair endothelium-dependent pulmonary artery relaxation in patients with severe COPD.[19] Chawla et al[21] reported that IMA was significantly elevated in cardiac ischemia patients, compared with that in control individuals. IMA demonstrates a good discrimination between ischemic and nonischemic patients. Our results showed that serum IMA levels of COPD patients were significantly higher than those of control individuals. Systemic levels of IMA are increased positively in patients with GOLD Stages II, III, and IV, compared with control individuals. This finding shows that IMA is a useful marker for hypoxia and oxidative stress in COPD. Our findings are consistent with those of Turedi et al,[22] demonstrating that serum IMA levels were significantly higher in patients experiencing pulmonary embolism, compared with those in healthy individuals. In another study, Hackett et al[19] found that parenchymal tissue from COPD patients who were current smokers contained lower levels of total human serum albumin, but higher levels of carbonylated and oxidized human serum albumin, compared with patients with normal lung function. Based on our findings consistent with those of these studies, we speculate that IMA increases under the conditions of free radical production and hypoxia, such as COPD.

Oxidized LDL activates several transcription factors, and increases the chemotaxis of neutrophils and monocytes, secretion of chemokines and cytokines, and intracellular ROS production involved in the pathogenesis of COPD.[23] In our study, serum ox-LDL levels of COPD patients were significantly higher than those of control participants, and ox-LDL was increased, especially in patients with GOLD Stage IV. Shen et al[23] suggested that serum ox-LDL levels are increased in COPD patients, and that these levels are associated with lung function, inflammation, and oxidative stress in COPD. Cigarette smoking is the main pathological factor for COPD.[24] Yamaguchi et al[24] found that smokers demonstrated a significantly higher level of thiobarbituric acid-reactive substances and 8-hydroxydeoxyguanosine, as well as a significantly lower level of vitamin E than nonsmoker individuals. A subfraction assay of LDL showed an increase in oxidatively modified LDL, as expressed by lower levels of LDL-1 and higher levels of LDL-2. The results reported in these studies are also consistent with our results.

An imbalance between oxidative stress and antioxidative capacity plays an important role in the development and progression of COPD. We found that serum TOS levels of COPD patients were significantly higher than those of control individuals. Santos et al[25] found that the plasma concentration of protein carbonyls was significantly increased in COPD patients compared to that in control individuals. The activity of antioxidant enzyme superoxide dismutase was increased in erythrocytes, while glutathione peroxidase activity was decreased in total blood. Levels of selenium in plasma were also found to be lower in COPD patients, compared with those in control individuals. In a study by Nadeem et al,[26] it was found that red cell antioxidative enzyme activities were altered with lower activity of glutathione peroxidase, greater activity of superoxide dismutase, and similar activity of catalase in patients with COPD, compared with control individuals. Ferric-reducing antioxidant power of plasma was lower in patients, compared with that in control individuals, although

protein carbonyls were higher. In another study by Cristóvão et al,[27] a marker of oxidative stress, malondialdehyde, which is a lipid peroxidation-derived product, was found to be significantly higher in COPD patients, when compared with control participants. COPD patients had a significant decrease in antioxidant status, compared with the control group. Lin et al[28] determined that compared with healthy control individuals, COPD patients had significantly lower plasma concentrations of vitamins A, C, and E, alpha-and beta-carotene, and total carotenoids, but significantly higher H_2O_2-induced DNA damage in white blood cells.

It is well understood that antioxidants are altered in COPD. Some studies demonstrated a marked decrease in plasma antioxidant capacity, while other studies showed essentially opposite findings. We found no difference between serum TAS levels of COPD patients and control participants. A mucolytic drug such as NAC is prescribed for some COPD patients over long periods of time. NAC has a direct antioxidant property because of interaction between its thiol and ROS, and an indirect antioxidant property due to its role as a glutathione precursor. Treatment with NAC in humans changes the pulmonary oxidant−antioxidant imbalance.[29] Sadowska et al[30] showed that long-term oral administration of NAC reduces H_2O_2 formation in the airways of COPD patients and that there is evidence of antioxidant action of the drug.

In light of our results, no difference was found between serum triglycerides, total-C, and LDL-C levels of COPD patients and control individuals. Serum HDL-C levels of COPD patients were significantly lower than the corresponding levels of control individuals. Lowering of HDL-C levels may increase the risk of coronary disease. Basili et al[31] reported that total-C, HDL-C, LDL-C, and triglycerides showed similar levels between COPD patients and control individuals. However, an insufficient number of studies related to atherogenetic lipid pattern in COPD have been conducted. Therefore, additional studies are necessary to further elucidate the role of lipids in COPD cases.

In conclusion, our study showed that serum oxidative stress parameters such as IMA, ox-LDL, and TOS are elevated in patients with stable COPD. We consider that IMA, ox-LDL, and TOS may be increased as a result of chronic hypoxia, inflammation, and oxidative stress in patients with severe and very severe stable COPD and that antioxidants, which may repair the impaired oxidant−antioxidant balance in COPD, are needed to prevent the development of COPD.

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