Original Research Paper



Pulmonary Medicine

SERUM C- REACTIVE PROTEIN LEVEL IN COPD PATIENTS: A COMPARATIVE STUDY

Agale S. A.	Asst Prof, Dpt of Pulmonary Medicine, Grant Govt Medical College, Mumbai, India
Chopra R K	Consultant Pulmonologist, Ruby Hall Clinic, Pune
Pujari V. V.*	Asso Prof, Dpt of Pulmonary Medicine, Grant Govt Medical College, Mumbai, India *Corresponding Author

ABSTRACT INTRODUCTION: The severity and progression of Chronic Obstructive Airway Disease is measured by forced expiratory volume in 1 second (FEV1). However Biomarkers like Fibrinogen, C- Reactive Protein (CRP) etc could become suitable surrogates in the early detection of disease.

AIMS & OBJECTIVES: To study the association of Serum CRP level in COPD and its correlation with the severity of COPD

METHODOLOGY: this study was conducted on 50 stable COPD patients and a control group of 50 healthy persons. All the subjects were investigated with complete Blood Count, chest radiographs, spirometry and serum CRP levels.

RESULTS: Mean WBC count in the test group was 8795/cmm and in Control group was 6020 /cmm (p<0.0001). Mean CRP level in the test group was 3.85 mg/L and in control group was 0.38 mg/L (p<0.0001). CRP levels correlate with severity of COPD

CONCLUSION: Serum CRP levels can be used as a biomarker in the COPD which correlates with the disease severity.

KEYWORDS: COPD, FEV1, Serum CRP

INTRODUCTION:

C - reactive protein (CRP) is an acute phase protein synthesized predominantly by the hepatocytes in response to tissue damage or inflammation. It has been accepted that levels of CRP relate to the presence of airflow obstruction and also associated to disease severity, quality of life, exercise capacity, response to treatment and mortality [1-3]. Fibrinogen, IL 8, IL 6, neutrophils, TNF α are other inflammatory biomarkers which also increase in exacerbation.

The present study aims to evaluate the serum levels CRP as the biomarker of severity of COPD.

MATERIALS AND METHODS:

After obtaining approval of the ethics committee of the Medical institute, we conducted this prospective, observational study at our tertiary care institute.

The study was done over a period of 13 months. The study was carried out in 100 consecutive subjects over the period of 13 months, who visited our OPD and IPD. Out of these 100 subjects, 50 were normal healthy individuals forming control group & rest 50 patients were diagnosed COPD cases as per GOLD guidelines.

Patients with history suggestive of asthma or any other pre-existing pulmonary disease affecting lung function other than COPD as well as patients with other systemic diseases were excluded.

Detailed history and examination of patients, with mMRC scoring of dyspnoea was done. All patients were subjected to spirometery and diagnosis and staging of COPD was made based on GOLD guidelines. All the subjects had blood test done for CBC and serum CRP level. Using standard methods, results were analyzed.

RESULTS:

Table 1: Comparison of age in COPD and control group

Parameter	COPD (n=50)		Control (n=20)	
	Mean	SD	Mean	SD
Age (Yrs)	63.16	10.47	59.86	6.86

p>0.05

Table 2: Sex wise distribution of cases in COPD group

Sex	COPD		
Male	36		
Female	14		
Total	50		

Chi-square = 0.48, P>0.05

Table 3: Comparison of WBC in COPD and control group

Parameter	COPD (n=50)	Control (n=50)		
	Mean	SD	Mean	SD
WBC(cells/mm3)	8794.68	3619.27	6020.54	1914.76

P<0.0001

TABLE 4: Comparison of CRP level in COPD and control group

	COPD (n=50)		Control (n=50)		P Value
	Mean	SD	Mean	SD	
CRP level(mg/L)	3.85	5.41	0.38	0.25	< 0.0001

P<0.0001

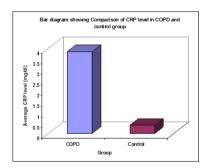


Fig 1: Graph of comparison of serum CRP level in COPD & control group

Table 5: Severity of disease wise distribution of cases in COPD

Severity of disease	COPD	Percentage
Mild	3	6%
Moderate	17	34%
Severe	20	40%
Very severe	10	20%
Total	50	

Table 6: Comparison of CRP level according to severity of disease in COPD group

Severity of disease	N	CRP level	CRP level (mg/L)	
		Mean	SD	
Mild	3	2.73	0.84	
Moderate	17	2.41	1.16	
Severe	20	3.04	3.26	
Very severe	10	8.25	10.34	

P<0.05

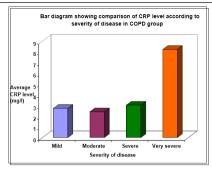


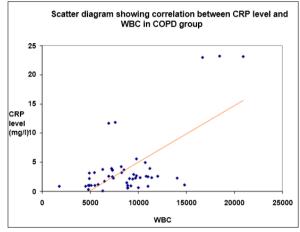
Figure 2: Graph of distribution of CRP level according to severity of COPD

Table 7: Comparison of WBC according to severity of disease in COPD group

COLD STORP				
Severity of disease	N	WBC (cells/mm3)		
		Mean	SD	
Mild	3	7933.33	1011.59	
Moderate	17	7686.12	2124.44	
Severe	20	8128.70	3047.18	
Very severe	10	12269.60	5147.14	

P<0.01

Fig 3: Graph of correlation between serum CRP level & WBC count with severity of COPD



DISCUSSION:

Mean age of our patients was 63.16 ± 10.47 yrs with minimum age of 36 yrs and maximum age of 85 yrs, maximum patients were in the age group of 51-60 yrs. In the similar studies conducted by Jain N K et al[4] and Hulya Koksal et al[5], they found mean age of the patients as 60.61 ± 10.36 yrs and 65.3 ± 7.39 yrs respectively. This result is consistent with the chronicity of the disease and its presentation being more in the elderly.

In our study we found that WBC count is increased in COPD patient as compare to control group. The mean WBC count in COPD patients was 8794.68x103 cells/mm3 with SD of 3619.27 (P<0.0001).

Few studies demonstrate elevated level of biomarkers seen in COPD & similar findings were observed in meta-analysis research of W Q Gan [6] et al, on CRP level in COPD patients; found that overall, circulating leucocytes along with CRP were higher in patients with COPD than in control subjects. The standardized mean difference was 0.44 units (95% CI 0.20 to 0.67; test for heterogeneity, p=0.003) or 0.886109 cells/1(95% CI 0.36 to 1.40)

In our study, significant difference was found in the serum CRP level in COPD patients and controls ($4.55\pm1.59\,\mathrm{mg/dl}$ versus $2.55\pm0.76\,\mathrm{mg/dl}$, respectively). P(<0.0001) suggested it as significant

In a study conducted by Groenewegan [7]and his colleagues in Masstricht University in the Netherlands on 277 patients, the serum levels of inflammatory biomarkers CRP, fibrinogen, and TNF α were

higher in COPD patients compared to controls. In another study performed by Valipour A [8] and co-workers on 30 COPD patients Austria, CRP (p<0.01) was higher in these patients compared to controls, along with other biomarker like CRP, VEGF, WBC & IL-6.

In our study, we found that as severity of COPD increases, there is increase in serum CRP levels

In our study we found significant correlation between CRP & severity of COPD. As severity of COPD increases, CRP protein accordingly increases. The mean CRP level in GOLD stage 1 is i.e mild COPD is 2.73mg/l with SD of 0.84. The CRP level is seen as increasing trend as severity of COPD increases. In GOLD stage, 3 & 4 show mean of 3.04 & 8.25 mg/dl respectively with p<0.05.

This trend is similar to Broekhuizen and colleagues[9] study where they found patients with GOLD stages III and IV had significantly higher CRP levels than those with GOLD stage II [II: 1.92 (0.36–16.00) mg/l; III: 4.43 (0.47–75.60) mg/l; IV: 4.90 (0.47–65.70) mg/l; both p,0.03].

CONCLUSION:

Serum CRP as a new & novel marker for severity of COPD is found useful according to many studies including landmark study- ECLIPSE study. Our short observational study also concluded its usefulness as a severity marker in both smoking & non-smoking COPD. As our sample size was small, further studies with larger sample size is recommended.

REFERENCES:

- Pinto-Plata VM, Mullerova H, Toso JF, Feudjo-Tepie M, Soriano JB, Vessey RS, Celli BR: C-reactive protein in patients with COPD, control smokers and non-smokers. Thorax 2006, 61(1):23–28.
 Dahl M, Vestbo J, Lange P, Bojesen SE, Tybjaerg-Hansen A, Nordestgaard BG: C-
- Dahl M, Vestbo J, Lange P, Bojesen SE, Tybjaerg-Hansen A, Nordestgaard BG: C-reactive protein as a predictor of prognosis in chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2007, 175(3):250.255.
 De Torres JP, Pinto-Plata V, Casanova C, Mullerova H, Cordoba-Lanus E, Muros de
- De Torres JP, Pinto-Plata V, Casanova C, Mullerova H, Cordoba-Lanus E, Muros de Fuentes M, Aguirre-Jaime A, Celli BR: C-reactive protein levels and survival in patients with moderate to very severe COPD. Chest 2008, 133(6):1336–1343.
- NK Jain, MS Thakkar, N Jain, KA Rohan, M Sharma. Chronic obstructive pulmonary disease: Does gender really matter? Lung India 2011;28:258-262
- 5) Hülya Köksal MD, Attila Saygı MD, Nesrin Sarıman MD, Emel Alıcı MD,Ş irin Yurtlu MD, Huri Yılmaz MD, and Yeliz Düzgun MD Evaluation of Clinical and Functional Parameters in Female Subjects With Biomass Smoke Exposure. Respiratory Care. March 2013; 58(3):424-430
- W Q Gan, S F P Man, A Senthilselvan, D D: Sin Association between chronic obstructive pulmonary disease and systemic inflammation: a systematic review and a metaanalysis; Thorax 2004; 59:574–580.
- Groenewegen KH, Postma DS, Hop WC, Wielders PL, Schlösser NJ, Wouters EF. COSMIC Study Group: Increased systemic inflammation is a risk factor for COPD exacerbations. Chest 2008; 133 (2): 350-7.
- Valipour A, Schreder M, Wolzt M, Saliba S, Kapiotis S, Eickhoff P, et al. Circulating vascular endothelial growth factor and systemic inflammatory markers in patients with stable and exacerbated chronic obstructive pulmonary disease. Clin Sci (Lond) 2008; 115 (7): 225-32.
- Broekhuizen R, Wouters E F M, Creutzberg E C, Schols A M W J. Thorax 2006;61:17-22.