



CORRELATION BETWEEN C-REACTIVE PROTEIN AND SEVERITY OF ASTHMA AND COPD.

Physiology

Dr. Poonam Kalsi MBBS, MD Physiology Demonstrator in the PG Department of physiology, GMC, Jammu.

Dr. Vimal Kumar MBBS, MD Medicine.

ABSTRACT

The high sensitivity C-reactive protein (hs-CRP) is an important marker in detecting systemic inflammation in asthma; indeed an association between serum hs-CRP level and severity of asthma has been suggested by the various studies. C-reactive protein (CRP) is a high sensitive marker of inflammation, infection and tissue damage which contributes host defence against infection by activating the complement pathways. This observational study was conducted in the Post Graduate Department of Medicine, Government Medical College, Jammu, with the aim to determine the association between C-reactive protein and severity of Asthma and Chronic obstructive pulmonary disorder. It was observed that in male patients, minimum PEFR% predicted was 58, maximum was 64 with a mean value of 62 ± 3 . hs-CRP values in asthmatic males were minimum of 3.76 mg/L, maximum was 21.72mg/L with a mean value of 9.84 ± 2.80 mg/L. Similarly in female patients, minimum PEFR% predicted was 49, maximum 77, with a mean value of 61 ± 6.36 , the minimum hs-CRP value was 3.76 mg/L, maximum value 19.86 mg/L and mean value of hs-CRP was 8.25 ± 3.16 mg/L. The study concluded that hs-CRP is reflector of chronic inflammation of respiratory tract, it correlates with severity of COPD and Bronchial Asthma, in which the pathology is same. It, therefore, is an important biomarker of severity of disease. hs-CRP is an predictor of morbidity and mortality of asthma and COPD, and also helps in the modulation of the treatment of the conditions.

KEYWORDS

Asthma, Chronic Obstructive Pulmonary Disease and C-reactive protein.

INTRODUCTION

In case of respiratory infectious diseases the systemic inflammation and reversible airflow narrowing is seen.¹

C-reactive protein (CRP) is a high sensitive marker of inflammation, infection and tissue damage which contributes host defence against infection by activating the complement pathways. The rise in CRP is driven by its rate of synthesis and falls rapidly when the pathological stimulus ceases with a plasma half life of approximately 19 hours. Smokers also show elevated hs-CRP level.^{2,3,4}

The high sensitivity C-reactive protein (hs-CRP) is an important marker in detecting systemic inflammation in asthma; indeed an association between serum hs-CRP level and severity of asthma has been suggested by the various studies.⁵

The increased levels of serum hs-CRP with a high frequency of airway hyper-responsiveness and low forced expiratory volume in one sec (FEV1) among subjects without heart disease suggesting that systemic inflammation may be associated with respiratory impairment.⁶

There is increasing evidence that chronic obstructive pulmonary disease (COPD) is a multi-organ systemic disease. Skeletal muscle weakness, wasting and impaired exercise performance have been well described as frequently occurring symptoms in advanced COPD and asthma. These features are poorly related to the severity of airflow limitation but appear to be linked to a systemic inflammatory response. Several systemic inflammatory mediators such as tumour necrosis factor- α (TNF- α), some interleukins (ILs), acute phase proteins [C-reactive proteins (CRP)], fibrinogen and lipopolysaccharide binding protein (LBP) and leucocytes are increased in COPD.⁷

Thus this prospective observational study was done to determine the association between C-reactive protein and severity of Asthma and Chronic obstructive pulmonary disorder.

Methodology

This observational study was conducted in the Post Graduate Department of Medicine, Government Medical College, Jammu, in November 2007 to October 2008 after obtaining approval from the institutional ethical committee.

After obtaining the informed consent a total of 100 patients attending the Medicine Outpatient department were included in the study.

Inclusion Criteria

1. Patients who were willing to participate.

2. Patients who were clinically diagnosed with COPD and Asthma.

Exclusion Criteria:

1. Patients under 18 years of age.

2. Patients who had co-morbidities.

Procedure Of Data Collection:

Whole procedure was explained to the patients. A detailed history and physical examination was done. Spirometry was done to diagnose and confirm the severity of COPD and Asthma and the serum C-reactive protein was analysed through laboratory investigations by estimation of plasma higher sensitivity C-reactive protein.

Data was tabulated, organized, analyzed and interpreted in both descriptive and inferential statistics i.e. frequency and percentage distribution, by using statistical package for social science software (SPSS), version 16. Categorical variables were expressed as number and percentage.

OBSERVATIONS AND RESULT

In this observational study 100 patients of COPD and Bronchial Asthma were included. Among them 30% patients were reported with Asthma and 70% with COPD.

It was observed that in male patients, minimum PEFR% predicted was 58, maximum was 64 with a mean value of 62 ± 3 . hs-CRP values in asthmatic males were minimum of 3.76 mg/L, maximum was 21.72mg/L with a mean value of 9.84 ± 2.80 mg/L. Similarly in female patients, minimum PEFR% predicted was 49, maximum 77, with a mean value of 61 ± 6.36 , the minimum hs-CRP value was 3.76 mg/L, maximum value 19.86 mg/L and mean value of hs-CRP was 8.25 ± 3.16 mg/L.

Table 1 Asthmatic Patients According To Severity

Variables	Males n(%)	Females n(%)	Male hs- CRP (mg/L) (Mean $\pm$ 1SD)	Female hs- CRP (mg/L) (Mean $\pm$ 1SD)
Mild (PEFR $\geq$ 80% with variability 20-30%)	4(30.76)	6(35.29)	6.84 ± 1.66	4.92 ± 1.12
Moderate (PEFR 60-80% with variability > 30%)	6(46.15)	8(47.05)	9.68 ± 2.78	7.86 ± 2.32
Severe (PEFR $\leq$ 60% with variability > 30%)	3(23.07)	3(17.64)	15.84 ± 4.12	13.90 ± 3.84

Table 1 depicted that the maximum number of male patients are in group with moderate severity i.e. 6 patients (46.15%), whereas highest

value of hs-CRP is in severe group of patients i.e. 15.84 ± 4.12 mg/L and in female patients 8 patients were with moderate severity, while the highest value of hs-CRP was observed in group with severe disease i.e. 13.90 ± 3.84 mg/L.

Table 2 COPD Males

Variables	Min	Max	Mean $\pm$ SD
Duration of smoking (in years)	25	60	41.56 ± 7.64
FEV1 (% Predicted)	30	68	51 ± 8.14
FVC (% Predicted)	57	83	71 ± 6.54
FEV1/FVC (% Predicted)	50	90	71 ± 11.06
hs-CRP (mg/L)	3.80	21.72	9.13 ± 4.02

Table 2. showed that there were 37 males COPD patients in this study, with a minimum duration of smoking of 25 years and maximum smoking duration of 60 years, mean duration of smoking was 41.56 ± 7.64 years, minimum, maximum and mean FEV1 (% predicted) values were 30, 68 and 51 ± 8.14 (%), respectively. The minimum FVC (% predicted) was 57, maximum 83 with a mean value of 71 ± 6.54 %. As regards FEV1/ FVC (% predicted), its minimum value was 50, maximum 90 and mean value was 71 ± 11.06 (%). The minimum value of hs-CRP was 3.80 mg/L, maximum value of 21.72 mg/L and mean value 9.13 ± 4.02 mg/L.

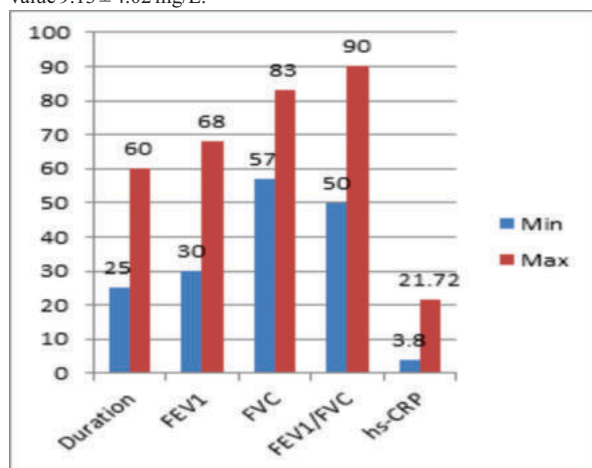


Figure 1. COPD males

Table 3 Distribution Of COPD Male Patients According To Severity Of Disease

Variables	No. of Patients (%age)	hs-CRP (mg/L) (Mean $\pm$ 1 SD)
Mild (FEV1 $\geq$ 80% predicted, FEV1/FVC < 70%)	11(29.72%)	4.80 ± 1.2
Moderate (FEV1 < 80% predicted, FEV1/FVC < 70% and 50%)	12(32.43%)	6.72 ± 2.6
Severe (FEV1 < 50% predicted, FEV1/FVC < 70% and 30%)	9 (24.32%)	10.84 ± 4.8
Very Severe (FEV1 < 30% predicted, FEV1/FVC < 70% predicted)	5 (13.51%)	15.68 ± 6.8

Table 3 represents that the maximum number of patients are in group with moderate severity i.e. 12 patients (32.43%), whereas highest value of hs-CRP is in very severe group of patients i.e. 15.68 ± 6.8 mg/L.

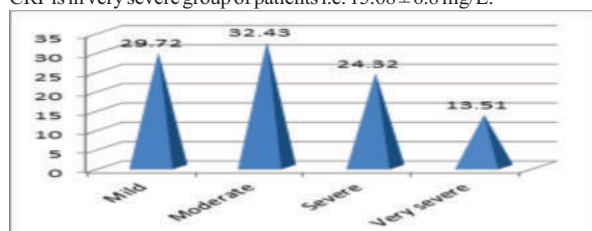


Figure 2. Distribution Of COPD Male Patients According To Severity Of Disease

Table 4 COPD Females

Variables	Min	Max	Mean $\pm$ 1SD
Duration of smoking (in years)	25	50	40 ± 5.22
FEV1 (% Predicted)	33	85	44.48 ± 10.06
FVC (% Predicted)	52	102	74.40 ± 12.93
FEV1/FVC (% Predicted)	43	73	58.30 ± 12.22
hs-CRP (mg/L)	3.70	17	9.60 ± 3.73

Table 4 depicted that there were 33 female COPD patients in this study, with a minimum duration of smoking of 25 years and maximum smoking duration of 50 years, mean duration of smoking was 40 ± 5.22 years. The minimum, maximum and mean FEV1 (% predicted) values were 33, 85 and 44.48 ± 10.06 (%), respectively. The minimum FVC (% predicted) was 52, maximum 102 with a mean value of 74.40 ± 12.93 %. As regards FEV1/FVC (% predicted), its minimum value was 43, maximum 73 and mean value was 58.30 ± 12.22 (%). The minimum value of hs-CRP was 3.70 mg/L, maximum value of 17 mg/L and mean value 9.60 ± 3.73 mg/L.

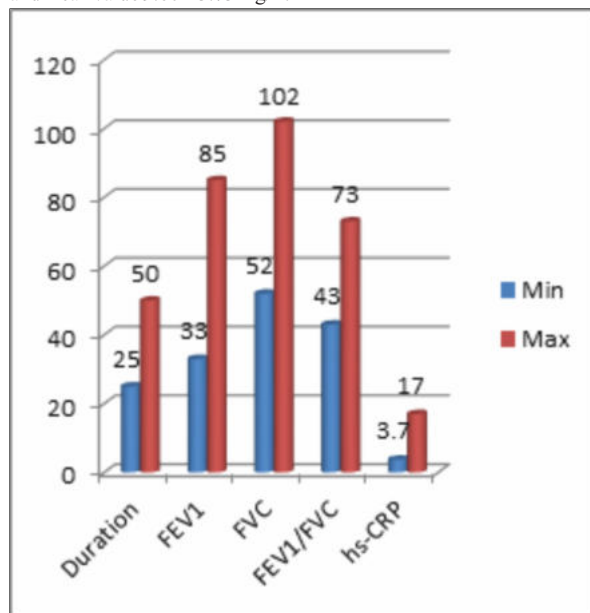


Figure 3. COPD Females

Table 5 Distribution Of COPD Female Patients According To Severity Of Disease

Variables	No. of Patients (%age)	hs-CRP (mg/L) (Mean $\pm$ 1 SD)
Mild (FEV1 $\geq$ 80% predicted, FEV1/FVC < 70%)	8 (25%)	4.32 ± 1.08
Moderate (FEV1 < 80% predicted, FEV1/FVC < 70% and 50%)	11 (33.33%)	6.92 ± 2.4
Severe (FEV1 < 50% predicted, FEV1/FVC < 70% and 30%)	07 (21.87%)	10.36 ± 3.24
Very Severe (FEV1 < 30% predicted, FEV1/FVC < 70% predicted)	07 (21.87%)	15.84 ± 4.82

Table 5 showed that the maximum female patients are in group with moderate severity i.e. 11 patients (33.33%), whereas highest value of hs-CRP is in very severe group of patients i.e. 15.84 ± 4.82 mg/L.

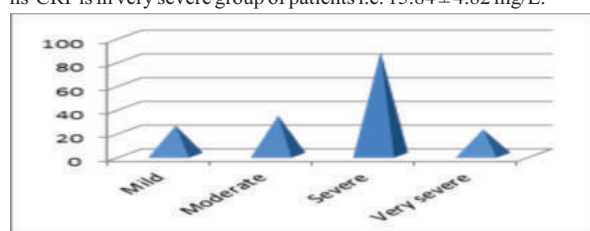


Figure 4. Distribution Of COPD Female Patients According To Severity Of Disease

DISCUSSION

Respiratory diseases are the leading and increasing cause of morbidity and mortality worldwide. In this study 100 patients, who were clinically diagnosed with COPD and Asthma were included. Detailed examinations and investigations were carried out in all the cases. Data was analyzed and discussed with previous literature.

Smoking is a well known risk factor associated with COPD. In our study, 100% of the patients with COPD were smokers. Similarly, 100% patients in the study by Takemura *et al.* (2006) were smokers. None of the patients in asthma group were smokers in our study.⁸ On the contrary, in a study by Olafsdottir *et al.* (2004), about 27.8% patients were smokers.⁹

Mean PEFr% predicted in case of asthmatic males and females was 72% each in a study by Takemura *et al.* (2005), whereas in our study it was $62 \pm 3\%$ and $61 \pm 6.36\%$ in case of male and female asthmatic patients, respectively.⁸

In a study by Stolz *et al.* (2007), percentage of patients with mild, moderate, severe and very severe asthma was 8.4, 22.2, 45.5 and 24 %, respectively, whereas in our study the percentage of mild, moderate, severe and very severe patients was 29.72, 32.43, 24.32 and 13.51%, respectively in case of males and 25, 33.3, 21.87 and 21.87 %, respectively in case of females.¹⁰

In our study, mean hs-CRP value in case of male asthmatics was 9.84 ± 2.80 mg/L. In mild, moderate and severe disease, it was 6.84 ± 1.66 , 9.68 ± 2.78 and 15.84 ± 4.12 mg/L, respectively. In asthmatic females, the mean hs-CRP value was 8.25 ± 3.16 mg/L and it went on increasing with severity of disease *i.e.* in mild, moderate and severe disease, it was 4.92 ± 1.12 , 7.86 ± 2.32 and 13.90 ± 3.84 mg/L, respectively. In case of COPD males, the mean hs-CRP value was 9.13 ± 4.02 mg/L and its values varied with increasing severity *i.e.* mild, moderate, severe and very severe disease, it was 4.80 ± 1.2 , 6.72 ± 2.6 , 10.84 ± 4.8 and 15.68 ± 6.8 mg/L, respectively. In case of COPD females, the mean value of hs-CRP was 9.60 ± 3.73 mg/L, whereas in case of mild, moderate, severe and very severe disease, it was 4.32 ± 1.08 , 6.92 ± 2.4 , 10.36 ± 3.24 and 15.84 ± 4.82 mg/L, respectively.

In other studies by Qian *et al.* (2008), the values of hs-CRP were 0.23-0.51 mg/L, 0.51-1.42 mg/L and > 1.42 mg/L in mild, moderate and severe asthma, respectively¹¹, whereas in a study by Soferman *et al.* (2008), the mean values of hs-CRP in severe asthma were 14.28 ± 8.45 mg/L.¹²

In another study by Panaszek *et al.* (2007), the serum concentrations of hs-CRP ranged from 0.20 to 14.5 mg/L in both male and female asthmatic patients.¹³

The values of serum hs-CRP concentration ranged from 12.9 mg/L to 50.6mg/L in male and female COPD patients (mild to very severe disease) in a study by Stolz *et al.* (2007).¹⁰

The value of serum hs-CRP ranged from 3.33 to 12.85 mg/L in male and female asthmatic patients in a study by Broekhuizen *et al.* (2005).¹⁴ It ranged from 2.9 to 13.7 mg/L in COPD male and female patients in a study by Schneider *et al.* (2006).¹⁵

High sensitivity C-reactive protein (hs-CRP), which is an inflammatory marker, in the present study had a strong association with COPD and asthma both in males and females with interaction p-values in case of male asthmatics (0.003), female asthmatics (0.01), COPD males (0.001) and COPD females (0.001). Above observations of our study are generally in confirmation of the results by studies conducted by Broekhuizen *et al.* (2005), Olafsdottir *et al.* (2004), Pinto-Plata *et al.* (2005), Schneider *et al.* (2006), Takemura *et al.* (2005), Panaszek *et al.* (2007), Qian *et al.* (2008) and Soferman *et al.* (2008) with the value of hs-CRP being directly proportional to the severity of disease both in asthma and COPD.^{14,9,16,15,8,13,11,12}

CONCLUSION

This observational study was conducted in Government medical college. The study concluded that hs-CRP is reflector of chronic inflammation of respiratory tract, it correlates with severity of COPD and Bronchial Asthma, in which the pathology is same. It, therefore, is an important biomarker of severity of disease. hs-CRP is an predictor of morbidity and mortality of asthma and COPD, and also helps in the

modulation of the treatment of the conditions.

REFERENCES

1. Wouters EF. The systemic face of airway diseases: the role of C-reactive protein. *Eur Respir J* 2006;27:877-9.
2. Pepys MB and Hirschfield GM. C-reactive protein : a critical update. *J Clin Invest* 2003; 11 : 1805-1812.
3. Vigushin DM, Pepys MB and Hawkins PN. Metabolic and scintigraphic studies of radiiodinated human C-reactive protein in health and disease. *J Clin Invest* 1993; 91 : 1351-1357.
4. Ridker PM. High- sensitivity C-reactive protein potential adjunct for global risk assessment in the primary prevention of cardiovascular disease. *Circulation* 2001; 103 : 1813-1818.
5. Savykoski T, Harju T, Paldanius M *et al.* Chlamydia pneumonia infection and inflammation in adults with asthma. *Respiration* 2004; 71 : 120-125.
6. Kony S, Zureik M, Driss F, Neukirch C, Leynaert B and Neukirch F. Association of bronchial hyper-responsiveness and lung function with C-reactive protein (CRP) : a population based study. *Thorax* 2004; 59 : 892-896.
7. P. J. Barnes, B. R. Celli. Systemic manifestations and comorbidities of COPD. *European Respiratory Journal*, 2009; 33 : 1165-1185
8. Takemura M, Matsumoto H, Niimi A *et al.* High sensitivity C-reactive protein in asthma. *Eur Respir J* 2006; 27 (5) : 908-912.
9. Olafsdottir IS, Gislason T, Thjodleifsson B *et al.* C-reactive protein levels are increased in non-allergic but not allergic asthma : a multicentre epidemiological study. *Thorax* 2005; 60 : 451-454.
10. Stolz D, Christ-Crain M, Morgenthaler NG *et al.* Copeptin, C-reactive protein and procalcitonin as prognostic biomarkers in acute exacerbation of COPD. *Chest* 2007; 131 : 1058-1067.
11. Qian FH, Zhang Q, Zhou LF *et al.* High-sensitivity C-reactive protein: a predicative marker in severe asthma. *Respirology* 2008; 13 (5) : 664-669.
12. Soferman R, Glatstein M, Sivan Y and Weisman Y. hs-CRP levels : measurement of airway inflammation in asthmatic children. *Pediatr Int* 2008; 50 (1) : 12-16.
13. Panaszek B, Liebhart E, Liebhart J, Paw A, Owicz R and Fal AM. Serum concentration of C-reactive protein is not a good marker of bronchial hyper-responsiveness. *Arch Immunol Ther Exp (Warsz)* 2007; 55 (5) : 341-345.
14. Broekhuizen R, Vernooy JH, Schols AM *et al.* Leptin as local inflammatory marker in COPD. *Respir Med* 2005; 99 : 70-74.
15. Schneider A, Dinant GJ, Maag I *et al.* The added value of C-reactive protein to clinical signs and symptoms in patients with obstructive airway disease : results of a diagnostic study in primary care. *BMC Fam Pract* 2006; 7 : 28.
16. Pinto-Plata VM, Mullerova H, Toso JF *et al.* C-reactive protein in patients with COPD, control smokers and non-smokers. *Thorax* 2006; 61 : 23-28.