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A PROSPECTIVE STUDY OF SERUM PROCALCITONIN AND CRP AS A SEVERITY OF ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Internal Medicine

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ABSTRACT

Background and Aim: The level of procalcitonin (PCT) and high-sensitivity C-reactive protein (CRP) in the acute exacerbation of COPD (AECOPD) was investigated. Aim of the study is to evaluate the method of PCT guided therapeutic strategy for patients with AECOPD and its importance on the planning of NIV treatment and to evaluate other possible predictors. **Method:** Prospective study was conducted among 100 patients admitted (in-patient) with acute exacerbation of COPD under the department of General Medicine, Mahatma Gandhi Hospital to study the serum procalcitonin and crp as a severity of acute exacerbation of chronic obstructive pulmonary disease **Results:** Comparison of Procalcitonin(ng/mL) among the study subjects according to NIVoutcome and it was found that mean±SD values of procalcitonin (ng/mL) among subjects having NIV outcomes as success was 0.68±0.29 and in failure cases was 2.03±0.47. the results were statistically significant with p value <0.01. Comparison of C-reactive protein (mg/Ml) among the study subjects according to NIVoutcome and it was found that mean±SD values of C-reactive protein (mg/Ml) among subjects having NIV outcomes as success was 9.14±5.75 and in failure cases was 37.82±17.01. The results were statistically significant with p value <0.01. **Conclusion:** The serum PCT levels, and CRP levels can be used as an auxiliary indicator in diagnosis of acute exacerbation of COPD. The measurement of serum PCT levels and CRP levels of AECOPD patients may be helpful to guide treatment.

KEYWORDS

Procalcitonin; PCT; COPD; Chronic obstructive pulmonary disease; AECOPD; COPD exacerbation

INTRODUCTION:

Chronic obstructive pulmonary disease (COPD) was initially defined as 'a disease state characterized by chronic airflow limitation due to chronic bronchitis and emphysema'. Chronic bronchitis has been defined in clinical terms as 'the presence of chronic productive cough for at least 3 consecutive months in 2 consecutive years. Other pulmonary or cardiac causes of chronic productive cough must be ruled out'. Emphysema, on the other hand, has been defined by its pathologic description: 'an abnormal enlargement of the air spaces distal to the terminal bronchioles accompanied by destruction of their walls and without obvious fibrosis'.

The prevalence of COPD reported in different population based studies from India is highly variable. The disease is distinctly more common in males. The prevalence was found to increase with increasing age, especially in the males, in those with more than 20 pack–yrs of smoking and in low income subjects. The male to female ratio had varied from 1.32:1 to 2.6:1 in different studies with a median ratio of 1.6:1.

Exacerbations and comorbidities contribute to the overall severity in individual patients. Globally, COPD has emerged as the major cause of morbidity and mortality expected to become the 3rd most leading cause of death and the 5th leading cause of loss of 'Disability Adjusted Life Years' (DALYs) as per projection of the Global Burden of Disease Study (GBDS). According to the projections, COPD will be the seventh leading cause of disability-adjusted life-years lost worldwide in 2030. However, COPD is not just a pulmonary disease; it is also associated with systemic manifestations and co-morbid conditions.

An exacerbation of COPD is an acute event characterized by a worsening of the patient's respiratory symptoms that is beyond normal day to day variations and leads to a change in medication. COPD exacerbations cause hospital admissions, morbidity and mortality, directly leading to the deterioration of health related quality of life. It is generally believed that exacerbations are important targets for treatments and prevention of disease progression of COPD.

The bacterial infection plays an important role in the exacerbation of COPD patients. Quick and accurate recognition of these patients along with aggressive and prompt intervention may be the only action that prevents frank respiratory failure.

C-reactive protein (CRP), procalcitonin (PCT), interleukin-6 (IL-6) are objective and quantitative indicators, which can be quickly completed the detection.

Procalcitonin (PCT) is a peptide precursor of hormone calcitonin, the later being involved with calcium homeostasis. It is composed of 116 amino acids and is produced by the parafollicular cells (C cells) of the thyroid and by the neuroendocrine cells of the lung and the intestine. The level of procalcitonin raises in a response to a proinflammatory stimulus, especially of bacterial origin. The investigations identified PCT as part of the complex pro-inflammatory response of the innate immune system. In vitro stimulation of macrophages with either bacteria or endotoxin results in rapid synthesis and release of tumor necrosis factor, (TNF), interleukin (IL) -1 and IL-6. Serum PCT serum levels are detectable as early as 3–4 h after the invasion, which is much earlier than the increase in the C-reactive protein level or erythrocyte sedimentation rate. Thus far, elevated PCT levels have not been noted for other inflammatory conditions, such as inflammatory bowel disease, temporal giant cell arteritis, polyarteritis nodosa, systemic lupus erythematosus, gout, and Still disease. Available data indicate that PCT levels are not influenced by therapy with glucocorticoids or nonsteroidal anti-inflammatory agents. PCT levels do not increase or increase only modestly in patients with infection due to respiratory viruses.

AIM AND OBJECTIVES:

To evaluate the method of PCT guided therapeutic strategy for patients with AECOPD.

1. To compare PCT levels, CRP levels, in patients with AECOPD with NIV failure or success.
2. To determine the predictive levels of serum PCT, CRP, and PaCO2 for assessing the need of IMV therapy.

MATERIAL AND METHODS:

- Type of Study: A prospective study
- Place of Study: Mahatma Gandhi Medical College & Hospital, Jaipur
- SELECTION OF CASES: All cases of Acute exacerbation of copd
- SAMPLE SIZE: 100 patients admitted (in-patient) with acute exacerbation of copd under the department of General Medicine, Mahatma Gandhi Hospital.

Inclusion criteria:

- Age 40-80 years
- Male or female
- Copd diagnosed according to gold guidelines.
- history of smoking now or in the past.
- Informed consent obtained

Exclusion criteria:

- Unstable cardiovascular disease such as uncontrolled high blood pressure, congestive cardiac failure, angina etc.
- Severe hepatic or renal dysfunction, malnutrition, malignant tumor, and severe anemia.
- History of taking regular corticosteroids or other immuno suppressive agents.
- Participation in other studies within past 6 weeks.
- Infections other than pneumonia.

Exclusion criteria related to lung:

- Diagnosis of other chronic lung disease (such as bronchiectasis, cystic fibrosis, asthma, interstitial lung disease, lung cancer etc.), a history of pulmonary bulla, or pneumonectomy or other lung surgery.
- Active pulmonary tuberculosis
- History of chest radiation therapy, pulmonary rehabilitation therapy, or other therapies before attending this study

RESULTS:

Table 1: Symptoms among the study subjects

Symptoms	N	%
Cough	23	23
Breathlessness	57	57
Pedal edema	14	14
Fever	12	12
Chest tightness	10	10

Table 1, shows distribution of subjects according to symptoms and it was found that 57% of subjects had breathlessness , 23% had cough, 14% had pedal edema, 12% had fever & 10% had chest tightness.

Table 2: Spirometry among the study subjects

Spirometry	Mean	SD
FEV1 (L)	1.33	0.68
FEV1 (%N)	48.4	12.43
Ratio of FEV1 to FVC	0.61	0.14

Table 2 shows spiromteric analysis of study subjects and it was found that mean±SD value of FEV1 was 1.33±0.68 and ratio of FEV1 to FVC was 0.16±0.14

Table 3: Comparison of Procalcitonin(ng/mL) among the study subjects according to NIV outcome

NIV	Procalcitonin (ng/mL)		t test	p value
	Mean	SD		
Success	0.68	0.29	14.93	<0.01*
Failure	2.03	0.47		

*: statistically significant

Table 3 shows comparison of Procalcitonin(ng/mL) among the study subjects according to NIVoutcome and it was found that mean±SD values of procalcitonin (ng/mL) among subjects having NIV outcomes as success was 0.68±0.29 and in failure cases was 2.03±0.47. the results were statistically significant with p value <0.01.

Table 4: Comparison of C-reactive protein (mg/Ml) among the study subjects according to NIV outcome

NIV	C-reactive protein (mg/Ml)		t test	p value
	Mean	SD		
Success	9.14	5.75	10.05	<0.01*
Failure	37.82	17.01		

*: statistically significant

Table 4 shows comparison of C-reactive protein (mg/Ml) among the study subjects according to NIV outcome and it was found that mean±SD values of C-reactive protein (mg/Ml) among subjects having NIV outcomes as success was 9.14±5.75 and in failure cases was 37.82±17.01. The results were statistically significant with p value <0.01.

Table 5: Predictive levels of serum PCT and CRP for assessing the need of IMV therapy

Parameters	PCT (ng/ml)	CRP (mg/ml)
Cut off	0.34	16
Sensitivity (%)	82.5	77.3
Specificity (%)	83.8	92.6
AUC (95%CI)	0.87 (0.76–0.93)	0.85 (0.77–0.90)

Table 5 shows Predictive levels of serum PCT and CRP for assessing the need of IMV therapy and it was found that cut off value of PCT & CRP was 0.34 (ng/ml) & 16 (mg/ml) respectively. 82.5% and 83.8% were sensitivity and specificity of PCT whereas 77.3% and 92.6% were sensitivity and specificity of CRP. AUC was checked at 95% CI ; PCT value was 0.87 whereas CRP value was 0.85.

DISCUSSION

Chronic obstructive pulmonary disease (COPD) is a preventable and treatable disease characterized by the airflow obstruction. COPD mainly affects the lungs, but can also bring adverse effects to other parts of the body. Due to the high morbidity, mortality, and heavy social and economic burden on the family of patients, COPD has become a critical threat to public health. There are many etiological factors behind the acute exacerbations of chronic obstructive pulmonary disease (AECOPD) and the pathogenesis has been revealed to be complex in these cases.

Many modalities have been used for the early diagnosis of COPD. Currently, inflammatory markers can also be used for COPD. These markers include serum procalcitonin (PCT), serum interleukin-6 (IL-6), IL-8 and IL-18, tumor necrosis factor-α (TNF-α), copeptin, soluble CDl4, macrophage inflammatory protein-1α (MIP-1α) and white blood cell count (WBC). Among the above-mentioned inflammatory markers, C-reactive protein (CRP) & PCT are commonly used in clinical practice

Hence the present study was conducted among 100 patients admitted (in-patient) with acute exacerbation of COPD under the department of General Medicine, Mahatma Gandhi Hospital from March 2021 to Sep 2022, to study the serum procalcitonin and CRP as a severity of acute exacerbation of chronic obstructive pulmonary disease.

Gender

71% of subjects were male and 29% of subjects were female in the present conducted study.

In a study done by Halim AA et al[42] (2015) it was found that 21% of subjects were male, Daubin et al [39](2008) stated 67% of male subjects and the results were similar to the current study marking the severity of lung diseases in male subjects.

Age

Maximum subjects (54%) were under the age group of 51 to 60 years and least (9%) were in the age group of 31-50 years. 37% subjects had age more than 60 years.

Wang et al[51] (2019) stated that maximum (70%) subjects were in the age group of 51-60 years and the results were similar to our study showing the incidence of lung diseases in this age group.

Smoking & Biomass Exposure

53% of total subjects currently had deleterious habit of smoking with male predominace of 43%. Remaining 31% had habit of smoking in the past. Biomass exposure was found in 14% of subjects with 10% of female predominance.

Halim et al[42] (2015) showed among the AECOPD subjects 20% had habit of smoking and 8% were current smokers these results were

dissimilar to our study where percentage of smokers were greater than ex smokers and this may be due to difference in sample size among both the studies.

Bmi

In the current study 43% of subjects had BMI between 18.5-24.9 kg/m^2, 36% had 25-29.9 and 21% had BMI greater 29.9 kg/m^2.
In a study done by Wang et al[51] the mean BMI of subject was found to be 25.2±2.7 (kg/m^2) and the results were quite similar to our study.

Location

Out of total 100 subject 63% were living in urban area whereas 37% were living in rural area suggesting the occurrence of lung diseases more in subjects living in urban population due to extra exposure to polluted environment as compared to ones living in village type area.

COPD Classification

COPD among the study subjects according to GOLD criteria and it was found that maximum number of subject (37%) fall under the Gold B criteria followed by 28% (Gold C), 26% (Gold A) & 9% (Gold D).

Twenty nine patients (74%) had severe or very severe COPD in a study by Daubin et al[39] (2008), & 76 % of subjects were in the criteria of GOLD III stated Stolz et al[38] (2007) in their study.and the results were similar to our study in which most of the patients fall in the category of GOLD B & C and the reason is these are the stages where lung disease start showing problems in a body and clinical findings can be derived by various investigations.

AECOPD Classification

In the present study subjects were distributed according to AECOPD using Anthonisen criteria. 46 % of subjects come under category I, 23% were in category II & 31 % were in category III.

Connors et al[64] (1996) in their study got most subjects in category I (47.9%), 21.6% in category II & 30.5% in category III. These results were similar to our study.

Co-Morbidities

In the current study following co morbidities were found- 19% subjects were dealing with problem of hypertension, 13% had diabetes mellitus, 5% had gastritis, ulcer, GERD, 4% had coronary artery disease and 2% had post tuberculosis.

Daubin et al[39] (2008) showed hypertension (38%) & diabetes mellitus (33%) as the most common co morbidities with AECOPD which was common in the current study results also.

Other Symptoms

The other symptoms found in subjects were breathlessness (57%) , cough (23%), pedal edema (14%), fever (12%) & chest tightness (10%).

Dyspnea, cough, rales, wheezing & fever were some of the other symptoms present in other studies in past literature as these symptoms accompany the lung diseases in one or another subject.

Spirometry

Spiromteric analysis of study subjects shows that mean±SD value of FEV1 (L) was 1.33±0.68, FEV1 % was 48.4±12.43 and ratio of FEV1 to FVC was 0.16±0.14.

The mean value of FEV1, (L) was 0.892 ± 0.397 & FEV1, % predicted was 39.9 ±16.9 in a study done by Gao et al[46] (2017) and these results were dissimilar to our study.

NIV

NIV outcome of study subjects of the current research showed that success rate was 74% and failure rate was 26%.

Study done by Wang et al[51] in 2019 showed the success rate of 70% among NIV subjects and a 30% of failure rate and results show similarity to our findings and reason is after the procdure the survival rate of subjects is increased .

PROCALCITONIN

Mean±SD value of procalcitonin (ng/mL) among the study subjects was 1.38±0.67. Comparison of Procalcitonin(ng/mL) to NIVoutcome revealed mean±SD values of procalcitonin (ng/mL) among subjects having NIV outcomes as success was 0.68±0.29 and in failure cases was 2.03±0.47. The results were statistically significant with p value <0.01.

Serum PCT, levels were higher, in the NIV failure group compared with the NIV success group (all P<.05) in a study by Wang et al[51] (2019). Rammaert et al [65] showed high mortality rates in patients whose PCT levels were >0.24 ng/mL. In another study, PCT levels >0.25mg/L in patients with COPD treated at the ICU were found to be related with mortality

C-reactive protein

Mean±SD value of C-reactive protein(mg/Ml) among the study subjects was 16.23±13.81

Comparison of C-reactive protein(mg/Ml) to NIVoutcome revealed mean±SD values of C-reactive protein(mg/Ml) among subjects having NIV outcomes as success was 9.14±5.75 and in failure cases was 37.82±17.01. The results were statistically significant with p value <0.01.

In agreement to previous studies, (Dev D et al[66], Jochberger S et al[67]) CRP levels were significantly elevated at the exacerbation and decreased substantially thereafter. Elevated CRP is known to be a predictor of adverse events in cardiovascular disease and to be associated with decline in lung function and worsening of chronic COPD.

Need Of IMV Therapy

Predictive levels of serum PCT and CRP for assessing the need of IMV therapy shows that cutoff value of PCT & CRP was 0.34 (ng/ml) & 16 (mg/ml) respectively. 82.5% and 83.8% were sensitivity and specificity of PCT whereas 77.3% and 92.6% were sensitivity and specificity of CRP. AUC was checked at 95% CI ; PCT value was 0.87 whereas CRP value was 0.85.

PCT cut-off value for has been determined to be 0.10 ng/mL in research of Pazarli AC et al (2012). The cut off values to achieve the highest Youden index were 0.31 ng/mL for PCT (sensitivity, 83.3%; specificity, 83.7%), 15.0mg/mL for CRP (sensitivity, 75.6%; specificity, 93.0%). The area under the curve (AUC) was 0.854 (95%CI: 0.793–0.914) for PCT, 0.849 (95% CI: 0.787–0.911) for CRP as revelaed by Wang et al[51] (2019) . Hurst et al reported that systemic biomarkers were not helpful in predicting the severity of AECOPD. In the present study, serum PCT levels, CRP levels, accurately predicted the need of IMV treatment. Each parameter itself had accurate diagnostic ability, but combining the measurements increased the AUC, which is a very significant value.

CONCLUSION

In conclusion, the serum PCT levels, and CRP levels can be used as an auxiliary indicator in diagnosis of acute exacerbation of COPD. The measurement of serum PCT levels and CRP levels of AECOPD patients may be helpful to guide treatment.

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