HIGH SENSITIVITY C-REACTIVE PROTEIN IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND ASTHMA- A PROSPECTIVE STUDY IN NORTH INDIA

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ABSTRACT

BACKGROUND
High sensitivity C-reactive protein (hs-CRP) is an acute phase reactant with well documented sensitivity that is commonly used to diagnose infections and inflammatory conditions like COPD and Asthma. We wanted to study the plasma hs-CRP levels in patients of COPD and asthma.

METHODS
This is a prospective study conducted for a period of one year from Nov. 2017- Oct. 2018, conducted at GMC, Jammu, which is a tertiary care centre. In our study, out of 100 patients who were studied, 50 were male (50%) and 50 were female (50%) with male: female ratio of 1:1.

RESULTS
Thirty (30%) patients were asthmatics and seventy (70%) patients had COPD, with asthma to COPD ratio of 1:2.3.

CONCLUSIONS
High sensitivity C-reactive protein (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).

BACKGROUND

COPD is a leading and increasing cause of morbidity and mortality worldwide[1] and at present over 600 million people worldwide have COPD, the morbidity and mortality continue to escalate at an alarming rate. Asthma is a chronic condition involving the respiratory system in which the airways occasionally constrict, become inflamed and are lined with excessive amounts of mucous, often in response to one or more triggers. Although asthma is more common in affluent countries, it is by no means a problem restricted to affluent only. WHO estimates that there are between 15 and 20 million asthmatics in India. Globally, asthma is responsible for around 180, 000 deaths annually. High sensitivity C-reactive protein (hs-CRP) is an acute phase reactant with well documented sensitivity that is commonly used to diagnose infections and inflammatory conditions like COPD and asthma.[2] Recent population based studies showed associations of increased levels of serum hs-CRP with a high frequency of airway hyper-responsiveness and low forced expiratory volume in one second (FEV_1) among subjects without heart disease suggesting that systemic inflammation may be associated with respiratory impairment.[3]

METHODS

This prospective study entitled High Sensitivity C-Reactive Protein in COPD and Asthma was carried out in the GMC, Jammu for a period of one-year w.e.f. Nov. 2017 to Oct. 2018. A detailed history, complete physical, clinical, systemic examination and lab investigations were done. Immunoturbidimetric method was employed for quantitative determination of hs-CRP.

Inclusion Criteria
All patients who had history along with clinical signs and symptoms with the complaint of chronic productive cough, breathlessness with seasonal variability and with history of smoking and occupational smoke and dust exposure suggestive of COPD and Asthma and confirmed by spirometry were included.

Exclusion Criteria
1. Diabetes mellitus.
2. Chronic inflammatory diseases like rheumatoid arthritis, SLE.
3. Atherosclerosis associated heart disease.
4. Pulmonary Kochs.
5. Interstitial lung disease.
6. Pneumothorax.
7. Pleural effusion.

RESULTS
The present study was carried out on 100 patients of COPD and Bronchial Asthma. The objective of this study was to study the plasma hs-CRP levels in these patients in Government Medical College Hospital, Jammu so as to

correlate the values of plasma hs-CRP levels with degree of severity of COPD and asthma.

Age (in Years)	Asthmatic		COPD	
	Males (n = 13) No. (%)	Females (n = 17) No. (%)	Males (n = 37) No. (%)	Females (n = 33) No. (%)
20-29	6 (46.15)	6(35.29)	—	—
30-39	6 (46.15)	11 (64.70)	—	—
40-49	1 (7.69)	—	1 (2.7)	2 (6.06)
50-59	—	—	6 (16.21)	5 (15.15)
60-69	—	—	20 (54.05)	25 (75.75)
70-79	—	—	10 (27.02)	1 (3.03)
Total	13 (100)	17(100)	37 (100)	33 (100)

Table 1. Age and Sex Distribution of Asthmatic and COPD Patients

Presentation	No. of Patients	Percentage (%)
Asthma	30	30
COPD	70	70

Table 2. Distribution of Patients According to Presentation

Variables	Asthmatic		COPD		Healthy	
	Males (n = 13)	Females (n = 17)	Males (n=37)	Females (n = 33)	Males (n = 10)	Females (n - 10)
Age in years (Mean ± 1 SD)	31.37 ± 6.64	31.67 ± 5.63	65.48 ± 7.55	61.93 ± 6.18	52.23 ± 14.58	43.33 ± 10.64
Height in meters (Mean ± 1 SD)	1.61 ± 0.09	1.54 ± 0.04	1.68 ± 0.04	1.53 ± 0.043	1.65 ± 0.61	1.52 ± 0.13
Weight in Kgs (Mean ± 1 SD)	54 ± 4.44	50.38 ± 4.05	60 ± 7.44	44.69 ± 4.78	59.94 ± 4.50	46.16 ± 5.24

Table 3. Various Demographic Characteristic Measurements of Male and Female Patients and Healthy Subjects

Variables	PEFR% Predicted			hs-CRP Values (mg/L)		
	Minimum	Maximum	Mean ± 1 SD	Minimum	Maximum	Mean ± 1 SD
Males (n=13)	58	64	62 ± 3	3.76	21.72	9.84 ± 2.80
Females (n=17)	49	77	61 ± 6.36	3.76	19.86	8.25 ± 3.16

Table 4. Asthmatic Patients (Male and Female)

Variables	Minimum	Maximum	Mean ± 1 SD
Duration of smoking (in years)	25	60	41.56 ± 7.64
FEV$_1$ (% Predicted)	30	68	51 ± 8.14
FVC (% Predicted)	57	83	71 ± 6.54
FEV$_1$/FVC (% Predicted)	50	90	71 ± 11.06
hs-CRP (mg/L)	3.80	21.72	9.13 ± 4.02

Table 5. COPD Males (n = 37)

Variables	Minimum	Maximum	Mean ± 1 SD
Duration of smoking (in years)	25	50	40 ± 5.22
FEV$_1$ (% Predicted)	33	85	44.48 ± 10.06
FVC (% Predicted)	52	102	74.40 ± 12.93
FEV$_1$/FVC (% Predicted)	43	73	58.30 ± 12.22
hs-CRP (mg/L)	3.70	17	9.60 ± 3.73

Table 6. COPD Females (n = 33)

DISCUSSION

This study was done on 100 patients who presented to Government Medical College Hospital, Jammu with the history of smoking, occupational exposure and family history of asthma. Seventy out of 100 patients were COPD and 30 were asthmatics. The objective of this study was to find out the plasma hs-CRP levels in patients of asthma and COPD and to correlate the values of hs-CRP levels with degree of severity of asthma and COPD.

In our study, out of 100 patients who were studied, 50 were male (50%) and 50 were females (50%) with ratio of male: female was 1 : 1. Thirty (30%) patients were asthmatics and 70 (70%) patients had COPD, with asthma to COPD ratio of 1: 2.3. In case of asthma, there were 13 male and 17 female patients with a male: female ratio of 0.76: 1, whereas in case of COPD, there were 37 males and 33 females with male: female ratio of 1.12: 1. Maximum number of male and female patients (i.e. 20% and 25% respectively) were in the age group of 60-69 years. Male: Female ratio in our study in case of COPD was 1.2: 1, whereas in the studies by Pinto-Plata et al[4] and Dahl[5] was 1.43: 1 and 1.26: 1, respectively. 66% of the patients were female in the study of Takemura et al (2006),[6] whereas the percentage of female patients in the study by Dahl (2006)[5] was 40%. In the studies by Stolz et al[7] and Higashimoto et al,[8] the percentage of female patients was 55% and 42%, respectively.

In our study, the mean age of patients in case of asthma was 31.37 years in males and 33.07 years in females, whereas it was 65.48 years in COPD males and 61.93 years in COPD females. On the other hand, mean age in case of controls i.e. healthy male and female subjects was 43.43 years. Whereas the average age in case of various studies by Olafsdottir et al,[9] Takemura et al[6] was 41.6 years and 48 ± 21 years, respectively in case of asthma, while in case of COPD, the average age in different studies by Broekhuizen et al,[10] Pinto-Plata et al[4] and Stolz et al[7] was 46 years, 63 years, 66 years and 70 years, respectively. 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[6] were smokers. None of the patients in asthma group were smokers in our study. On the contrary, in a study by Olafsdottir et al[9] about 27.8% patients were smokers.

In our study, the BMI in case of male asthmatics, female asthmatics, COPD males and COPD females was 20.84, 21.25, 21.27 and 20.08 kg/m², respectively, whereas in a study by Olafsdottir et al[9] it was 25.04 and 26.01 kg/m in case of male asthmatics and female asthmatics, respectively. Takemura et al[6] reported 22 ± 3 and 23 ± 4 kg/m BMI in male and female asthmatics in their study.

In case of COPD, Pinto-Plata et al[4] reported 27.04 and 26.54 kg/m BMI in males and females, respectively. Mean PEFR% predicted in case of asthmatic males and females was 72% each in a study by Takemura et al,[6] whereas in our study it was 62 ± 3% and 61 ± 6.36% in case of male and female asthmatic patients, respectively.

In a study by Stolz et al,[7] 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.

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 valued varied with increasing severity i.e. in 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,[11] 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, respectively, whereas in a study by Soferman et al,[12] the mean values of hs-CRP in severe asthma were 14.28 ± 8.45 mg/L.

In another study by Panaszek et al,[13] the serum concentrations of hs-CRP ranged from 0.20 to 14.5 mg/L in both male and female asthmatic patients. The values of serum hs-CRP concentration ranged from 12.9 mg/L to 50.6 mg/L in male and female COPD patients (mild to very severe disease) in a study by Stolz et al.[7] In a study by Pinto-Plata et al,[4] the serum concentrations of hs-CRP in both male as well as female patients was reported to be between 3.7 to 6.3 mg/L.

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.[10] It ranged from 2.9 to 13.7 mg/L in COPD male and female patients in a study by Schneider et al.[14]

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,[10] Olafsdottir et al,[9] Pinto-Plata et al,[4] Schneider et al,[14] Takemura et al,[6] Panaszek et al,[13] Qian et al[11] and Soferman et al[13] with the value of hs-CRP being directly proportional to the severity of disease both in asthma and COPD.

CONCLUSIONS

As hs-CRP reflects 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. In addition, if follow-up studies are done, hs-CRP may also be predictor of morbidity and mortality of the above-mentioned entities, thereby helping in the modulation of the treatment of the conditions. Many anti-inflammatory drugs can then be tried for experimental purpose to decelerate the progress of chronic inflammatory disease. Atorvastatin is a potent anti-inflammatory drug used in treating various anti-inflammatory diseases like rheumatoid arthritis. Its use in COPD and asthma can be contemplated.

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