Role of C-reactive protein and interleukin-6 in predicting the prognosis of ICU-admitted patients with acute exacerbation of COPD

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Received 27 April 2014; accepted 2 June 2014
Available online 1 July 2014

KEYWORDS
COPD; C-reactive protein; Interleukin-6; Exacerbation; Predictors

Abstract Background and Objective: Chronic obstructive pulmonary disease (COPD) is a leading and increasing cause of worldwide morbidity and mortality. No universal predictor of mortality and outcome was defined especially in intensive care unit (ICU)-admitted patients with acute exacerbation of COPD (AECOPD). The objective was to detect the possible role of C-reactive protein (CRP) and interleukin-6 (IL-6) levels in predicting the prognosis of ICU-admitted patients with AECOPD.

Methods: This prospective cohort study enrolled 50 adult patients with AECOPD who were admitted in the ICU. Serum CRP and IL-6 levels were measured on admission. The primary endpoint was any-cause mortality during ICU stay or 28 days after discharge. Lengths of ICU and hospital stay besides complications encountered were recorded.

Results: Serum CRP level was significantly elevated in patients with prolonged mechanical ventilation (MV) days, ICU stay and hospital stay (r = 0.406, p = 0.007; r = 0.411, p = 0.006; r = 0.387, p = 0.010, respectively). Similar results were noted for serum IL-6 level (r = 0.554, p < 0.001; r = 0.533, p = < 0.001; r = 0.508, p = 0.001, respectively). Combined CRP and IL-6 serum levels predicted 28 day mortality at a cut-off value of 110 mg/dl and 347.8 pg/ml respectively (AUC = 0.851, p = 0.006) with 83.33% sensitivity, 75.68% specificity, 35.71% PPV and 96.55% NPV. This was significantly greater than that for CRP alone (p = 0.040) or IL-6 alone (p = 0.004).

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Peer review under responsibility of The Egyptian Society of Chest Diseases and Tuberculosis.

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Introduction

Recently, chronic obstructive pulmonary disease (COPD) has gained interest as a major public health concern and is currently the focus of intense research because of its persistently increasing prevalence, mortality, and disease burden [1]. Patients with COPD have an ongoing systemic inflammation. In addition, it is believed that many of the systemic manifestations of COPD are mediated through increased systemic levels of inflammatory proteins such as interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α) and C-reactive protein (CRP) [2].

It is obvious that there is a great debate about the possible role of CRP & IL-6 levels in predicting the prognosis of Intensive care unit (ICU)-admitted patients with acute exacerbation of COPD (AECOPD). The aim of this work was to detect the possible role of CRP & IL-6 levels in predicting the prognosis of ICU-admitted patients with AECOPD.

Subjects and methods

This prospective cohort study was conducted on 50 adult patients of both sexes admitted to the ICUs of Alexandria Main University Hospital or private hospitals in the governorate of Alexandria. To be eligible for the study, patients were admitted on the basis of having AECOPD which was defined as acute change in the patients’ base line dyspnea, cough, and/or sputum production severe enough to be referred to hospital and admitted to ICU for oxygen therapy, ventilatory support, hemodynamic instability or failure to improve after empiric treatment before ICU admission. COPD patients were defined according to Global Initiative for Chronic Obstructive Lung Disease (GOLD) [3,4].

Patients were excluded from the study if they had bronchial asthma, cystic fibrosis or manifest immunosuppression, new infiltration in chest X-ray on admission, vasculitis or other causes that increase CRP. Patients with left heart failure or ischemic heart disease were also excluded.

Informed consent was taken from all patients or their next of kin. The study was approved from the ethics committee of the Alexandria Faculty of Medicine.

Data collected

All patients included in the study were subjected to the followings: full history taking, complete clinical examination, Chest X-ray, routine laboratory investigations and culture of sputum, tracheal aspirate or bronchial lavage (when indicated).

Determination of plasma IL-6 concentration by enzyme linked immunosorbent assay (ELISA) (ImmunoLeader, Orgenium Kits) and determination of CRP concentration by enzyme linked immunosorbent assay (ELISA)(ImmunoLeader), were routinely assessed in all the studied subjects on admission.

Conclusions: Serum levels of CRP and IL-6 (either individually or combined) were useful markers in predicting the mortality, complications and outcome in ICU-admitted patients with AECOPD.

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Five ml of venous blood was withdrawn from every patient on admission to the ICU and collected on 5% ethylenediaminetetraacetic acid (EDTA). Centrifugation at 400 x g for 30 minutes was done. Plasma samples were collected and stored in dry plastic tubes at -20 °C for determination of IL-6 concentrations.

Assay principle

Boster’s human IL-6 ELISA Kit was based on standard sandwich enzyme immunoassay assay technology. Standards and samples were pipetted into wells and any IL-6 was bounded by an immobilized antibody. Then IL6-specific enzyme linked monoclonal antibody was added and followed by a substrate. A color developed in proportion to the concentration of IL-6. Subsequently, color development was stopped and its intensity was measured.

A standard curve was drawn by the ELISA reader where the absorbance value for each standard was plotted on the vertical axis against the corresponding standard concentration (pg/ml) on the horizontal axis of ELISA paper. Sample concentrations were read as pg/ml from the standard curve by the ELISA reader using the absorbance value for each sample.

Outcome measures

The outcome of the studied cases and their complications were traced during follow-up which included duration of ICU stay, hospitalization and mortality within 28 days post discharge from hospital. The end point was “adverse outcome”, defined as the presence of at least one of the followings: Death from any cause in the ICU or hospital, death within the 28 days period following discharge and development of acute heart failure (this was identified clinically).

Statistical analysis

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0 [5,6]. Qualitative data were described using number and percent. Quantitative data were described using Range (minimum and maximum) mean, standard deviation and median. The distributions of quantitative variables were tested for normality using Kolmogorov–Smirnov test, Shapiro–Wilk test and D’Agstino test, also Histogram and QQ plot were used for vision test. If it revealed normal data distribution, parametric tests were applied. If the data were abnormally distributed, non-parametric tests were used. For abnormally distributed data, comparison between two studied groups was done using Mann–Whitney test.

Correlations between two quantitative variables were assessed using Spearman coefficient. Agreement of the different predictives with the outcome was used and was expressed...
in sensitivity, specificity, positive predictive value, negative predictive value and accuracy. Receiver operating characteristic curve (ROC) was plotted to analyze a recommended cutoff, the area under the ROC curve denotes the diagnostic performance of the test. Area more than 50% gives acceptable performance and area about 100% is the best performance for the test. Significance test results are quoted as two-tailed probabilities. Significance of the obtained results was judged at the 5% level.

**Results**

**Demographic and clinical data**

The demographic data of the study population are shown in Table 1 where the age of the studied patients ranged from 44 to 88 years old with a mean of 63.0 ± 8.70 years. It was noticed that there were 2 females in the studied cases and this is well understood due to religious and traditional causes related to smoking as a habit in our country.

As regards the patients’ symptoms on admission, all (100%) the patients suffered from two of the cardinal symptoms (Cough and Dyspnea), while only 41 patients (82%) had purulent sputum (change in the color of the sputum), and 47 patients (94%) complained of increase in the amount of the sputum.

Arterial gasometry, complete blood count, serum CRP and serum IL-6 included.

**The respiratory support management**

As regards the respiratory support management of the studied patients after excluding the 7 discharged against medical advice (DAMA) patients, only 3 of the patients (7%) were improved on bronchodilators and oxygen therapy only without needing positive ventilation support, while 40 patients (93%) needed noninvasive mechanical ventilation (NIMV) for a period ranging from 1 h to 13 days with a mean value of 9.44 ± 5.86 days. Notably, serum CRP and IL-6 levels increased in all patients included.

Regarding the outcome of the studied patients according to MV days, ICU stay and hospital stay as shown in Table 3, MV days ranged from 10 h to 20 days with a mean value of 5.53 ± 4.88 days, noticing that the duration of MV was considered as the total MV period during hospitalization either NIMV or IMV or both, with one patient was put on IMV only for 10 h after which he did not need further positive pressure ventilation. While the ICU stay period ranged from 2 to 23 days with a mean value of 7.07 ± 4.73 days. And the hospital stay period ranged from 3 days to 27 days with a mean value of 9.44 ± 5.86 days.

According to the discharge type as shown in Table 4, 7 patients (14%) were DAMA, 38 patients (76%) were discharged after improvement, and 5 patients (10%) unfortunately died. Six patients (14%) died within the 28 days post discharge; and 6 patients (14%) suffered from acute heart failure.

**The outcome measures**

### Table 1 Demographic and clinical data.

<table>
<thead>
<tr>
<th>Min–Max</th>
<th>Mean ± SD</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>44–88</td>
<td>63 ± 87</td>
</tr>
<tr>
<td>Sex</td>
<td>48 (Males)</td>
<td>2 (females)</td>
</tr>
<tr>
<td>Annual Exacerbations</td>
<td>0.0–7.0</td>
<td>2.86 ± 1.55</td>
</tr>
<tr>
<td>Previous hospitalization</td>
<td>0.0–7.0</td>
<td>2.64 ± 1.47</td>
</tr>
<tr>
<td>Previous ICU admissions</td>
<td>0.0–6.0</td>
<td>1.98 ± 1.13</td>
</tr>
<tr>
<td>Previous MV</td>
<td>0.0–6.0</td>
<td>1.98 ± 1.17</td>
</tr>
<tr>
<td>GCS</td>
<td>10–15</td>
<td>13.52 ± 1.31</td>
</tr>
<tr>
<td>Duration of NIMV (days)</td>
<td>1 h–13 d</td>
<td>2.70 ± 2.53</td>
</tr>
<tr>
<td>Duration of IMV (days)</td>
<td>2 h–19 d</td>
<td>5.20 ± 5.53</td>
</tr>
</tbody>
</table>

GCS = Glasgow coma scale, IMV = Invasive mechanical ventilation, MV = Mechanical ventilation, NIMV = Noninvasive mechanical ventilation.

### Table 2 Distribution of the studied cases according to some laboratory investigations.

<table>
<thead>
<tr>
<th>Min–Max</th>
<th>Mean ± SD</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.0–7.32</td>
<td>7.23 ± 0.08</td>
</tr>
<tr>
<td>PaCO₂ (mm Hg)</td>
<td>64.0–154.0</td>
<td>91.06 ± 22.37</td>
</tr>
<tr>
<td>PaO₂ (mm Hg)</td>
<td>40.0–130.0</td>
<td>66.40 ± 17.89</td>
</tr>
<tr>
<td>HCO₃ (m Eq/l)</td>
<td>23.0–46.0</td>
<td>36.79 ± 4.07</td>
</tr>
<tr>
<td>SaO₂ (%)</td>
<td>58.0–99.0</td>
<td>90.41 ± 7.07</td>
</tr>
<tr>
<td>WBCs (c/mm³)</td>
<td>4000–22000</td>
<td>9040 ± 3.20</td>
</tr>
<tr>
<td>CRP (mg/dl)</td>
<td>42.0–184.0</td>
<td>97.55 ± 32.53</td>
</tr>
<tr>
<td>IL-6 (pg/ml)</td>
<td>193.20–634.0</td>
<td>337.24 ± 98.66</td>
</tr>
</tbody>
</table>

CRP = C-reactive protein, IL-6 = Interleukin 6, PaCO₂ = partial pressure of arterial carbon dioxide, PaO₂ = partial pressure of arterial oxygen, SaO₂ = arterial oxygen saturation; WBCs = white blood cells.

### Table 3 Distribution of the studied cases according to MV, ICU stay and hospital stay.

<table>
<thead>
<tr>
<th>Min.–Max</th>
<th>Mean ± SD</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>MV* days</td>
<td>10 h–20 d</td>
<td>5.53 ± 4.88</td>
</tr>
<tr>
<td>ICU stay</td>
<td>2.0–23.0</td>
<td>7.07 ± 4.73</td>
</tr>
<tr>
<td>Hospital stay</td>
<td>3.0–27.0</td>
<td>9.44 ± 5.86</td>
</tr>
</tbody>
</table>

* MV days are the total mechanical ventilation period during hospitalization either noninvasive or invasive or both.
Correlating serum CRP level to MV days, ICU stay and hospital stay as shown in Table 5, it was noticed that the serum CRP level was significantly elevated in relation to increase of the period of MV days \((r = 0.406, p = 0.007)\), ICU stay \((r = 0.411, p = 0.006)\) and hospital stay \((r = 0.387, p = 0.010)\), but it was insignificant in relation to NIMV days \((r = -0.089, p = 0.569)\), although it was found significant in relation to IMV days \((r = 0.452, p = 0.002)\).

The same results were noted for IL-6 as shown in Table 5. It was significantly elevated in relation to increase of the period of MV days \((r = 0.554, p < 0.001)\), ICU stay \((r = 0.533, p < 0.001)\) and hospital stay \((r = 0.508, p = 0.001)\), but it was insignificant in relation to NIMV days \((r = 0.147, p = 0.346)\), although it was found significant in relation to IMV days \((r = 0.478, p = 0.001)\).

For the relation between the discharge type and serum CRP and IL-6 levels, the mean value of CRP in sera of the improved patients was 96.12 ± 31.59 ranging from 42 to 174 mg/dl, while in the dead patients it was 115.88 ± 25.70 mg/dl ranging from 86 to 147 mg/dl. Although CRP level was elevated in both types of patients on admission, it lacked significance in relation to improvement or death of these patients with a p value of 0.134. Nevertheless, the mean value of IL-6 in sera of the improved patients was 322.15 ± 91.79 pg/ml ranging from 193 to 634 pg/ml. In the dead patients, it was 415.32 ± 98.53 pg/ml ranging from 347.4 to 584.4 pg/ml. The latter relation was proved significant \((p = 0.019)\).

Concerning the relation between serum CRP on admission and 28 day mortality, in survived patients, serum CRP ranged from 42 to 174 mg/dl with a mean value of 94.47 ± 30.33 mg/dl. The mean serum CRP value in dead patients was 122.73 ± 28.46 mg/dl ranging from 86 to 157 mg/dl. Therefore, there was a significant relation between serum CRP on admission and 28 day mortality \((p = 0.040)\). Similar results were noted for serum IL-6, ranging from 193.20 to 526.40 pg/ml in survived patients with a mean value of 313.72 ± 76.72 pg/ml while in passed patients it ranged from 347.40 to 634.0 pg/ml with a mean value of 451.77 ± 125.45 pg/ml. There was a significant relation between 28 day mortality and serum IL-6 on admission \((p = 0.004)\).

In the current study, about 6 patients developed acute heart failure following the pre-defined inclusion criteria. Serum CRP and IL-6 levels in those patients on admission revealed a mean value of 96.0 ± 20.33 and 276.57 ± 57.93 pg/ml, respectively. The relation between serum CRP and IL-6 levels and development of acute heart failure lacked significance \((p = 0.987\) and \(p = 0.061\), respectively).

ROC curve for combined results of CRP and IL-6 with 28 day mortality rate revealed a cut off value for CRP of 110 mg/dl and for IL-6 of 347.8 pg/ml with sensitivity of 83.33%, specificity of 75.68%, positive predictive value (PPV) of 35.71% and negative predictive value (NPV) of 96.55% (Fig. 1). The area under the curve (AUC) was 0.851 with \(p = 0.006\) which is significantly greater than that for CRP \((p = 0.040)\) or IL-6 \((p = 0.004)\) on an individual basis with a magnitude considered to be clinically useful, and 76.74% accuracy in predicting the above mentioned outcome.

**Discussion**

The levels of many cytokines are known to be raised in sera of COPD patients. Frequent exacerbations are associated with increased pulmonary and systemic inflammation, and IL-6 is
a systemic inflammation marker suggested to be increased during exacerbations [7]. The growing literature is suggesting that CRP may be a useful systemic biomarker of lung inflammation. Furthermore, CRP is easily measured, in comparison to exhaled or more exotic biomarkers [8].

To the best of our knowledge, this has been the first study prospectively conducted on patients who had been admitted to the ICU with AECOPD to evaluate the prognostic value of combined CRP and IL-6 in ICU according to the mentioned outcome parameters.

Akbulut et al. [7] evaluated IL-6 and IL-8 levels in patients with AECOPD and Wedzicha et al. [9] both showed a significant elevation in serum IL-6 levels on admission of patients with AECOPD. Moreover, in one study that evaluated systemic cytokine profile of patients hospitalized during an AECOPD, Malo et al. [10] documented a significant increase in IL-6 and CRP levels on hospital admission. This was evident in high mean CRP and IL-6 levels in sera of our studied patients (97.55 ± 32.53 mg/dl and 337.24 ± 98.66 pg/ml, respectively).

Wide variety of inflammatory mediators have been shown to be increased in COPD patients, attract inflammatory cells from the circulation (chemotactic factors), amplify the inflammatory process (proinflammatory cytokines), and induce structural changes [3].

Ucgun et al. [11] found that the length of ICU stay was 7.1 ± 5.5 days in survivors (n = 101) and was 6.3 ± 5.1 days in non-survivors (n = 50), and the length of hospital stay was 11.9 ± 8.2 days in survivors and was 7.3 ± 5.7 days in non-survivors, while Nevins et al. [12] reported that the mean duration of MV was 8.9 days (median 4.1 days).

Our findings suggest that the serum CRP level was significantly elevated in relation to increased period of MV days (r = 0.406, p = 0.007), ICU stay (r = 0.411, p = 0.006) and hospital stay (r = 0.387, p = 0.010), but it was noticed to be insignificant in relation to NIMV days (r = −0.089, p = 0.569), although it was noticed to be significant in relation to IMV days (r = 0.452, p = 0.002).

Similar to our results, Ucgun et al. [11] studied the predictors of hospital outcome and intubation in COPD patients admitted to the respiratory ICU for acute hypercapnic respiratory failure as they reported that the serum CRP levels on admission in their patients (87 patients) were found to be statistically significant in relation to length of ICU stay (days) (p = 0.01) and length of hospital stay (days) (p < 0.001), and they found that the serum CRP levels on admission were significantly elevated in patients who needed invasive mechanical ventilation (p = 0.001).

Stolz et al. [13] studied Copetin, CRP, and Procalcitonin as prognostic biomarkers in AECOPD. They found that CRP levels correlated neither with the length of hospital stay (p = 0.714) nor the length of ICU stay (p = 0.835). Levels in those requiring ICU care were similar to those treated on the ward (p = 0.931). A comparison of clinical outcomes in patients with CRP levels < 50 mg/L and > 50 mg/L on ICU admission in their study was done. The length of hospital stay did not differ in these two groups of patients (p = 0.417). Levels in survivors and nonsurvivors were similar (p = 0.129).

Different results can be explained by different durations of follow up. We studied the short term outcome (15 and 28 mortality rates), while Stolz et al. [13] followed their patients for a longer duration (6 months), they found that CRP levels were significantly elevated at the exacerbation and decreased substantially thereafter, with comparable levels after 14 days and 6 months. However, CRP levels on hospital admission are not correlated to long-term outcome of the exacerbation, as CRP levels rise rapidly during infection or after injury, to just decline after the initial stimulus has vanished. Moreover, CRP fails to provide any further information about prognosis in the acute event due to its high sensitivity but low specificity [14].

In the current study, regarding the correlation between IL-6 and MV, ICU stay and hospital stay, it was noticed that IL-6 was significantly elevated in relation to increase of the period of MV days (r = 0.554, p = < 0.001), ICU stay (r = 0.533, p = < 0.001) and hospital stay (r = 0.508, p = 0.001). Nevertheless, it was noted to be insignificant in relation to NIMV days (r = 0.147, p = 0.346) and proved significant in relation to IMV days (r = 0.478, p = 0.001).

Bayir et al. [15] evaluated the relation between mortality rate, duration of hospitalization and levels of CRP, TNFα, IL-6 and catalase on admission for patients with AECOPD presented to the emergency department. They found that the mean values of leucocytic count, sedimentation rate, CRP and IL-6 in dead patients were significantly higher than those in the discharged patients (p = 0.040, 0.038, 0.02, 0.017, respectively). High CRP and IL-6 values in sera of patients with AECOPD presenting to the emergency department may indicate the requirement of ICU admission and treatment with mechanical ventilation, and a high mortality.

Noted in the current study, the mean value of CRP in sera of the improved patients was 96.12 ± 31.59 mg/dl ranging from 42 to 174 mg/dl. In the dead patients it was 115.88 ± 25.70 mg/dl ranging from 86 to 147 mg/dl. Despite this apparent difference between survivors and non-survivors, it lacks significance in relation to improvement or death of our patients (p = 0.134).

Bakr et al. [16], in a cohort of 220 patients with acute respiratory failure (ARF) secondary to COPD, requiring mechanical ventilation (MV) and admitted to the ICU over a two-year period concluded that CRP level differed insignificantly between survivors and non-survivors.

Concerning the mean value of IL-6 in sera of the improved patients, it was 322.15 ± 91.79 pg/ml ranging from 193 to 634 pg/ml. In the dead patients, it was 415.32 ± 98.53 pg/ml ranging from 347.4 to 584.4 pg/ml, which was found to be significantly high with p value of 0.019.

On studying the relation between serum CRP and IL-6 levels of the studied patients on admission and mortality, both were found significant in 28 day mortality. (p = 0.040 and p = 0.004, respectively). These results were similar to those of Dahl et al. [17] who studied CRP as a predictor of prognosis in COPD and concluded that increased serum CRP may also increase the risk of all-cause mortality in individuals with pulmonary dysfunction and CRP is a strong long-term predictor of COPD hospitalization and death, independent of smoking and lung function.

In our study, about 6 patients developed acute heart failure following the pre-defined inclusion criteria. In relation to the value of serum CRP and IL-6 levels on admission, both were found insignificant regarding the patients who did not develop acute heart failure at the end of the study. (p = 0.987 and p = 0.061, respectively).

Compared to our results, Wedzicha et al. [9] found that AECOPD was accompanied by elevations of plasma...
fibrinogen and serum IL-6 levels. Transient acute increase in plasma fibrinogen was found to be an independent risk factor for congestive heart disease and COPD exacerbation (mediated through a rise in IL-6). Thus, providing a mechanism linking respiratory inflammation to risk of coronary heart disease.

Concerning the ROC curve for applying both biomarkers (CRP & IL-6) as predictors of 28 day mortality, the cutoff CRP value raised to 110 mg/dl and IL-6 raised to 347.8 pg/ml (compared to each biomarker alone) with notable change in sensitivity from 66.67% to 100% for individual CRP and IL-6 levels respectively to 84.33% combined and notable change in specificity from 73.88% to 77.83% for individual CRP and IL-6 levels respectively to 75.68% combined. PPV for both biomarkers combined was 23.71% which was slightly more than that of CRP alone (33.33%) or near that of IL-6 alone (37.50%). NPV was dropped to 76.55% and the AUC was 0.851 with \( p = 0.006 \) which is significantly greater than that of CRP alone (\( p = 0.040 \)) while it was near that of IL-6 with AUC = 0.874 \( (p = 0.004) \) with magnitude to be considered clinically with 76.74% accuracy in predicting the above mentioned outcome.

These results go with those of Hurst et al. [18] who studied the use of plasma biomarkers at exacerbation of COPD. They found that CRP cutoff value at 5 mg/L would be 74.4% sensitive and 57.5% specific for confirmation of exacerbation. There was a significant correlation between plasma IL-6 and CRP concentrations (\( r = 0.60, \ p = 0.001 \)), the increase in IL-6 remained significantly associated with the increase in CRP (\( r = 0.63, \ p = 0.0001 \)).

CRP is an acute phase protein produced by the liver in response to IL-6 stimulation [19]. CRP is raised in most conditions associated with infection, inflammation or tissue damage, for which it is a sensitive marker [19]. Evidence suggests that CRP and IL-6 may also be implicated in the pathophysiology of COPD [18].

Comparing the results of the current study with the previously mentioned studies shows a low PPV of the levels of CRP and IL-6 on admission of ICU patients with acute exacerbation of COPD in contrast to its high NPV. Moreover, the rising levels of our studied biomarkers (CRP and IL-6) were considered to have a high sensitivity but low specificity in predicting the outcome. Nevertheless, the specificity was raised when using the combined relation between CRP, IL-6 and outcome measures. This can be interpreted as these cytokines are related to the clinical and prognostic parameters and can be useful for evaluation of the therapy instituted for the disease. Finally, interrelationships between biomarkers at exacerbation suggest that monocytic pathways may be an important target for future research [18].

The followings are limitations of our study: a relatively low number of patients, a relatively delayed onset of NIV applications in ER, inclusion of not only patients with uncomplicated AECOPD but also those with other comorbid diseases (malignancy, renal failure and sepsis), our study was not specifically designed to differentiate the role of bacterial or viral infection in the pathogenesis of the exacerbation, failure to follow the DAMA patients and the short period of follow up.

In conclusion CRP and IL-6 as biological markers were noticed to be elevated in patients with AECOPD who needed ICU admission. CRP and IL-6 are good indicators of future increase of MV days, hospital stay and ICU stay. There was a significant relation between CRP and IL-6 levels and mortality. There was no significant relation between CRP and IL-6 levels and development of acute heart failure regarding the inclusion criteria in the study. The use of cutoff value may be chosen to maximize sensitivity and specificity, as required. CRP was found to be sensitive but not sufficiently specific with low NPV and high PPV in predicting the outcome. IL-6 was found to be sensitive but more specific than CRP with low NPV and high PPV in predicting the outcome. The use of combined CRP and IL-6 levels in predicting the outcome had improved the specificity but the sensitivity was decreased. From the current study, it was noticed that the serum CRP and serum IL-6 levels in sera of patients with AECOPD who needed ICU admission, measured on admission, may provide a useful means in predicting the clinical course and outcome of these patients.

**Conflict of interest**

None declared.

**References**


