

Correlation of serum fatty acid binding protein-4 and interleukin-6 with airflow limitation and quality of life in stable and acute exacerbation of COPD

Mohammad Reza ASLANI^{1,2} , Zeynab GHAZAEI³ , Hassan GHOBADI^{4,*} 

¹Lung Inflammatory Diseases Research Centre, Faculty of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran

²Neurogenic Inflammation Research Centre, Mashhad University of Medical Sciences, Mashhad, Iran

³Faculty of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran

⁴Internal Medicine Department (Pulmonary Division), Faculty of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran

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Background/aim: The serum fatty acid binding protein 4 (FABP-4) level increases in chronic inflammatory diseases. The present study aimed to examine serum FABP-4 and interleukin (IL)-6 levels in patients with stable and acute exacerbation of chronic obstructive pulmonary disease (COPD) and the correlation of these markers with airflow limitation.

Materials and methods: We measured serum FABP-4 and IL-6 levels in 60 COPD patients [30 stable COPD (SCOPD), and 30 acute exacerbation of COPD (AECOPD)], and 30 healthy subjects and compared them with airflow limitation according to the COPD stage in the Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD) criteria, peripheral O₂ saturation (SpO₂), and COPD Assessment Test (CAT) score. We also tested the association between serum FABP-4 levels and some characteristics of study parameters.

Results: Both serum FABP-4 and IL-6 levels increased with increasing severity of GOLD grades in SCOPD ($P < 0.01$ for both) and AECOPD groups ($P < 0.001$ and $P < 0.01$, respectively). It also increased in patients with AECOPD group compared with SCOPD group in GOLD grades I-II ($P < 0.01$) and GOLD grades III-IV ($P < 0.05$). In addition, there was a significant positive correlation between serum FABP-4 level with IL-6, CAT score, and smoking history and inversely with FEV₁ and SpO₂.

Conclusion: The study revealed that serum FABP-4 level was elevated with increasing GOLD grades in COPD patients, markedly in acute exacerbation phase. The increase was associated with elevated serum levels of IL-6 and severity of hypoxia. Thus, it seems that FABP-4 may be involved in the pathogenesis of COPD.

Key words: Chronic obstructive pulmonary disease, fatty acid binding protein 4, interleukin-6, airflow limitation

1. Introduction

Chronic obstructive pulmonary disease (COPD) is one of the diseases that deeply affects morbidity and mortality in the world [1]. The limitation of air flow is the main characteristic of the disease, which is usually associated with airway inflammation [1]. On the other hand, acute exacerbation of COPD (AECOPD) is characterized by increased systemic inflammation, worsening of pulmonary function tests, increased sputum production, worsening of dyspnoea and cough, and reduced health-associated quality of life, all of which affect the patient's survival [2]. Similar to other diseases that are not characterized by specific aetiology, various factors contribute to the pathogenesis of the disease, including abnormal immune responses, environmental and hormonal factors, and variable gene expression [3].

It has been well-known that under the conditions of AECOPD there is severe airway and systemic inflammation

[4]. Additionally, systemic inflammatory markers and cytokines such as interleukin-6 (IL-6), IL-8, fibrinogen, α_1 -antitrypsin, myeloperoxidase, C-reactive protein (CRP), and tumor necrosis factor alpha (TNF- α) are high with COPD in the exacerbation phase [3,4]. Despite extensive evidence, the precise mechanism of systemic inflammation in AECOPD is not completely clear. It has been reported that a variety of markers and cytokines peak during AECOPD.

Adipokines (also known as adipocytokines) are adipocyte-secreted protein mediators that not only regulate energy metabolism, but they also control inflammatory responses in many chronic diseases [5–7]. Much evidence has shown that adipokines are involved in the lung inflammatory diseases, such as asthma and COPD [8,9]. One of the recently suggested adipokines, fatty acid binding protein 4 (FABP-4) (also known as

* Correspondence: h.ghobadi@arums.ac.ir

adipocyte-protein 2 or aP2), is produced by various cells such as adipocytes, endothelial cells, and macrophages [10]. It has been shown that FABP-4 has a regulatory role in lipid and glucose homeostasis, reactive oxygen species (ROS) production, the inflammatory processes, and secretion of leukotrienes [11,12]. FABP-4 promotes the secretion of proinflammatory cytokines such as IL-6 and TNF- α which exacerbate the severity of the inflammatory diseases [13]. On the other hand, it has been shown that by inhibiting the expression of FABP-4 by pharmacological and genetic studies, many inflammatory signals are inhibited, including the production of inducible nitric oxide synthase (iNOS), cyclooxygenase 2 (COX-2), and inflammatory cytokines such as IL-6, IL-1 β , TNF- α [14]. In animal studies with an allergic airway inflammation model in FABP-4-knockout mice, reduced levels of cytokines and inflammatory cells in the lung tissue have been shown [15]. In addition, elevated serum levels of FABP-4 have been reported in chronic inflammatory diseases, such as asthma, rheumatoid arthritis, hypertension, insulin resistance, obesity, cardiac dysfunction, type 2 diabetes, atherosclerosis, acute lung injury, and female stable COPD [16]. The present study was conducted to evaluate serum FABP-4 and IL-6 levels in men with stable and acute exacerbation of COPD. Another aim of this study was to evaluate the relationship between serum FABP-4 levels and the severity of disease based on Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD) grades and clinical assessment of disease severity based on COPD Assessment Test (CAT) in patients with COPD.

2. Materials and methods

2.1. Study participants

In the current study, 90 subjects were divided into 3 groups including 30 patients with stable COPD (SCOPD), 30 patients with acute exacerbation of COPD (AECOPD), and 30 healthy subjects who were enrolled from April 2017 to March 2018. All subjects were male and matched for age. Patients with a diagnosis of SCOPD were recruited from a respiratory clinic and patients with AECOPD were selected from among those admitted to the emergency department of Ardabil Imam Khomeini Educational and Clinical Hospital, Ardabil, Iran. The control group consisted of subjects with normal spirometry with no respiratory symptoms who were selected from the same hospital who visited in other outpatient clinics.

The SCOPD and AECOPD were diagnosed according to the American Thoracic Society (ATS) guidelines [17]. The AECOPD refers to a sudden worsening of COPD symptoms in the form of shortness of breath, chronic worsening of the cough, and increased volume or discoloration of the phlegm. The inclusion criterion for COPD patients was a ratio of the forced expiratory

volume in 1 s (FEV1) to forced vital capacity (FVC) < 70%. Exclusion criteria were the history of hospitalization in the previous 4 weeks, cardiac ischemia, chronic inflammatory diseases, infectious disease, diabetes, metabolic syndrome, chronic renal failure, and cancer.

The pulmonary function testing was performed using a spirometer (Chest Inc., 801, Tokyo, Japan) according to ATS guidelines under standard conditions. Pulmonary function and biochemical tests were conducted on the same day for SCOPD and control subjects, but for the AECOPD patients they were carried out one day after admission to the hospital. The GOLD grades and COPD assessment test (CAT) questionnaire were fully completed for all patients described previously [18].

2.2. Biochemical measurements

Approximately 3–5 mL of blood samples were taken from all patients to determine serum levels of FABP-4 and IL-6. Serum FABP-4 and IL-6 concentrations were measured using a commercial kit (Crystal day, China) and an electrochemiluminescent method with an Elecsys 2010 automated analyser (Roche Diagnostics). The results were reported as ng/mL.

2.3. Statistical analysis

The results are presented as mean \pm standard deviation (SD), or median and 25th–75th percentiles. Continuous variables were compared using the student's t-test. Comparison between groups was made by ANOVA test was performed with Tukey Kemar post hoc test; alternatively, the Kruskal–Wallis test; if significant, it was followed by the Mann–Whitney U test for post hoc analysis. Correlation coefficients were assessed using the Pearson's (or Spearman rank order) correlation test. Linear regression analyses were performed using FABP-4 as dependent variable and IL-6, FEV1, cigarette history (pack/year), GOLD grade, and SpO₂ as independent variables. A value of P < 0.05 was considered significant. SPSS version 16.0 (SPSS Inc., Chicago, IL, USA) and Graph Pad Prism 5 software were used for statistical analysis.

3. Results

3.1. Baseline characteristics of study population

The study population consisted of 90 men, comprising 30 control subjects, 30 patients with SCOPD, and 30 patients with AECOPD. In the control group the mean age was 58.13 ± 7.36 years and that of the COPD group was 58.70 ± 8.01 years (P = 0.730) (Table 1).

The serum FABP-4 levels were significantly higher in the AECOPD group than in the control and SCOPD groups (P = 0.000 for both, Figure 1a). In addition, there was a significant difference in FABP-4 serum level between SCOPD and control subjects (P = 0.010, Figure 1a). Further, IL-6 results revealed higher levels of IL-6 in

Table 1. Baseline characteristics of patients with COPD and control subjects.

Parameters	Control group	COPD group		P-value
	(n = 30)	SCOPD (n = 30)	AECOPD (n = 30)	
Mean age (year)	58.13 ± 7.36	57.97 ± 9.27	59.43 ± 6.59	0.730
Body mass index (kg/m ²)	26.29 ± 3.52	26.27 ± 4.83	24.47 ± 4.38	0.174
Pulmonary function test:				
FEV1 (% of predicted)	90.33 ± 7.98	53.56 ± 23.20	34.04 ± 14.01	0.000
FVC (% of predicted)	85.40 ± 9.26	68.20 ± 22.26	49.53 ± 21.72	0.000
FEV1/FVC	86.70 ± 4.21	58.76 ± 9.77	55.08 ± 11.24	0.000
FABP-4 (ng/mL)	0.80 (0.70–0.90)	0.90 (0.80–1.20)	1.10 (1–1.40)	0.000
IL-6 (ng/mL)	53.50 (43–58)	56 (53–61)	90.50 (76–109)	0.000

Data are presented as mean ± SD or median (25th–75th percentiles). AECOPD: acute exacerbation of COPD, SCOPD: stable COPD, FEV1: forced expiratory volume in 1 s, FVC: forced volume capacity, FABP-4: fatty acid binding protein 4, IL-6: interleukin 6.

AECOPD group than in control and SCOPD groups ($P = 0.000$ for both, Figure 1b). On the other hand, serum levels of IL-6 in SCOPD group were higher than control subjects ($P = 0.023$, Figure 1b).

3.2. Severity of chronic obstructive pulmonary disease and baseline characteristics of the study population

Baseline parameters of the study population for COPD severity based on GOLD grade are presented in Table 2. There were statistically significant differences in SpO₂ ($P = 0.003$), smoking history (pack/year) ($P = 0.002$), CAT score ($P = 0.000$), FABP-4 level ($P = 0.000$), and IL-6 ($P = 0.000$) between the COPD groups based on GOLD grade. However, we found no significant differences in age ($P = 0.849$) and BMI ($P = 0.735$) according to the stages of COPD.

All grade III-IV patients have higher levels of FABP-4 and IL-6 than the patients with lower grades both in AECOPD and stable groups ($P < 0.01$ to $P < 0.001$, Table 2). The AECOPD patients had higher FABP-4 and IL-6 than stable patients in all COPD grades ($P < 0.05$ and $P < 0.001$, respectively) (Figure 2a and 2b).

The results showed that in both AECOPD and SCOPD groups, CAT scores were statistically higher in GOLD grades III-IV compared to stages I-II ($P = 0.000$ for both) (Table 2).

3.3. Relationship between serum levels of fatty acid binding protein-4 plus IL-6 and parameters of pulmonary function

With regard to study parameters, serum FABP-4 levels were significantly associated with FEV1_{% predicted} ($r = -0.716$,

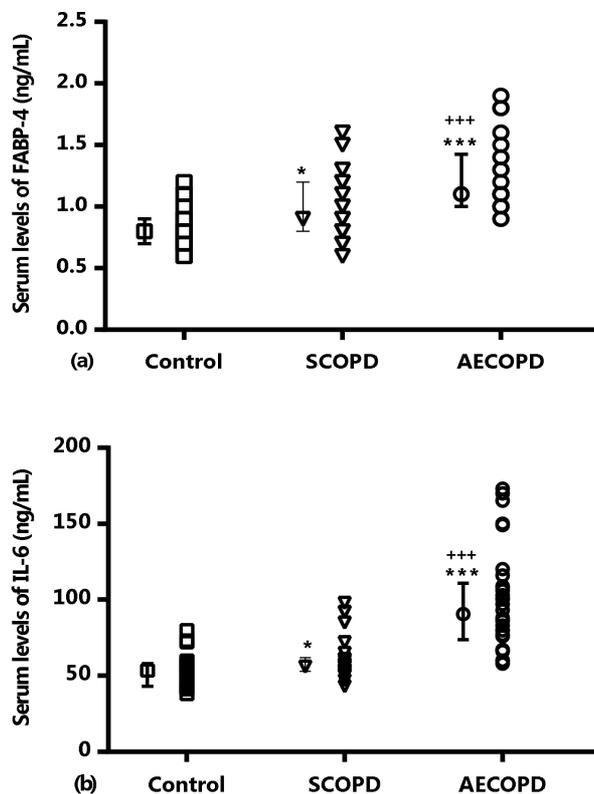


Figure 1: Individual values and median (25th to 75th percentiles) of serum levels of (a): FABP-4 and (b): IL-6 in study groups. For statistical differences between control group and other groups: *, $P < 0.05$, ***, $P < 0.001$. For statistical differences between stable COPD with acute exacerbation of COPD: +++, $P < 0.001$. FABP-4: fatty acid binding protein 4, IL-6: interleukin-6.

Table 2. GOLD groups and baseline characteristics of the study population.

Variables	GOLD I-II		GOLD III-IV	
	SCOPD	AECOPD	SCOPD	AECOPD
Number	14	8	16	22
Age (year)	57.21 ± 9.20	60.50 ± 11.60	58.62 ± 9.59	59.05 ± 3.82
BMI (kg/m ²)	25.46 ± 4.06	24.47 ± 4.21	26.98 ± 5.44	24.48 ± 4.53
Smoking (pack per year)	22 (20–28)	30 (15–58)	32.5 (27–39)	44.5 (35–78)
P1		NS	NS	P < 0.01
P2				P < 0.05
FEV1 (% predicted)				
P1	74.78 ± 13.50	52.98 ± 2.50	35.00 ± 9.68	27.15 ± 9.08
P2		P < 0.001	P < 0.001	P < 0.05
FVC (% predicted)				
P1	87.64 ± 14.69	70.75 ± 5.95	51.18 ± 10.48	41.82 ± 20.14
P2		P < 0.01	P < 0.001	NS
FEV1/FVC (%)				
P1	65.00 ± 3.16	58.97 ± 5.62	53.31 ± 10.40	53.66 ± 12.49
P2		P < 0.01	P < 0.001	NS
SpO ₂ (%)				
P1	96 (92–96)	89 (85.50–89.50)	92 (89–95)	85.50 (81–88)
P2		P < 0.001	P < 0.05	P < 0.001
CAT score				
P1	11 (9–16)	14 (13–15)	27 (21.50–31)	26.5 (22–28)
P2		NS	P < 0.001	NS
IL-6 (ng/mL)				
P1	53.50 (51–56)	67 (63.50–80)	61 (55.50–85)	102 (86–120)
P2		P < 0.001	P < 0.01	P < 0.001
FABP-4 (ng/mL)				
P1	0.80 (0.70–0.90)	1 (0.90–1)	1.10 (0.90–1.25)	1.25 (1.10–1.60)
P2		P < 0.01	P < 0.01	P < 0.05
				P < 0.001

Data are depicted as mean ± SD or median (25th to 75th percentiles). GOLD: the Global Initiative for Chronic Obstructive Lung Disease, SCOPD: stable of chronic obstructive pulmonary disease, AECOPD: acute exacerbation of chronic obstructive pulmonary disease, BMI: body mass index, FEV1: forced expiratory volume in 1 s, FVC: forced volume capacity, SpO₂: O₂ saturation, FABP-4: fatty acid binding protein 4, IL-6: interleukin-6, CAT: COPD assessment test, NS: nonsignificant. P1: statistical differences between SCOPD with AECOPD groups. P2: statistical differences between GOLD I-II with GOLD III-IV in study groups.

P = 0.000; Figure 3a), FVC_{% predicted} (r = -0.670, P = 0.000), GOLD grades (r = 0.603, P = 0.000), and smoking history (pack/year) (r = 0.619, P = 0.000; Figure 3b). There were also significant correlations between serum FABP-4 levels and CAT score (r = 0.639, P = 0.000), and SpO₂ (r = -0.537, P = 0.000; Figure 3c) (Table 3).

Further, the results showed that there were significant associations between IL-6 and FEV1_{% predicted} (r = -0.666, P = 0.000; Figure 3d), smoking history (pack/year) (r = 0.644, P = 0.000; Figure 3e), and SpO₂ (r = -0.640, P = 0.000; Figure 3f). Interestingly, there were also significant correlations between serum levels of FABP-4 and IL-6 (r = 0.692, P = 0.000; Figure g).

Finally, a multiple regression was run to predict FABP-4 from IL-6, CAT score, and SpO₂. These variables significantly predicted FABP-4, with F (4, 55) = 30.88, P < 0.001, R² = 0.692. The results showed that the most significant predictors of FABP-4 were IL-6 and CAT score (P < 0.01 and P < 0.001, respectively) (Table 4).

4. Discussion

In this study, serum FABP-4 and IL-6 levels were significantly elevated with disease severity based on GOLD grades in patients with stable and acute exacerbation of COPD. Further, the serum FABP-4 and IL-6 levels were significantly higher in patients with stages III-IV COPD

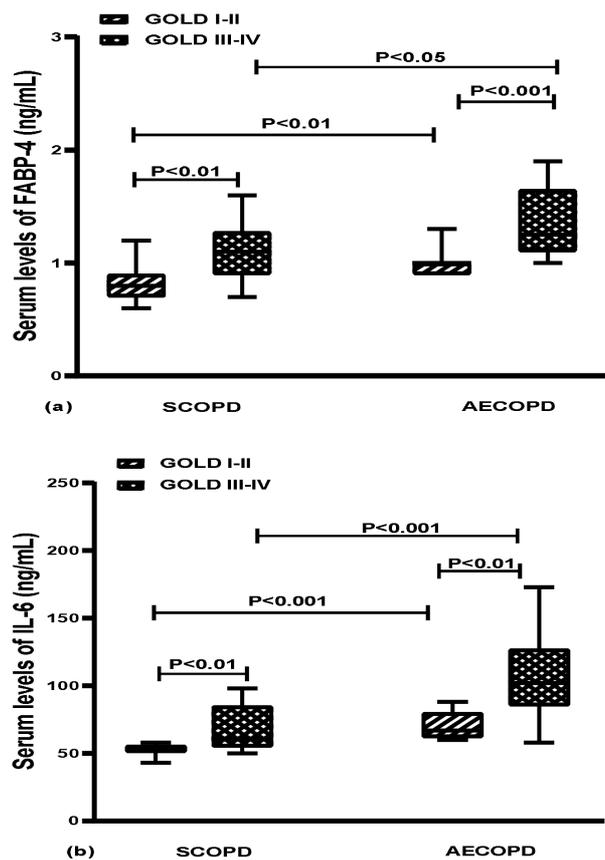


Figure 2: Serum levels of (a): FABP-4 and (b): IL-6 based on GOLD grade in stable and acute exacerbation of COPD patients. Data are depicted as median and quartiles range. GOLD: the Global Initiative for Chronic Obstructive Lung Disease, SCOPD: stable of chronic obstructive pulmonary disease, AECOPD: acute exacerbation of chronic obstructive pulmonary disease, FABP-4: fatty acid binding protein 4, IL-6: interleukin-6.

than in stages I-II according to GOLD grade. There was a negative correlation between serum FABP-4 levels and SpO_2 as well as with FEV1. On the other hand, there was a positive correlation between serum FABP-4 levels and IL-6 as well as with severity of COPD based on GOLD grade.

The main symptom of COPD, especially its acute exacerbation phase, is the high level of inflammation that plays a key role in the development of disease [3]. It has been shown that in patients with SCOPD and AECOPD there is an over-production of various types of inflammatory cytokines such as IL-6, TNF- α , and IL-1 β , likely to stimulate downstream of cytokines to exacerbate pulmonary tissue damage [3, 19]. IL-6 is a pro-inflammatory cytokine produced predominantly by a variety of pulmonary cells, including airways epithelial cells, endothelial cells, alveolar macrophage, and fibroblast [20]. Our results indicated that serum IL-6 levels of

AECOPD patients were higher than those in healthy subjects. In addition, it was found that the amount of IL-6 serum levels in AECOPD of patients were higher than those in SCOPD patients. Also, the results of IL-6 serum levels based on the severity of the disease revealed that in stages III-IV the amount of IL-6 was higher than stages I-II, which was in line with previous studies [20].

Many studies have shown that a variety of adipokines play an important role in chronic inflammatory diseases such as asthma and COPD [13, 21]. Indeed, adipokines are modulating mediators of inflammatory and immune responses [22]. FABP-4, as adipokine, is a cytosolic protein that is involved in the lipid trafficking and signalling [23]. Many evidence reported that elevated FABP-4 concentrations have been associated with insulin resistance, obesity, asthma, hypertension, cardiac dysfunction, type 2 diabetics, atherosclerosis, acute lung injury, and stable COPD [16]. It has been indicated that FABP-4 has a regulatory role in the allergic airway inflammation and that blocking FABP-4 causes a decline in airway inflammation in lung diseases [15]. However, there are few studies about the association of FABP-4 with COPD severity of disease, especially in acute exacerbation phase. Zhang et al. revealed that there was a gender difference in serum FABP-4 level in patients with stable COPD [13]. In their study, it was found that in patients with stable COPD, the serum level of FABP-4 in females was higher than that in males and correlated negatively with pulmonary function tests and positively with TNF- α , CRP, and adiponectin levels [13]. In the current study, we found that the serum FABP-4 level in male patients with SCOPD was higher than control subjects. Although it is not clear to us whether there is a statistical difference between the levels of FABP-4 in men in our study and the study of Zhang et al., it seems that in our study, the higher BMI may have an effect on FABP-4 results, which requires further studies.

Our results also showed that serum FABP-4 level was higher in patients with AECOPD than in healthy subjects as well as SCOPD patients. In fact, these results indicate that FABP-4 may play a critical role in the development of COPD. Previous studies have reported that FABP-4 worsens inflammatory responses in inflammatory diseases by increasing levels of inflammatory cytokines or by recruiting inflammatory cells [24]. Perhaps FABP-4 plays a key role in the pathogenesis of COPD in the activation of transcription factors and release of inflammatory factors in macrophages. Since smoking has been shown to induce and activate macrophages, due to the strong correlation between FABP-4 and smoking in our study, at least in part, it can reflect the role of macrophages and their relationship with FABP-4 in pathogenesis of disease, especially in AECOPD condition. Animal studies have

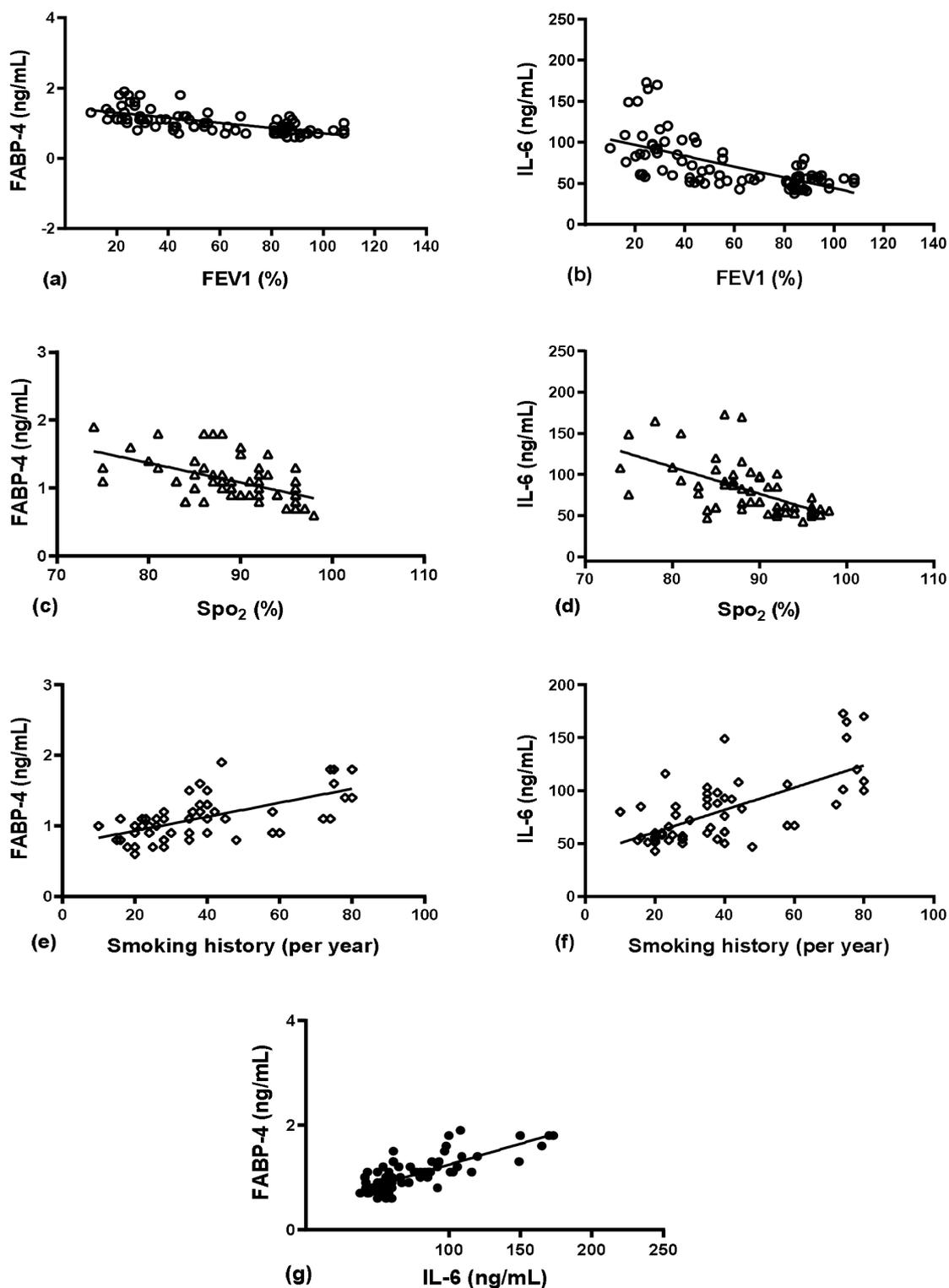


Figure 3: Spearman rank order correlation analysis of (a): FEV1 and FABP-4 serum levels (correlation coefficient = -0.716 , $P = 0.000$), (b): smoking history and FABP-4 serum levels (correlation coefficient = 0.619 , $P = 0.000$), (c): O₂ saturation and FABP-4 serum levels (correlation coefficient = -0.537 , $P = 0.000$), (d): FEV1 and IL-6 serum levels (correlation coefficient = -0.666 , $P = 0.000$), (e): smoking history and IL-6 serum levels (correlation coefficient = 0.644 , $P = 0.000$), (f): O₂ saturation and IL-6 serum levels (correlation coefficient = -0.640 , $P = 0.000$), and (g): serum levels of FABP-4 and IL-6 (correlation coefficient = 0.692 , $P = 0.000$). FEV1: forced expiratory volume in 1 s, FABP-4: fatty acid binding protein 4, IL-6: interleukin-6, SpO₂: O₂-saturation.

Table 3. Spearman correlation analysis of study parameters with FABP-4 in COPD patients (n = 60)

Variables	FABP-4	
	R	P-value
Age	0.069	0.599
Smoking history (per year)	0.608	0.000
FEV1 (% predicted)	-0.672	0.000
FVC (% predicted)	-0.651	0.000
FEV1/FVC	-0.242	0.060
GOLD grade	0.603	0.000
SpO ₂	-0.537	0.000
CAT score	0.693	0.000

FEV1: forced expiratory volume in 1 s, FVC: forced volume capacity, FABP-4: fatty acid binding protein 4, IL-6: interleukin 6, SpO₂: O₂ saturation, GOLD: the Global Initiative for Chronic Obstructive Lung Disease, CAT: COPD assessment test.

revealed that FABP-4-deficient macrophages have reduced inflammatory function and decreased inflammatory cytokines, such as IL-6, TNF- α , and MCP-1 [monocyte chemoattractant protein 1] [25]. In fact, mechanically, pharmacological or genetic inhibitors of FABP-4 had protective effects against inflammation through diminished chemokine and cytokine secretion, polarization of cells towards antiinflammatory M2 condition, and production suppression of proinflammatory factors in hepatic tissue [11,26,27]. In addition, our study results showed that there was a strong correlation between FABP-4 and IL-6 levels in patients with COPD, suggesting that adipokines such as FABP-4 may play a critical role in systemic inflammation of COPD patients. Particularly, the results revealed that serum levels of FABP-4 and IL-6 in the AECOPD patients were much higher than those in SCOPD patients. On the other hand, serum levels of FABP-4 in patients with AECOPD based on the severity of the disease in stages III-IV were greater than stages I-II, indicating that FABP-4 plays a major role in the development and persistence of inflammation in patients with COPD. Accordingly, increased levels of FABP-4 in patients with COPD can be indicative of local or systemic inflammation. Although adipose tissue and inflammatory cells such as macrophage are the main secretor sources of FABP-4, it has also been shown that levels of FABP-4 are high in acute lung injury [28]. Of course, it should be noted that the authors did not rule out other pathways other than the inflammatory pathway of FABP-4 in patients with COPD. In patients with rheumatoid arthritis, it has been shown that increased levels of FABP-4 were associated with lipid profiles,

Table 4. Associations between FABP-4 and study parameters.

FABP-4			
Variables	B	95% CI for B	P-value
SpO ₂	-0.059	-0.013-0.007	0.538
IL-6	0.420	0.001-0.002	0.001
CAT score	0.361	0.007-0.021	0.000
Cigarette smoking	0.172	-0.000-0.006	0.093

B: unstandardized coefficient. CI: confidence intervals, FABP-4: fatty acid binding protein 4, IL-6: interleukin-6, SpO₂: O₂ saturation.

independent of the severity of the disease, which indicates the predominant role of FABP-4 in lipid metabolism rather than inflammation pathway [14].

A significant negative correlation between SpO₂ and FABP-4 levels in our study may reveal another pathophysiological role of FABP-4 in COPD patients. In patients with COPD, one of the pathways activated as a result of hypoxia is endoplasmic reticulum stress response (ER stress). It has been shown that diminished FABP-4 can reduce the apoptosis mediated by ER stress [29]. Therefore, elevated FABP-4 level in patients with COPD, especially in the AECOPD phase may have an effect on ER stress markers and may affect oxygenation changes which required further studies.

In this study, we additionally found a positive association between serum FABP-4 levels and CAT score plus mMRC scales. It has been reported that physical activity significantly decreases in patients with higher stages of COPD [30]. Another study also proposed that the increase in levels of inflammatory factors such as C-reactive protein, IL-6, and fibrinogen is the main cause for this diminished activity [31]. The rise in serum FABP-4 and IL-6 levels with increasing GOLD grades of COPD could correlate with the effect of systemic inflammation on health status.

Our study had some limitations. Since previous studies have shown that there was sex differences in FABP-4 levels, we did not measure serum FABP-4 levels in female patients with COPD in the acute exacerbation phase. Further, we did not measure other inflammatory markers other than IL-6. Therefore, we are not able to determine the correlation between serum levels of FABP-4 and other inflammatory markers of COPD. Finally, the sample size of our study was small, and such evaluations should be performed with a large sample size.

In conclusion, in this study, we found that serum FABP-4 and IL-6 levels increases with the enhanced GOLD grades in patients with COPD, markedly in acute

exacerbation phase. The increase of FABP-4 had a strong relationship with elevated serum level of IL-6 and severity of hypoxia. Thus, serum FABP-4 levels merit consideration as a useful marker in the pathogenesis of COPD patients.

Acknowledgement/Disclaimers/Conflict of Interest

This is a report of a database from the study of "Evaluation of serum levels of Fatty Acid Binding Protein-4 and IL-6 in exacerbation phase of COPD patients" that was registered

and funded by Research Committee of Ardabil University of Medical Sciences. The authors have declared that there is no conflict of interest.

Informed Consent

The study was approved by the Ethics Committee of Ardabil University of Medical Sciences and all of the study participants signed the written consent forms (No. IR.ARUMS.REC.1397.038).

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