Section: Respiratory Medicine

Original Research Article

ROLE OF C-REACTIVE PROTEIN LEVELS IN PREDICTING BACTERIAL VS. NON-BACTERIAL EXACERBATION IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Abstract

Background: COPD is a chronic inflammatory lung disease that causes obstructed airflow from the lungs. It is a major cause of death and disability worldwide. Exacerbations are acute episodes of worsening respiratory symptoms that can lead to hospitalization and even death. The cause of exacerbations is complex and thought to involve a combination of factors, including host immune response, respiratory viruses, airway bacteria, and pollution. **Aim:** The aim of this study was to investigate the role of serum C-reactive protein (CRP) levels in differentiating bacterial and non-bacterial exacerbations in patients with acute exacerbations of COPD (AECOPD). **Materials and Methods:** This hospital-based cross-sectional study was conducted at the Government Thanjavur Medical College, Thanjavur, India, from December 2021 to May 2022. All COPD patients who were diagnosed according to the GOLD guidelines and were over 40 years of age were included in the study with their informed and written consent. At admission, participants underwent blood investigation (serum CRP) and sputum culture for non-tuberculous mycobacteria. **Results:** A total of 80 COPD patients were included in the study, of whom 73 were males and 7 were females. Fifty-five patients were smokers and 25 were non-smokers. Fifty-five patients had bacterial AECOPD. The mean serum CRP levels were significantly higher in the subgroup with bacterial AECOPD than in non-bacterial AECOPD. The most common non-tuberculous mycobacteria isolated from sputum were Pseudomonas aeruginosa (18 patients), Klebsiella pneumoniae (16 patients), Acinetobacter (11 patients), Enterobacter (6 patients), Escherichia coli (2 patients), Haemophilus influenzae (1 patient), and Klebsiella oxytoca (1 patient). The ideal cut-off point for distinguishing bacterial AECOPD from non-bacterial AECOPD was 18.82 mg/L. **Conclusion:** In adult patients with AECOPD symptoms, an elevated serum CRP level of >18.82 mg/L is a useful clinical marker for bacterial exacerbation and may guide antibiotic therapy.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) encompasses two distinct conditions: chronic bronchitis and emphysema. Chronic bronchitis is defined as "the presence of a daily productive cough lasting for a minimum of three consecutive months over two consecutive years".[1,2] In 1962, the American Thoracic Society (ATS) provided a definition for emphysema as "an anatomical alteration of the lung characterized by abnormal enlargement of the air spaces beyond the terminal, non-respiratory bronchioles, accompanied by destructive changes in the alveolar walls".[3] In 1984, the National Heart, Lung and Blood Institute described emphysema as "a lung condition characterized by abnormal, permanent enlargement of airspaces distal to the terminal bronchiole, accompanied by the destruction of their walls, and without obvious fibrosis".[4] McDonough et al. have further elucidated that "the permanent enlargement of the distal airspaces may serve merely as a structural biomarker, resulting from secondary effects of small airway inflammation and destruction".[5] These definitions highlight that COPD involves not only airway abnormalities but also airspace abnormalities.

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The prevalence of COPD varies significantly depending on the diagnostic and classification methods employed. Typically, COPD manifests after the age of 40, with its incidence increasing as individuals age. The following chart illustrates that the prevalence rate rises with advancing age. Remarkably, COPD stands as the fourth leading global cause of death, with projections indicating that it will become the third leading cause in the future.

An exacerbation of COPD is defined as "a sustained deterioration in the patient's condition, extending beyond normal day-to-day variations, with an acute onset that necessitates modifications to regular medication in individuals with underlying COPD".[6]

C-reactive protein (CRP) belongs to the pentraxin family of proteins and is primarily synthesized in the liver. Serum CRP levels surge in response to acute infections, inflammatory conditions, and trauma, typically exceeding 10 mg/l, alongside elevated erythrocyte sedimentation rates (ESR). Hepatocytes are the main source of CRP production, with cytokines, particularly IL-6 and IL-1, regulating CRP at the transcriptional level. The CRP gene is located on chromosome 1's short arm.

MATERIALS AND METHODS

This cross-sectional study was conducted at Government Thiruvotteswarar Hospital of Thoracic Medicine, Otteri and Government Kilpauk Medical College, Kilpauk, Chennai -10, Tamil Nadu, India. This study lasted 6 months (Feb 2022 – July 2022). The sample size of this study was 80 patients. All COPD patients are diagnosed as defined in the GOLD guidelines and are above 40 years old. After the informed written consent by the patients, the study was preceded by the approval of the local ethical committee. All the patients were selected based on the inclusion and exclusion criteria and were taken into the study with their informed and written consent.

All the participants must undergo blood investigation (Serum CRP) and Sputum for Non-tuberculous culture sensitivity at admission. An early morning deep-coughed sputum sample was collected from all participants according to a standard guideline. Within 24 hrs of admission, patients were asked to collect sputum into a sterile, wide-mouthed container with a screw cap after rinsing the mouth twice with water and antiseptic solution to avoid oral contamination of the sample collected. The relationship between Serum CRP and the bacterial colonies in sputum was assessed and interpreted.

Data collected was analysed using IBM SPSS Statistics 23.0. Descriptive stats, frequency, and percentages analysed categorical variables, while mean and SD assessed continuous ones. For comparing independent groups, the Independent sample t-test was employed. Pearson's Correlation examined variable relationships, with a significance level set at $p < 0.05$.

RESULTS

In 80 COPD patients, <50 years (3.8%), 51-60 years (16.8%), 61-70 years (50.0%), 71-80 years (22.5%), and >80 years (5.0%).

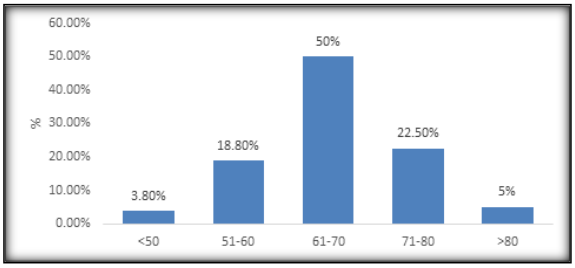

Figure 1: Distribution of Age group

The distribution by gender shows that females account for 8.8%, while males make up 91.3%.

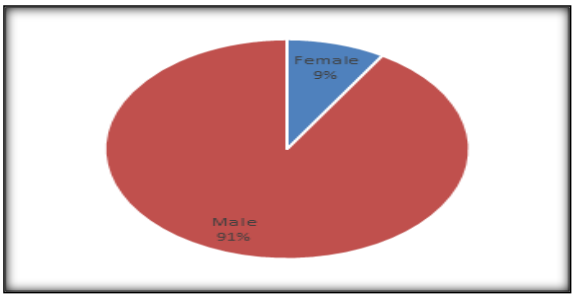

Figure 2: Distribution of Gender

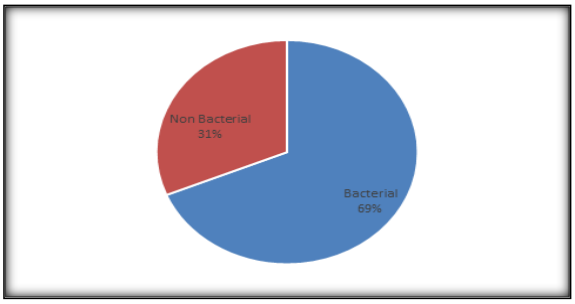

Figure 3: Distribution of Bacterial vs. non-bacterial Exacerbation

The distribution of NT C/S results reveals the following percentages for different pathogens: Acinetobacter baumannii (21.8%), Enterobacter cloacae (10.9%), Escherichia coli (3.6%), Haemophilus influenza (1.8%), Klebsiella oxytoca (1.8%), Klebsiella pneumonia (27.3%), and Pseudomonas aeruginosa (32.7%).

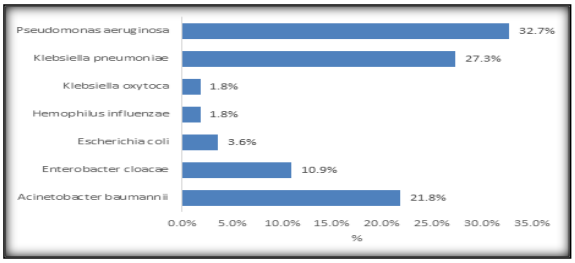

Figure 4: Distribution of NT C/S

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Table 3 shows that the comparison of Serum CRP Levels with NTCS by Independent sample t-test was t-value=41.153, p-value=0.0005<0.01, which shows a high statistical significance difference at $p < 0.01$ level.

Table 1: Comparison of Serum CRP Levels with NTCS by Independent sample t-test

Variable	NTCS	N	Mean	SD	t-value	p-value
Serum CRP Levels	Bacterial	55	18.82	3.14	41.153	0.0005 **
	Non Bacterial	25	0.82	0.55		

DISCUSSION

This study indicates that a CRP level of 18.82 ± 3.14 mg/L serves as a valuable biomarker for detecting bacterial infections, particularly in patients experiencing Acute Exacerbations of Chronic Obstructive Pulmonary Disease (AECOPD).7 Our research also noted that individuals with positive sputum cultures tended to exhibit elevated CRP values, possibly due to bacterial exacerbations inducing more extensive systemic damage compared to nonbacterial exacerbations. Notably, Hurst et al. found a direct correlation between systemic inflammatory response and the presence of bacterial pathogens, with exacerbations featuring potentially pathogenic microorganisms (PPMs) in sputum demonstrating significantly increased systemic inflammation.[7]

In our geographical area, Pseudomonas aeruginosa, the predominant causative agent, played a substantial role in 27.3% of exacerbations, while Hemophilus influenzae was only observed in 1.8% of exacerbations, differing from other studies.[8,9] This variance might arise from varying antibiotic pressures in different regions and the exclusion of pneumonia patients. For instance, in cases of community-acquired pneumonia, CRP levels were higher for Klebsiella pneumophila.[10,11] Nevertheless, in patients with AECOPD, no significant differences in CRP values were observed among different pathogens, suggesting that bacterial pathogens were associated with the host's inflammatory immune responses. Furthermore, colonization-induced inflammation likely contributed to COPD development, as evidenced in stable COPD patients, aligning with our study findings.

Several limitations merit acknowledgment. Firstly, our study exclusively focused on bacterial cultures, potentially underestimating the prevalence of atypical pathogens in AECOPD cases with mucoid sputum. Future investigations should encompass atypical pathogens to validate these results. Secondly, we employed a noninvasive diagnostic approach; therefore, invasive diagnostic procedures might yield different outcomes. Nonetheless, our study demonstrated the clinical reliability of spontaneously expectorated sputum culture as a method for assessing the presence and type of bacterial infections.[12] Thirdly, we lacked comprehensive information regarding patient treatments and did not thoroughly explore the relationships between clinical outcomes and baseline CRP levels. While a weak correlation was observed, further investigation with a larger sample size is warranted. Finally, our study exclusively included hospitalized patients, limiting the generalizability of our findings to exacerbations managed at home.

CONCLUSION

In adult patients with AECOPD symptoms, an elevated serum CRP level of >18.82 mg/L is a useful clinical marker for bacterial exacerbation and may guide antibiotic therapy.

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