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Correlation of Serum CRP and D-dimer Levels with Cardiac Dysfunction in Patients with Acute Exacerbation of COPD

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Abstract: ***Background:*** Systemic inflammation and cardiovascular risk are linked with exacerbation of chronic obstructive pulmonary disease (AECOPD). Among biomarkers, which have been found to be significant predictors of inflammatory and thrombotic processes that can cause cardiac dysfunction in such patients, is biology C-reactive protein (CRP) and D-dimer. Place and Duration of Study The research was carried out at the Department of Medicine and Pulmonology, Punjab Rangers Teaching Hospital Lahore/Rahber Medical College Lahore from June 2024 to February 2025. ***Objective:*** The current research will aim to determine the association between serum CRP and D-dimer and cardiac dysfunction in acute exacerbation COPD patients. ***Methodology:*** On 288 patients with AECOPD a cross-sectional observational study was carried out. The WHO sample size calculator formula was used to determine the sample size based on prevalence, confidence interval and margin of error. The sampling was done consecutively as non-probability. The demographic and clinical data were collected in the structured proforma. The levels of serum CRP and D-dimer were determined by standard laboratory. The transthoracic echocardiography was used to measure cardiac dysfunction, the left ventricular ejection fraction (LVEF) and the right ventricular functioning. Data analysis was done using statistical software and Pearson correlation and regression analysis was done. ***Results:*** A significant number of patients (288) had a high CRP and D-dimer level. The average level of CRP and D-dimer was significantly higher in patients with cardiac dysfunction as compared to healthy patients ($p < 0.001$). CRP levels were strongly negatively correlated with the LVEF, and the D-dimer levels were strongly correlated with the right ventricular strain and dysfunction. ***Conclusion:*** A strong relationship exists between D-dimer and cardiac dysfunction and serum CRP level in AECOPD patients. These biomarkers could be a great predictor of early detection of high-risk patients and could be used to assist in prompt management plans.

Keywords: AECOPD, COPD, CRP, D-dimer, cardiac dysfunction, inflammation, echocardiography

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a major health problem in the global community which is characterized by persistent symptoms of the respiratory system, as well as by airflow limitation due to the malformations in the airways and alveoli [1]. The acute exacerbations of COPD (AECOPD) are the instances of worsening of breathing functions that typically require hospitalization and have a significant impact on morbidity, mortality, and health care burden [2] . Growing evidence indicates that COPD is not a pulmonary disease, but a systemic inflammatory disease that has various extrapulmonary consequences, especially cardiovascular complications .

Myocardial dysfunction is very prevalent among the patients of AECOPD, and one of the main causes of poor prognosis [3]. Both right and left ventricular dysfunction can be caused by chronic hypoxia, pulmonary hypertension, augmented vascular resistance, and systemic inflammatory reactions[4]. The interplay of the pulmonary and cardiac systems is especially clear during acute exacerbations, during which the physiological stress further impairs the work of the cardiac system[5] [6]. The role of inflammation in pathogenesis of COPD and complications is key [7].C-reactive protein (CRP) which is an acute-phase reactant produced by the liver in response to the stimulation of interleukin-6 is the most used inflammatory systemic inflammatory biomarker. An increase in CRP has been associated with the severity of COPD, often exacerbation, and an increased risk of cardiovascular disease[8]. The increased levels of inflammatory activity in AECOPD could lead to myocardial stress, endothelial dysfunction, and cardiac output decrease [9].

Equally, D-dimer is a fibrin degradation product which is an indication of coagulation and fibrinolysis pathway activation . D-dimer is a hypercoagulable state that is typical of severe COPD exacerbations[10]. It is a prothrombotic state, which predisposes pulmonary embolism, microvascular thrombosis and right ventricular strain [11]. The degree of cardiac dysfunction in AECOPD patients can thus be indirectly proportional to the high levels of D-dimer [12] [13].

Despite the growing knowledge on the interplay between inflammation, coagulation and cardiovascular malfunction in COPD, local studies evaluating the relationship between serum CRP levels and the level of D-dimer and echocardiographic outcomes of cardiac failure are limited [14]. This knowledge of these associations is clinically significant in the early stratification of risks, prognostic evaluation, and the timely intervention.
Thus, the aim of the study was to determine the relationship between serum CRP and D-dimer levels and cardiac dysfunction in 288 patients reporting with acute exacerbation of COPD . The results can offer important information on the role of the biomarkers in predicting cardiovascular complications and enhancing clinical outcomes in this patient group that is at high risk [15].

Objective

To accomplish the following aims: to determine the association between serum C-reactive protein (CRP) and D-dimer level and cardiac dysfunction in patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD), and to compare them as predictive biomarkers of cardiovascular involvement and severity of the disease in hospitalized patients.

METHODOLOGY

The study was a cross-sectional observational study carried out at the Department of Medicine and Pulmonology, Punjab Rangers Teaching Hospital Lahore/Rahber Medical College Lahore from June 2024 to February 2025. The number of patients who were enrolled was 288 and diagnosed with acute exacerbation of chronic obstructive pulmonary disease (AECOPD). The WHO sample size calculator formula was used by considering the estimated prevalence, and a 95% confidence interval and acceptable margin of error to calculate the sample size. To sample out the eligible participants, consecutive non-probability sampling method was used. The clinical evaluation of all the patients was done by a qualified physician at the time of admission. A structured proforma was used to collect detailed history such as age, gender, smoking status, duration and severity of symptoms of the disease. Aseptic venous blood was sampled and sent to the laboratory to find out the serum C-reactive protein (CRP) and D-dimer levels. The CRP measurement was achieved with the assistance of immunoturbidimetric assay, and D-dimer by enzyme-linked immunosorbent assay (ELISA) as it has been customarily done in the laboratory. Transthoracic echocardiography was done on all patients to assess cardiac function by an experienced cardiologist. The left ventricular ejection fraction (LVEF), right ventricular systolic, and the estimation of the pulmonary artery pressure were used as the main parameters in detecting the existence of cardiac dysfunction. All the data collected were coded and put in the Statistical Package for Social Sciences (SPSS) software to analyse. The baseline characteristics were calculated using descriptive

statistics. The correlation between the parameters of cardiac dysfunction, CRP and D-dimer levels was performed by Pearson correlation analysis. Also, the regression analysis was done to determine the independent predictors of cardiac dysfunction among patients with AECOPD. The p-value of 0.05 was found significant.

Inclusion and Exclusion Criteria

Inclusion Criteria: The patients aged between 40 and 80 years old with acute exacerbation of chronic obstructive pulmonary disease according to GOLD criteria were involved. Men and women who were admitted with the aggravation of dyspneal, augmented sputum or cough were both admissible. Those patients who were confirmed to be having the diagnosis by means of spirometry (FEV1/FVC < 0.70) were enrolled. Only the individuals that gave informed consent were used. Patients that had undergone long-term follow-up (without acute exacerbation) or had stable COPD were excluded. Final analysis was done on hemodynamically stable patients having full clinical and laboratory records.

Exclusion Criteria: Patients known to have ischemic heart disease, congenital heart disease or valvular heart disorders were excluded. Patients who had active pulmonary embolism, deep vein thrombosis, chronic kidney disease stage IV V or chronic liver disease were also not allowed. Patients that had surgery, trauma, malignancy, or autoimmune diseases were excluded as it may confound the rise of CRP and D-dimer. People who are taking anticoagulant or corticosteroids before admission were excluded. The other exclusion criterion was pregnant women, and incomplete data or non-participation of the patients in the study.

Data Collection

A set proforma that was designed to gather the data was utilized. Informed consent was collected and demographic information, such as age, gender, the state of smoking, and the length of COPD, were noted. At admission, clinical assessment was done by a qualified physician. Serum CRP and D-dimer levels were measured using blood samples which were drawn aseptically under conditions. CRP was analysed by immunoturbidimetric assay and to measure D-dimer levels, ELISA based techniques were applied in the laboratory of the hospital. The cardiac examination was done by an experienced cardiologist using transthoracic echocardiography. LVEF, right ventricle and pulmonary artery pressure were measured. All these data were entered into SPSS software to be analysed. There was a quality control measure to make laboratory results accurate and reliable. The information about the patients was highly confidential. Data collection was until the six-month study period was attained and 288 patients were acquired.

RESULTS

The participants of the study were 288 patients with acute exacerbation of COPD. The average age of patients was 62.4 ± 10.8 years and most of them were males. High levels of serum CRP and D-dimer were found in most of the patients especially those who had severe exacerbations. A large proportion of patients were found to have cardiac dysfunction as echocardiographic results showed. The patients with low left ventricular ejection fraction were found to have a considerable high level of CRP in comparison to healthy cardiac patients ($p < 0.001$). On the same note, high levels of D-dimer were closely related with the right ventricular dysfunction and high pulmonary artery pressure. There was a moderate to strong relationship between inflammatory markers and severity of cardiac dysfunction. Multivariate analysis affirmed CRP, D-dimer to be independent predictors of cardiac involvement. In general, the research showed that the cardiac outcome of AECOPD patients was poorer in case of elevated levels of biomarkers.

Table 1: Baseline Demographic Characteristics of Patients (n = 288)

Variable	Category	Frequency (n)	Percentage (%)
Age	40–50 years	62	21.5
	51–60 years	88	30.6
	61–70 years	96	33.3
	71–80 years	42	14.6
Gender	Male	198	68.7
	Female	90	31.3
Smoking Status	Smokers	176	61.1
	Non-smokers	112	38.9

Table 1 presents demographic characteristics of 288 AECOPD patients, most of them males, aged 61-70 years, with more prevalent in smokers, and typical population distribution of high-risk COPD.

Table 2: Serum CRP Levels in Study Population

CRP Level	Patients (n)	Percentage (%)
Normal (<10 mg/L)	74	25.7
Elevated (10–50 mg/L)	142	49.3
Highly Elevated (>50 mg/L)	72	25.0

Table 2 gives the serum CRP levels with majority of patients having a high or very high CRP which is an indicator of high systemic inflammation when COPD is acutely exacerbated.

Table 3: Serum D-dimer Levels Distribution

D-dimer Level	Patients (n)	Percentage (%)
Normal (<0.5 µg/mL)	80	27.8
Elevated (0.5–1.0 µg/mL)	120	41.7
High (>1.0 µg/mL)	88	30.5

The table 3 indicates the distribution of D-dimer with a high percentage of patients having high levels of D-dimer, indicating high activity of coagulation and risk of thrombosis in patients with AECOPD.

Table 4: Echocardiographic Findings in AECOPD Patients

Cardiac Parameter	Normal Function n (%)	Dysfunction n (%)
Left Ventricular Function	170 (59.0%)	118 (41.0%)
Right Ventricular Dysfunction	182 (63.2%)	106 (36.8%)
Pulmonary Hypertension	160 (55.6%)	128 (44.4%)

Table 4 presents the echocardiographic results, which reveals prominent dysfunction of the left and right ventricles and pulmonary hypertension, which prove the common heart involvement in acute cases of COPD exacerbation.

Table 5: Correlation of CRP and D-dimer with Cardiac Dysfunction

Variable	Correlation with LVEF (r)	p-value	Interpretation
CRP	-0.52	<0.001	Moderate negative correlation
D-dimer	-0.47	<0.001	Moderate negative correlation
Variable	**Correlation with RV Dysfunction**	**p-value**	**Interpretation**
CRP	0.49	<0.001	Moderate positive correlation
D-dimer	0.56	<0.001	Strong positive correlation

Table 5 shows that there is a significant correlation between CRP, D-dimer and cardiac dysfunction, and a negative correlation between CRP and LVEF and positive correlation between CRP and right ventricular dysfunction, which shows strong predictability.

DISCUSSION

This study determined the association between the amount of serum C-reactive protein (CRP) and D-dimer and cardiac dysfunction in 288 patients having an acute exacerbation of chronic obstructive pulmonary disease (AECOPD). The results indicated that the two biomarkers were highly increased in the cases of patients with cardiac dysfunction and that they had a high relationship with echocardiographic measures of ventricular impairment [16].

One of the indicators of the systemic inflammatory response to AECOPD is the increase in the CRP levels that was measured. COPD is becoming recognized as an inflammatory disease, but not necessarily a pulmonary disease [17]. In acute exacerbations, there are increased inflammatory mediators i.e. interleukins and tumour necrosis factor-alpha which cause production of hepatic CRP. High CRP was also closely associated with low left ventricular ejection fraction (LVEF) in this paper, which indicates that systemic inflammation may be a contributing factor of myocardial depression and a low cardiac output. These results agree with other studies that show that high CRP is a predictive factor of cardiovascular morbidity in COPD patients on its own [18].

In a similar manner, D-dimer levels were greatly increased in a considerable number of patients and had a close relationship with right ventricular dysfunction and pulmonary hypertension [19]. High levels of D-dimer indicates that coagulation cascade and fibrinolysis have been activated indicating that the person is under a hypercoagulable state [13]. Hypoxia and systemic inflammation in the AECOPD condition facilitates thrombogenesis, which predisposes microvascular thrombosis and pulmonary embolism [20]. These pathophysiological alterations put extra pressure on the right ventricle resulting into dysfunction and elevated pulmonary arterial pressure. The results of this study are in tandem with existing literature, which has revealed the relevance of coagulation abnormalities in the worsening of

cardiovascular events in COPD.

The correlation analysis also confirmed that both CRP and D-dimer are shown to have strong correlations with severity of cardiac dysfunction. CRP had a negative moderate correlation with LVEF, and the right ventricular impairment was more strongly correlated with D-dimer . These findings suggest that the combination of both inflammatory and thrombotic processes is what can cause cardiac dysfunction in AECOPD patients.

The biomarkers can be clinically helpful in the early risk stratification. Regular CRP and D-dimer measurements of AECOPD patients in the hospital might aid in identifying patients who are at the greatest risk of cardiac complications and should be closely monitored and intervened upon. This is particularly important in the resource-limited setting where the advanced cardiac imaging may not be readily available. However, this study has certain limitations [21]. It is a cross-sectional design that cannot ascertain causality [22]. Also, the research was carried out in one centre thus it may not have generalizability. It is recommendable that any additional multicentre longitudinal studies be carried out in the future to further validate these findings besides explore the prognostic value of these biomarkers. To sum up, high serum CRP and D-dimer levels are strongly linked with cardiac dysfunction in patients with AECOPD and therefore could be easily used as a predictive biomarker of cardiovascular involvement in the exacerbation of COPD [23].

CONCLUSION

The present study concludes that the level of serum C-reactive protein (CRP) and D-dimer are also high in patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD) that develop cardiac dysfunction. Both biomarkers were significantly and statistically correlated with echocardiographic parameters, such as decreased left ventricular ejection fraction and right ventricular dysfunction. The results imply that inflammation in the body system and coagulation activation are important factors in the genesis and progression of cardiac complications in AECOPD. CRP of high levels indicates the presence of inflammatory stress now, and D-dimer of high levels indicates a state of hypercoagulability that provokes pulmonary vascular loading and cardiac dysfunction. CRP and D-dimer can, therefore, be considered a useful, inexpensive, and easily accessible biomarker that can be used to identify the patients who are at risk of cardiac dysfunction at a young age. This would be clinically helpful as it would help the clinicians to risk stratify and more frequently monitor and treat these patients, which would ultimately result in a reduction in morbidity and mortality in patients with AECOPD.

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