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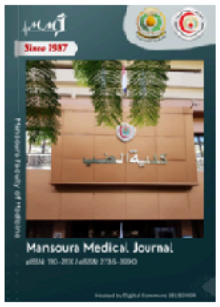

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# Association between serum procalcitonin level with exacerbation severity in chronic obstructive pulmonary disease patients

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ORIGINAL STUDY

# Association Between Serum Procalcitonin Level With Exacerbation Severity in Chronic Obstructive Pulmonary Disease Patients

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**Abstract**

*Background*: **There is a significant impact on morbidity, mortality, and quality of life due to chronic obstructive pulmonary disease (COPD) exacerbations. Individuals with acute exacerbation of COPD had considerably higher mean serum procalcitonin (PCT) levels compared to individuals with stable COPD, according to previous investigations.**

*Objective*: **This study aimed to assess whether PCT levels were associated with the severity of exacerbations in patients with COPD.**

*Patients and methods*: **Thirty-nine patients who were suffering from an acute exacerbation of COPD were included. Included patients were classified as having either acute respiratory failure non life threatening or acute respiratory failure life threatening. Serum PCT level was measured.**

*Results*: **PCT serum levels were not substantially associated with the severity of exacerbation in studied patients ($P = 0.4$). There was no correlation between PCT level and pack-year index, modified medical research council dyspnea, COPD assessment test, exacerbation history, exacerbation severity, respiratory rate, or $pCO_2$ level.**

*Conclusion*: **The results of our research proved a nonsignificant association between PCT level and exacerbation severity of COPD patients.**

*Keywords:* Chronic obstructive pulmonary disease, Exacerbation, Exacerbation severity, Procalcitonin

## 1. Introduction

The hormone calcitonin's precursor, procalcitonin (PCT), has been used as a biomarker for the identification of bacterial infection or sepsis and can tell bacterial pneumonia apart from viral pneumonia (Meynaar *et al.*, 2011). In contrast to viral infections and other inflammatory diseases, bacterial infections were shown to have greater PCT levels (Wacker *et al.*, 2013). Antibiotic resistance, on the other hand, calls for increased efforts to limit antibiotic misuse. Antibiotics are commonly administered for acute respiratory tract infections even though viruses, not bacteria, are the most common cause of these infections (Samsudin and Vasikaran, 2017). There is a significant impact on morbidity, mortality, and quality of life due to chronic obstructive pulmonary disease (COPD) exacerbations and comorbidities (Donaldson *et al.*, 2005).

Inadequate knowledge exists on the causes and effects of severe COPD exacerbations despite the disease's clinical and societal importance. A higher risk of exacerbation is connected with the acquisition of novel bacterial strains and rates of infection with bacteria (Sethi and Murphy, 2001) and viruses (Rohde *et al.*, 2003) are increased during exacerbations (Sethi *et al.*, 2002).

It has been shown that not all individuals respond equally to antibiotics when they are used to treat COPD exacerbations; hence, there is a need for biomarkers that could potentially identify such occurrences (Pandey *et al.*, 2019).

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Therefore, this study aimed to assess whether PCT levels were associated with the severity of exacerbations in patients with COPD.

## 2. Patients and methods

Thirty-nine patients who were admitted to the Chest Medicine Department, Mansoura University Hospitals (during the period from September 2022 to March 2023) and suffering from an acute exacerbation of COPD were included in this cross-sectional study. Our University's institutional review board gave its stamp of approval for this study (R.22.09.1825). Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2022 (Venkatesan, 2022) criteria were used to diagnose COPD. Patients with no respiratory failure or conditions such as pneumonia, extrapulmonary infections, active malignancy, recent surgery, severe trauma, or a history of either were not included.

Included patients were classified as having either an acute respiratory failure that is not life threatening or life threatening respiratory failure according to GOLD 2022 (Venkatesan, 2022).

Participants' demographic information was recorded, including their age, sex, pack-year smoking index, COPD assessment test (CAT), and modified medical research council dyspnea score (mMRC).

Enzyme-linked immunosorbent assay kits (Bioassay Technology Laboratory, Jiaxing, Zhejiang, China) were used to determine serum PCT concentrations (ng/ml).

### 2.1. Statistical analysis

The information was analyzed using SPSS V.26 (Chicago, USA). Continuous data was presented as the mean (SD) or median (minimum–maximum) depending on the outcomes of the Shapiro–Wilk test for the assumption of normal data distributions. The data was reported numerically (as a percentage) for the categories. Significance testing was performed using the $\chi^2$ and Fisher's exact tests for categorical variables, Welch's $t$ test for parametric data, and the Mann–Whitney $U$ test for nonparametric variables. Using Spearman's correlation, we analyzed whether or not there was a connection between PCT and other factors. The 5% cutoff for significance was decided upon.

## 3. Results

This study involved 39 male COPD patients with acute exacerbation (mean age, 65 years). The severity of their exacerbation was life threatening in 51.3% of cases. However, 48.7% of these patients manifested with acute respiratory failure non life threatening. Regarding COPD classification, all patients in the study were placed in group D. Regarding the mMRC score, 64.1% of the examined patients had grade 4, 25.6% had grade 3, 10.3% had grade 2, and no enrolled patients with grade 1 or 0. The mean serum PCT concentration among the patients studied was 0.13 ng/ml (Table 1).

Age, pack-year smoking index, and PCT serum level were not substantially associated with the severity of exacerbation in patients studied ($P = 0.4$). Nonetheless, a significant association was found between exacerbation severity and both CAT and mMRC score ($P = 0.001$ and 0.03, respectively) (Table 2).

Regarding the association between the serum PCT level and patients' characteristics, there was no correlation between PCT level and pack-year index, mMRC dyspnea score, CAT, exacerbation history, exacerbation severity, respiratory rate, or $pCO_2$ level (Table 3).

## 4. Discussion

The GOLD recommendations suggest using antibiotics for treating moderate to severe acute exacerbations of COPD (Pauwels *et al.*, 2001). Although purulent sputum and the growth of bacterial pathogens suggest infection, pinpointing the root cause of acute exacerbations can be difficult due to the possibility of chronic colonization. It has been suggested that measuring serum PCT can help differentiate bacterial infection from infection due to viruses or other noninfectious reasons (Falsey *et al.*, 2012).

*Table 1. Characteristics of the studied patient.*

| | $N = 39$ [$n$ (%)] |
|---|---|
| Age (years) (mean ± SD) | 65.5 ± 10 |
| Pack-year index median (minimum–maximum) | 50 (0–600) |
| CAT (mean ± SD) | 29.7 ± 6.5 |
| mMRC 0/1/2/3/4 | 0/0/4/10/25 (0/0/10.3/25.6/64.1) |
| Exacerbation severity | |
| ARF nonlife threatening | 19 (48.7) |
| ARF life threatening | 20 (51.3) |
| Exacerbations number/last year median (minimum–maximum) | 3 (1–6) |
| Exacerbations number/year need hospitalization median (minimum–maximum) | 1 (1–3) |
| Serum PCT level (ng/ml) median (minimum–maximum) | 0.13 (0.01–0.3) |

ARF, acute respiratory failure; CAT, COPD assessment test; mMRC, modified medical research council dyspnea score; PCT, procalcitonin.

*Table 2. Association between exacerbation severity and characteristics of the studied patients.*

| Parameters | ARF nonlife threatening ($N = 19$) | ARF life threatening ($N = 20$) | |
|---|---|---|---|
| Age (years) (mean ± SD) | 64.3 ± 10 | 66.9 ± 9.5 | *t*: −0.6 *P*: 0.4 |
| CAT mean ± SD | 26.3 ± 7.2 | 32.9 ± 3.7 | *t*: −3.6 *P*: 0.001 |
| mMRC [*n* (%)] | | | |
| 2/3 | 10 (71.4) | 4 (28.6) | $\chi^2$: 4.5 *P*: 0.03 |
| 4 | 9 (36) | 16 (64) | |
| Exacerbations number/year need hospitalization median (minimum–maximum) | 1 (1–3) | 1 (1–3) | *Z*: −0.09 *P*: 0.9 |
| Pack-year index median (minimum–maximum) | 50 (0–200) | 50 (20–600) | *Z*: −0.7 *P*: 0.4 |
| Exacerbations number/last year median (minimum–maximum) | 3 (1–6) | 3.5.5 (2–6) | *Z*: −0.7 *P*: 0.4 |
| Serum PCT level (ng/ml) median (minimum–maximum) | 0.09 (0.02–0.02) | 0.1 (0.01–3) | *Z*: −0.7 *P*: 0.4 |

CAT, COPD assessment test; mMRC, modified medical research council dyspnea score; PCT, procalcitonin.

*Table 3. Correlation between serum procalcitonin level and characteristics of the studied patients.*

| | Serum PCT level | |
|---|---|---|
| | Rho | *P* |
| mMRC | 0.12 | 0.4 |
| CAT | 0.13 | 0.4 |
| Pack-year index | 0.03 | 0.9 |
| Exacerbation severity | 0.11 | 0.4 |
| Exacerbations number/year | −0.2 | 0.06 |
| Exacerbations number/year need hospitalization | −0.2 | 0.1 |
| Respiratory rate | 0.1 | 0.5 |
| $pCO_2$ | −0.06 | 0.7 |

CAT, COPD assessment test; mMRC, modified medical research council dyspnea score; PCT, procalcitonin.

Individuals with acute exacerbation of COPD had considerably higher mean serum PCT levels compared to individuals with stable COPD, according to previous investigations (Pandey *et al.*, 2019; Halim and Sayed, 2015; Tasci *et al.*, 2008). In contrast to Pandey *et al.* (2019), where the mean PCT level was 1.3 ng/ml, we found that the median PCT level was 0.13 ng/ml. The omission of cases with pneumonia from our study may have led to this discrepancy in PCT levels. COPD patients admitted with pneumonia had a PCT level of 0.493 ng/ml (0.131–1.471) in Daubin *et al.* (2009).

Cases with pneumonia had greater PCT levels than those with acute COPD exacerbation, according to a study by Falsey *et al.* (2012). However, with a 0.25 ng/ml threshold for bacterial infection, there was little difference between viral and bacterial infection in patients with acute COPD exacerbation. However, Falsey *et al.* (2012) did not use GOLD criteria to categorize the severity of COPD cases' symptoms.

Pandey *et al.* (2019) also identified greater levels of PCT in individuals with COPD who had experienced multiple exacerbation events leading to hospitalization over the previous year. On the other hand, we discovered no statistically significant association between PCT concentration and past episodes of exacerbation.

In this study, we examined the association of PCT level with the exacerbation severity in patients with group D COPD. Our results showed a nonsignificant association between PCT serum level and severity of COPD exacerbation with respiratory failure. However, patients with no respiratory failure exacerbations were not present in our study. In contrast to our study, Halim and Sayed (2015) observed a statistically significant difference in PCT serum level between acute COPD exacerbation patients that needed ventilatory support and those who did not need mechanical ventilation.

Mortality and readmission rates from an acute exacerbation of COPD were greater in the PCT-positive group than in the PCT-negative group in the study by Gong *et al.* (2020). Our research was limited, because we did not follow up with our patients. However, in Davies *et al.* (2022), participants whose PCT levels were elevated (>0.25 ng/ml) were found to have a considerably higher risk of requiring ICU admission and a longer-than-usual hospital stay of more than 7 days. However, PCT levels were not linked to the readmission rate.

The small sample size, the absence of a non-respiratory failure exacerbation group, and the lack of patient follow-up were all limitations of our study.

### 4.1. Conclusion

Our research proved a nonsignificant association between PCT level and exacerbation severity of COPD patients.

## Conflicts of interest

There are no conflicts of interest.

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