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ORIGINAL RESEARCH

To assess the function of CRP as a biomarker in COPD acute exacerbation

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ABSTRACT

Aim: The purpose of this research is to assess the function of CRP as a biomarker in COPD acute exacerbation.

Methods: The Department of Respiratory Medicineconducted this cross-sectional research. After washing their mouths twice with plain water, all patients were advised to collect deep coughed up phlegm into a sterile wide mouth container with a screw cover. The samples were promptly sent to the microbiology laboratory and processed within 30 minutes of being collected. Gram staining was performed on a sputum sample and results were reported using Bartlett's grading method. A appropriate sample was defined as one with a score of 1 or above. Mac Conkey's agar, chocolate agar, and blood agar plates were inoculated with appropriate sputum samples. Standard microbiological procedures established by the American Society for Microbiology were used to identify the isolated organisms. Sputum samples cultured for pathogenic bacteria were classed as Bacterial exacerbations, whereas samples with no pathogenic bacteria or oral commensals were classified as Non bacterial exacerbations.

Results: Among the 100 patients, 65 had bacterial growth on culture and were classed as Bacterial COPD exacerbation. The other 35 instances in which no bacterial growth or oral commensals were found were classed as Non Bacterial COPD exacerbation. Using the crude odds ratio, it was determined that the chances of Bacterial Exacerbation for patients with COPD "≥5 years" are 2.87 (95 percent CI: [1.26,6.88]) times greater than persons with COPD "<5 years." Furthermore, smokers had a 3.77(95 percent CI[1.50,10.28]) greater risk of bacterial exacerbation than nonsmokers. In our investigation, the optimal CRP cut-off point for separating Bacterial COPD patients with Bacterial Exacerbation from those without Bacterial Exacerbation was 8.77 mg/L (sensitivity:97%; specificity:40%; PPV:75%; NPV:87%, AUC:0.77).

Conclusion: Higher CRP levels are related with individuals experiencing Bacterial COPD exacerbations rather than Non Bacterial COPD exacerbations. CRP levels might therefore be utilised to anticipate Bacterial exacerbations and also to recommend antibiotic treatment.

Keywords: CRP, acute exacerbation, COPD

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a prevalent illness condition defined by non-reversible airflow restriction. Acute exacerbations are common in the chronic course of the illness. Anthonisen et al criteria's are the most generally utilised in defining an acute

exacerbation of COPD (AECOPD). [1] AECOPD is evaluated when the prior stable condition worsens with some or all clinical signs such as increased dyspnea, increased sputum volume, and increased sputum purulence. Wheezing, coughing, chest tightness, tachypnea, heart rate of 20% over baseline, drowsiness, or pyrexia may accompany one of these symptoms. Although some of these symptoms may be due to increased airflow restriction, they might also be due to tracheobronchial tree infections. The majority of COPD exacerbations are caused by airway infections. [2] Bacterial infections cause around 50% of exacerbations; however, it is presently unable to distinguish bacterial from nonbacterial causes of acute exacerbations. [3,4]The shift in sputum colour from mucoid to purulent during exacerbations is thought to be caused by neutrophil recruitment in the airways, hence sputum purulence seems to be a reliable diagnostic of bacterial infections. C-reactive protein (CRP) is an inflammatory marker. Following an acute-phase stimulation, its levels may increase 10,000-fold, from!50 g/l to 1500 mg/l, indicating that it has a biological role. [5,6] Several investigations have recently revealed that blood CRP levels are elevated in patients with COPD[7,8], stable COPD (SCOPD)[9], and AECOPD[10], indicating that CRP levels are a sign of AECOPD but not necessarily of bacterial infection. A recent research, however, showed that CRP might be utilised as a measure of severe bacterial infection. CRP's utility as a predictive biomarker in AECOPD patients was studied further in two more trials, one of which suggested that a high blood CRP concentration 14 days after an initial exacerbation might be used to predict repeated exacerbations within 50 days, while the other did not. However, plasma levels of CRP, copeptin, and procalcitonin were all raised during acute exacerbations, with CPR being especially high in Anthonisen type 1 exacerbations. [12,11]

METHODS AND MATERIALS

The Department of Department of Respiratory Medicineconducted this cross-sectional research.

This research comprised 100 COPD patients who presented to our hospital with an acute exacerbation. COPD was characterized as a 70 percent FEV1 to FVC ratio with no substantial bronchodilator reversibility in FEV1 OR FVC (as per Global Initiative for Obstructive Lung Disease guidelines). Acute Exacerbation (AE) of COPD was examined in individuals with a history of COPD and increasing respiratory symptoms such as shortness of breath, cough, wheeze, and changes in sputum volume and colour. Following a comprehensive history and clinical examination, patients were submitted to a chest X-ray, ECG, complete blood count, CRP, and sputum (mucoid, mucopurulent) for culture and sensitivity. In suspected instances of bronchiectasis, a CT chest was performed. The institutional ethics committee granted ethical approval. CRP levels in patient blood samples were evaluated using nephelometric technology and the MISPA I2 specific protein analyzer.

MICROBIOLOGY

After washing their mouth twice with plain water, patients were advised to collect deep coughed up phlegm into a sterile wide mouth container with a screw closure. The samples were promptly sent to the microbiology laboratory and processed within 30 minutes of being collected. Gram staining was performed on a sputum sample and results were reported using Bartlett's grading method. A appropriate sample was defined as one with a score of 1 or above. [13]MacConkey's agar, chocolate agar, and blood agar plates were inoculated with appropriate sputum samples. Standard microbiological procedures established by the American Society for Microbiology were used to identify the isolated organisms. 14 Sputum samples cultured for pathogenic bacteria were classed as Bacterial exacerbations, whereas samples with no pathogenic bacteria or oral commensals were classified as Non bacterial exacerbations.

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STATISTICAL EVALUATION

Data from the research were analysed using descriptive statistics (frequency, percentage, mean, standard deviation) and SPSS statistical software version 24.0, which used the Chi-square test or Fisher's Exact test and the Independence samples t-test. P-values less than 0.05 were deemed statistically significant.

Results

AE were examined in 100 COPD hospitalised patients. Among the 100 patients, 65 had bacterial growth on culture and were classed as Bacterial COPD exacerbation. The other 35 instances in which no bacterial growth or oral commensals were found were classed as Non Bacterial COPD exacerbation. Tables 1 and 2 demonstrate the distribution of participants by age, gender, and duration of COPD.

The majority of the patients in the research were over 60 years old (60 cases (60 percent)), with a male preponderance (70 cases (70 percent)). Diabetes was detected in 22 instances (22 percent) while hypertension was seen in 31 cases (31 percent). Those with COPD for more than 5 years and a history of smoking had a higher risk of bacterial exacerbation. Using the crude odds ratio, it was determined that the chances of Bacterial Exacerbation for patients with COPD "≥5 years" are 2.87 (95 percent CI: [1.26,6.88]) times greater than persons with COPD "<5 years." Furthermore, smokers had a 3.77(95 percent CI[1.50,10.28]) greater risk of bacterial exacerbation than nonsmokers.

Using the Mann-Whitney U-test, it was shown that the median of C- reactive protein levels for Bacterial Exacerbation is considerably higher than for Non-Bacterial Exacerbation. The risk of COPD Bacterial Exacerbation is 50.36 (95 percent CI: [17.58,69.52]) greater in participants with higher CRP levels than in those with normal CRP levels (Table 3). In our investigation, the optimal CRP cut-off point for separating Bacterial COPD patients with Bacterial Exacerbation from those without Bacterial Exacerbation was 8.77 mg/L (sensitivity:97%; specificity:40%; PPV:75%; NPV:87%, AUC:0.77) (95 percent CI: [0.64,0.89]).

Table 1 demographic profile of the patients

Gender	Number	%
Male	70	70
Female	30	30
Age		
Below 60	40	40
Above 60	60	60
Duration of COPD		
Below 5	55	55
Above 5	45	45
Co morbidity		
Diabetic mellitus	22	22
Hypertension	31	31

Table 2 bacterial and non bacterial COPD

	Number	%
Bacterial COPD Exacerbation	65	65
Non-Bacterial COPD Exacerbation	35	35

Table 3: CRP levels in Bacterial COPD exacerbations and Non Bacterial COPD exacerbations

Factor	Overall	Bacterial COPD Exacerbation	Non-Bacterial COPD Exacerbation	P-value
CRPLevels(Mg/L)	48.5[12.48,61.53]	50.36[17.58,69.52]	35.33[4.69,55.31]	0.016*

Table 4: CRP level in COPD patients with Bacterial Exacerbation corresponding to the bacteria isolated.

Organism	Number of cases	Average CRP
Klebsiella	27	60.85
Acinetobacter	4	65.74
Citrobacter	4	70.69
Enterococcus species	5	65.85
Enterobacter species	4	70.36
Moraxella	6	69.12
Non-Fermenting GmNeg Bacilli	7	65.87
Pseudomonas	8	65.22
Staphylococcus	4	71.36
Streptococcus	2	65.74

Klebsiella(27) and pseudomonas(8) were the most common organisms isolated. Table 4 lists the other organisms that were isolated. In terms of median CRP levels, there were no statistically significant variations amongst Bacterial pathogens.

DISCUSSION

CRP is an acute-phase protein that, when increased, indicates an active tissue-damaging activity. As a result, its measurement serves as a quick screening test for active organic illness. Most bacterial infections cause an increase in CRP production, which is a highly early and sensitive response. CRP was also a reliable predictor of the severity of the exacerbations; individuals with high CRP levels. Hospitalization increased fourfold at 100 mg/L. CRP emerges as a useful biological marker for identifying severe exacerbations in COPD patients with advanced illness, which are mostly caused by bacterial infections caused by S. pneumoniae and H. influenza.Acute COPD exacerbations are to blame for the increased morbidity and mortality associated with COPD. They may be caused by a variety of reasons, the most common of which being bacterial or viral infections. [15,16]Early antibiotic treatment, particularly in cases of bacterial exacerbation of COPD, might enhance outcomes in these individuals. Biomarkers are critical in diagnosing the aetiology of exacerbations at the point of treatment, and various studies have been conducted to far to investigate the relevance of biomarkers such as CRP in predicting bacteria exacerbations in COPD patients. [17,18] Our results also shown that a CRP cut off of 8.77 mg/L might aid in the differentiation of these two groups (Bacterial and non-Bacterial COPD AE) with a sensitivity of 97% and specificity of 40%.

Peng et al. studied CRP levels in patients and bacteria isolated from these patients and discovered that Pseudomonas was responsible for exacerbations in 25% of the cases.
[17] Our results are comparable to those of this investigation; bacteria were recovered from individuals with AE COPD who had a high level of CRP in their blood. However, contrary to the findings of Peng et al. Klebsiella was found in 36.76 percent of COPD patients with exacerbations in our research. A recent research also linked an increase in CRP levels to the presence of Bacterial pathogens (both alone and in combination with viral/atypical

microorganisms). [19] We discovered that among the many demographic characteristics, COPD duration and smoking impact the development of exacerbations in patients, but other factors such as age and gender did not have a statistically significant effect. Tobacco use has been identified as a risk factor for the development of COPD exacerbations in COPD patients. [20-22] The CRP cut off at the point of treatment has been used to guide antibiotic prescription and has shown a 20% decrease in antibiotic usage in primary care patients. [19] Another goal of our research might be to utilise the CRP cut off value found in our study to guide treatment in a controlled trial with patients experiencing COPD exacerbations.

CONCLUSION

This research helped to prove that higher CRP levels are connected with individuals experiencing Bacterial COPD exacerbations rather than Non Bacterial COPD exacerbations. CRP levels might therefore be utilised to anticipate Bacterial exacerbations and also to recommend antibiotic treatment.

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