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D-Dimer And CRP As Biomarkers In COPD Patients: A Prospective Cohort

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Abstract

In the current scenario where there is more spread of COVID -19, it has become difficult to identify the severity of chronic obstructive pulmonary disease (COPD) in patients, as there is much hindrance to undergo pulmonary function test (PFT). We aimed to investigate the levels of D-dimer and CRP in COPD patients and their association with the severity of disease. Clinical and laboratory data were evaluated in 50 patients who were visiting the OPD of pulmonology department at our hospital attached to medical college. D-dimer and CRP levels of venous blood were evaluated in patients whose FEV_1 was below 80% by performing PFT. 50 subjects who met the inclusion criteria enrolled for study with a FEV_1 valuesless than 80%.23 subjects have showed an abnormal increase of D-dimer 0.57±0.024 (Mean±SD) and CRP 5.54±0.35 (Mean±SD) in severe cases were FEV_1 obtained was less than 50%. 27 subjects have showed normal level of D-dimer with 0.17±0.01 (Mean±SD) and CRP 1.84±0.55 (Mean±SD) in moderate cases were FEV_1 obtained was less than 80%. The analysed data by using ANNOVA have showed F value 32.57 (Brown Forsythe test), P=0.001 which was statistically

significant between columns treated (each column is one group) at 95% CI. Levels of CRP and D-dimer showed 100% specificity and sensitivity.Elevated levels of D-dimer and CRP maybereliable diagnostic biomarker to identity the severity of chronic obstructive pulmonary disease (COPD) in the absence of pulmonary function test.

Keywords

COPD, CRP, D-dimer and FEV_1

Introduction

After 2019, with the spread of pandemic Covid-19, chronic obstructive pulmonary disease (COPD) research and its management has obtained a priority. Lack of significant biomarker and simple haematological tests to detect stages of COPD early for a prospective treatment. Chronic obstructive pulmonary disease (COPD) is accounting for 3 million deaths annually and a major global health problem[1]. Data suggests that COPD is often associated with a wide variety of systemic complications, including systemic inflammation [2], thishyper-coagulable state can be triggered by inflammation, which promotes tissue-factor gene expression in endothelial cells [3,4].D-dimer an end product of degradation of fibrin by plasmin, have been increased in patients with COPD exacerbation, irrespective of presence of venous thromboembolism (VTE) [5,6]. The combination of an unlikely clinical decision rule and a normal D-dimer appears to have a similar safety in excluding pulmonary embolism irrespective of the presence of COPD [7]. On the other hand, there is a continuing debate about the VTE diagnostic efficiency of D-dimers tests in patients with stable COPD. A similar distribution of D-dimer results was found in 313 patients with and without COPD, suggesting that the presence of COPD had no influence on the diagnostic performance of the test for thromboembolic disease [8]. However, studies have showed that plasma level fibrinogen and other markers of coagulation are significantly higher in stable COPD patients than in healthy subjects, which may have important diagnostic and therapeutic implications[9,10]. We aimed to investigate the levels of D-dimer and CRP in COPD patients, and their association with the severity of disease.

Materials and Methods

We conducted a prospective cohort study at our general hospital, attached to a medical college, 250 subjects showed the signs and symptoms of COPDwho were visiting the outpatient department of pulmonology were enrolled for studyfrom May- December 2020. 50 COPD confirmed subjects were consider for study whose forced expiratory volume 1 (FEV_1) to forced vital capacity of less than 0.8 with the administration of broncho dilator salbutamol were included for the study. The severity of COPD was classified according to Gold standard criteria according to Global Initiative for Chronic Obstructive Lung Disease. Participants suffering with asthma and lung cancer, infectious disease use of anticoagulant therapy, diabetics, high blood pressure, heart failure and hormonal replacement therapy were excluded from the current study. The study protocol was reviewed and approved by the Institutional ethical committee (IEC). Informed consent was obtained before the start of the study from each participant. Demographic data, smoking habits, presence of comorbidities and use of type of corticosteroid were collected by a questionnaire provided. Pulmonary function test was performed by using computerized spirometer by administering bronchodilator. Blood samples were collected from all participants and D-dimer, C-reactive protein was performed by available immunoturbidimetric and

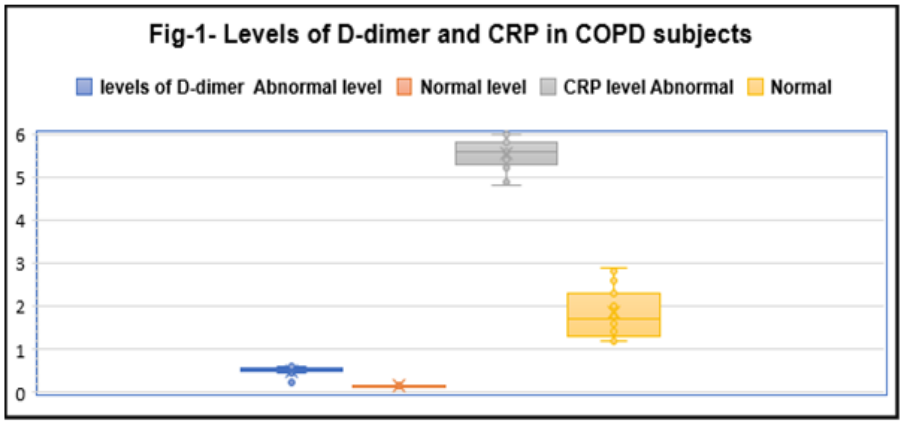
turbidimetric method on platform of Mindray auto analyser and kits supplied by the company. Standard operating procedure was adopted to avoid any error and bias during accessing the samples.

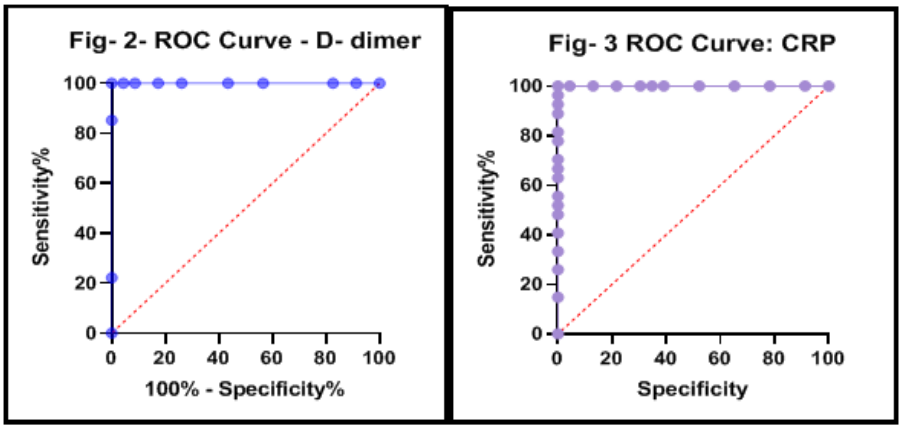
Statistical analysis

Obtained data was analysed by using graph pad prism 9 (USA), Mean±SDwas calculated by using one-way ANNOVA with Brown-forsythe test was applied to compare the variables. Statistical significance of $p<0.05$, at confidence interval of 95% with 80% power of the study was considered to be significant.

Result

A total no of 50 subjects who met the inclusion criteria enrolled for study showed a FEV_1 less than 80%. 27 subjects showed FEV_1 value of 50-79% and remaining 23 subjects showed less than 30-49%. Subjects enrolled for study were suffering with moderate to severe COPD (Gold stage of COPD). 23 subjects have shown an abnormal increase of D-dimer value 0.57±0.024 (Mean±SD), 0.004 (SEM), at 95% CI (0.562– 0.578), CRP 5.54±0.35 (Mean±SD), 0.075 (SEM) at 95%CI (5.388-5.699) in severe cases were FEV_1 obtained was less than 50%.27 subjects have showed normal level of D-dimer with 0.17±0.01 (Mean±SD), 0.002 (SEM) at 95% CI (0.167 – 0.772), CRP 1.84±0.55 Mean±SD, 0.107 (SEM) at 95%CI (1.621-2.061) in moderate cases were FEV_1 obtained was less than 80%. Oneway ordinary ANNOVA was applied to draw the statistical significance between the two groups (normal values of CRP and D-dimer, Abnormal Values of CRP and D-dimer), the analysed data have shown F value 32.57 (Brown Forsythe test), P=0.001 which was statistically significant between columns treated (each column is one group) at 95% CI (Fig-1). CRP and D-dimer showed 100% specificity and sensitivity (Fig-2,3).





Discussion

Current scenario of pandemic, people suffering with COPD are not undergoing pulmonary function test (PFT) due to its procedure and hindrance of getting infected with COVID-19. Simple blood test can reveal the status of stages of COPD. The raise of levels of D-dimer and CRP may prove use full to pulmonologist and physician to plan the line of treatment to people suffering with COPD and help them to monitor and recover. The D-dimers result from the breakdown of fibrin and can serve as a marker for fibrinolytic system activity, levels have been shown to be increased in a variety of diseases [11,12]. Previous studies have shown the evidence for the presence of a hypercoagulable state in COPD patients [9,10,13] . A case-control study demonstrated an increase in fibrinogen, D-dimer, factor VIII and von Willebrand factor [13]. In another study, enrolled 40 participants with COPD showed increase in plasma levels of thrombin antithrombin complex, fibrin peptide A, tissue plasminogen activatorplasminogen activator inhibitor and β-thromboglobulin [10] these studies support our study. A case control study found, an increase of levels of F1+2 fragments and D-dimer [9]. Hartmann and colleagues [8] reported in a large study that the distribution of D-dimer results was not influenced by the presence of COPD this study contradicts our study. However, the diagnosis of COPD in above study was based on clinical information and perhaps some misclassifications of COPD might have occurred. In our study, we found significant correlation between D-dimers, CRP and stages of COPD. There are evidences that reduced lung function associated with increased levels of systemic inflammatory markers in subjects with stable COPD [14,15].Moreover, fibrinogen, possibly a marker for chronic low-grade inflammation, is associated with modest deterioration of lung function in healthy young adults [16,17]. In a previous 12 month follow up study, changes in FEV_1 were significantly greater in COPD patients with high thrombin antithrombin complex or tissue plasminogen activator-plasminogen activator inhibitor levels [10], this study is in agreement with our findings. Another case-control study did not find a correlation between severity of obstruction and D-dimers [13].Levels of CRP were increased in all diseases, as more formation of fibrinogen may alter the levels of CRP [18]. Previous studies on COPD patients showed an abrupt increase of CRP levels, as it was having more prognostic value we have not emphasizing on its increase. A systematic review and meta-analysis showed an increase of baseline CRP level in COPD patients [18].Another study showed an increase of HS-CRP levels in COPD [19].These two-studies support increase of CRP in our studies. An increase of D-dimer is an indication of sever COPD.

Conclusion

COPD pathogenesis, progression of disease and mortality caused due to systemic inflammation. Although CRP is associated with the several conditions, assessing its levels in COPD patients along with D-dimer may be useful tool to identify the progression and severity of COPD.

Limitations of Study

Limitations of the present study was low sample size and not having control group. More studies are warranted with large sample size and with a control group.

References

1. Barnes PJ. Chronic obstructive pulmonary disease. N Engl J Med 2000; 343(4):269–280.

2. Stone AC, Nici L. Other systemic manifestations of chronic obstructive pulmonary disease. Clin Chest Med 2007; 28(3):553–557.
3. Libby P, Simon DI. Inflammation and thrombosis: the clot thickens. Circulation 2001; 103(13):1718–1720.
4. Akgun M, Meral M, Onbas O, Araz O, Koplay M, Aslan S, Mirici A. Comparison of clinical characteristics and outcomes of patients with COPD exacerbation with or without venous thromboembolism. Respiration 2006; 73(4):428–433.
5. Karwat K, Kosciuch J, Chazan R. Is micro embolism present and is it important element of COPD exacerbation? Pol Merkur Lekarski 2005; 18(106):385–388.
6. Sohne M, Kruip MJ, Nijkeuter M, Tick L, Kwakkel H, Halkes SJ, et al. Accuracy of clinical decision rule, D-dimer and spiral computed tomography in patients with malignancy, previous venous thromboembolism, COPD or heart failure and in older patients with suspected pulmonary embolism. J Thromb Haemost 2006; 4(5):1042–1046.
7. Alessandri C, Basili S, Violi F, Ferroni P, Gazzaniga PP, Cordova C. Hypercoagulability state in patients with chronic obstructive pulmonary disease. Chronic Obstructive Bronchitis and Haemostasis Group. Thromb Haemost 1994; 72(3):343–346.
8. Ashitani J, Mukae H, Arimura Y, Matsukura S. Elevated plasma procoagulant and fibrinolytic
9. markers in patients with chronic obstructive pulmonary disease. Intern Med 2002; 41(3):181–185.
10. Ginsberg JS, Wells PS, Brill-Edwards P, Donovan D, Panju A, van Beek EJ, Patel A. Application of a novel and rapid whole blood assay for D-dimer in patients with clinically suspected pulmonary embolism. Thromb Haemost 1995; 73(1):35–38.
11. Raimondi P, Bongard O, de MP, Reber G, Waldvogel F, Bounameaux H. D-dimer plasma concentration in various clinical conditions: implication for the use of this test in the diagnostic approach of venous thromboembolism. Thromb Res 1993; 69(1):125–130.
12. Aibar M, Laborda K, Conget F, Cornudella R. Hipercoagulability state and endotelial injury in stable chronic obstructive pulmonary disease patients. An Sist Sanit Navar 2010; 33: 43–50.
13. Gan WQ, Man SF, Senthilselvan A, Sin DD. Association between chronic obstructive pulmonary disease and systemic inflammation: a systematic review and a meta-analysis. Thorax 2004; 59(7):574–580.
14. Papaioannou AI, Mazioti A, Kiropoulos T, Tsilioni I, Koutsokera A, Tanou K, et al. Systemic and airway inflammation and the presence of emphysema in patients with COPD. Respir Med 2010; 104(2):275–282.
15. Engstrom G, Lind P, Hedblad B, Wollmer P, Stavenow L, Janzon L, Lindgarde F. Lung function and cardiovascular risk: relationship with inflammation-sensitive plasma proteins. Circulation 2002; 106(20):2555–2560.
16. Thyagarajan B, Jacobs DR, Apostol GG, Smith LJ, Lewis CE, Williams OD. Plasma fibrinogen and lung function: the CARDIA Study. Int J Epidemiol 2006; 35(4):1001–1008.
17. Leuzzi G, Galeone C, Taverna F, et al. C-reactive protein level predicts mortality in COPD: a systematic review and meta-analysis. Eur Respir Rev 2017; 26: 160070.

18. SA Alavi1, F Soati*1, K Forghanparast1, H Amani1. HsCRP in Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease. Iran Red Crescent Med J 2011; 13(10):713-718.