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CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD); FREQUENCY OF ELEVATED C-REACTIVE PROTEIN IN PATIENTS AT LIAQUAT UNIVERSITY HOSPITAL JAMSHORO/HYDERABAD

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ABSTRACT… Objectives: Chronic obstructive pulmonary disease (COPD) leads to partial reversible obstruction of airways. The objective of our study is to determine frequency of elevated C-reactive protein (CRP) level in patients of COPD at Liaquat University Hospital Jamshoro/Hyderabad. **Study Design:** Cross-sectional study. **Setting:** Medical Unit-I of Liaquat University Hospital Jamshoro/Hyderabad. **Period:** 1st March 2013 to 31st August 2013. **Patients and Methods:** Patients of either sex and ages from 40-80 years old and having COPD for at least two years duration were included. Patients below 40 years of age, having malignancies or autoimmune disorders were excluded from this study. **Results:** We enrolled 186 patients with COPD and their mean age was ± SD 57.63±8.45 years. Majority 182 (97.8%) had habit of smoking while 4(2.2%) were non-smokers. Mean CRP level in COPD patients was ± SD 1.26±0.79 (range 0.1- 3.0 mg/d1). Out of 186 COPD patients, 94(50.6%) have raised CRP level (higher than 1.0 mg/dl). Median value of CRP level during this study was 1.10 mg/dl. About 92(49.4%) patients have normal level of CRP (less than 1.0 mg/dl). **Conclusion:** On conclusion, frequency of raised C-reactive protein in our study was much higher (50.6%).

Key words: Frequency, C-reactive protein level (CRP), chronic obstructive pulmonary disease.

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a major health concern due to increasing prevalence throughout world. Although cigarette smoking is a major risk factor for COPD in world, yet there are some genetic and environmental factors implicated in its pathogenesis.[1] Moreover, non-smokers may also develop chronic airflow obstruction due to serious indoor air pollution caused by burning woods, animal dung, crop residues, coal in open fires or improper stoves.[1] In developing countries, indoor air pollution resulting from biomass cooking or heating in an important culprit for COPD.[2]

In COPD, inhalation of noxious gases and particulate matter is characterized by infiltration of chronic inflammatory cells and release of chemical mediators in airways and lung parenchyma. This persistent inflammation in lung tissues is often associated with systemic inflammatory reaction leading to adverse clinical effects and hence called as systemic effects of COPD.[3] The systemic inflammation in COPD arises due to unknown reasons. However, mechanism for regulation of inflammatory response in pulmonary and systemic compartments remain obscure but there is a clear evidence supporting role of some inflammatory markers which may rise in peripheral circulation.[3,4] Of blood-based biomarkers discovered, C-reactive protein (CRP) has shown promising role in its etiology.[5] The increased CRP level is often associated with impaired lung functions, decreased exercise capacity, poor quality of life and being predictor of all-cause mortality in COPD patients. Pinto-Plata VM[6-9] found 14% rise in serum CRP levels due to COPD. Furthermore, COPD by itself and smoking being commoner risk factor for it, is often associated with raised serum CRP levels.[10]

Based on current knowledge that COPD is a multi-

component disorder associated with raised serum CRP levels, we planned this study. The objective of our study was to find frequency of elevated CRP levels in COPD patients considering degree of pulmonary dysfunction, systemic inflammation and quality of life.

MATERIAL AND METHODS

This descriptive cross-sectional study was conducted at Medical Unit-I of Liaquat University Hospital Jamshoro/Hyderabad from 1st March 2013 to 31st August 2013. About 186 patients of either sex and ages from 40-80 years old and having COPD for at least two years duration were enrolled by non-probability consecutive sampling. All participants gave informed and written consent and study was approved by institutional ethical committee.

All COPD patients were recruited in medicine department who fulfill inclusion criteria. We exclude patients below 40 years of age, having concurrent malignancies, acute respiratory failure, auto-immune disorders with raised CRP levels. All data was collected in structured questionnaire designed by researcher and include information regarding age, demographic profile, smoking, lung function in COPD and CRP levels. About 2 mls of venous blood sample in fasting state at 9.00 am was taken from all subjects for CRP estimation. It was centrifuged immediately and obtained serum frozen at -80^{0}C until time of analysis. High sensitive CRP measurements were performed by using CRPH reagent, Beckman coulter (sensitivity ≤ 0.011 mg/dL) in conjunction with Beckman coulter Immage® Immunohistochemistry system, CA, USA nephelometer.

Data was entered and analyzed in statistical program SPSS Version 16.0. Frequencies and percentages were computed for qualitative variables like gender, economical and educational statuses, smoking habit and raised CRP. The numerical variables such as age (in years) were presented as mean ± standard deviation. The effect modifiers were controlled by stratification of age, gender, economical and educational statuses and smoking habits so that effects of these parameters could be assessed on raised CRP by using Chi-square test. All data was calculated on 95% confidence interval and p-value ≤ 0.05 was considered as statistically significant.

RESULTS

We enrolled 186 COPD patients during this study with mean age ± SD 57.63±8.45 years (range 40-80 years). About 175 (94.08%) were males and 11(5.92%) females with male to female ratio of 16:1. This is shown in tables-I and II. Majority of our patients 116 (62.4%) were between 51 to 60 years of age. This is shown in table-III. Most of studied patients 89 (48.1%) were illiterate and belonged to poor socio-economic status 104 (55.9%). This is shown in tables-IV and V. Similarity majority 182(97.8%) of patients had habit of active smoking and this is shown table-VI.

In present study, mean CRP level ±SD was 1.26±0.79 (range 0.1-3.0 mg/dl). The raised CRP level (higher than 1.0 mg/dl) was observed in 94 (50.6%) patients. The median CRP level was 1.10 mg/dl. Normal level (less than 1.0 mg/dl) of CRP level was seen in 92(49.4%) patients. This is shown in tables-VII and VIII. Our study showed gender, educational and socio-economic statuses to be significant causes for elevated CRP levels in COPD patients (p-value < 0.05), while habit of smoking was insignificant (p-value 0.98). This is shown in tables-X,XI,XII,XIII.

Mean	57.63
Median	56.0
Mode	51.0
Std. Deviation	8.45
Range	40 to 80 years
Minimum	40.0
Maximum	80.0

Table-I. Age distribution of patients (in years) N=186

Gender	Frequency	Percentage
Male	175	94.08%
Female	11	5.92%

Table-II. Gender distribution of patients N=186

Age in Groups	Frequency	Percentage
40 to 50 years	17	9.0%
51 to 60 years	116	62.4%
61 to 70 years	33	17.7%
71 to 80 years	20	10.8%

Table-III. Distribution of patients according to age group N=186

Educational Status	Frequency	Percentage
No Schooling	89	48.1%
Primary	55	29.6%
Secondary	29	15.4%
Graduation	13	6.9%

Table-IV. Frequency of Educational Status of Patients N=186

Socio-economic Status	Frequency	Percentage
Poor (monthly income <10,000)	104	55.9%
Middle (11 to 40,000)	57	30.6%
Upper (>40,000)	25	13.4%

Table-V. Frequency of Socio-Economics Status N=186

Smoking	Frequency	Percentage
Yes	182	97.8%
No	4	2.2%

Table-VI. Frequency of patients according to habit of smoking N=186

Mean	1.26
Median	1.10
Mode	0.4
Std. Deviation	0.79
Range	0.1 to 3.0 mg/dl
Minimum	0.1
Maximum	3.0

Table-VII. Distribution according to CRP level N=186

Raised CRP level	Frequency	Percentage
Yes (> 1.0 mg/dl)	94	50.6%
No (< 1.0 mg/dl)	92	49.4%

Table-VIII. Frequency of patients according to CRP level N=186

Age (in groups)	Raised CRP		Total	P value
	Yes N=94	No N=92		
40 to 50 years	10 (10.6%)	7 (7.6%)	17 (9.1%)	0.23*
51 to 60 years	52(55.3%)	64(69.6%)	116 (62.4%)	
61 to 70 years	19 (20.2)	14(15.2%)	33 (17.7%)	
71 to 80 years	13 (13.8%)	7(7.6%)	20(10.8%)	

Table-IX. Outcome of age (in groups) with CRP level N=186
*P value is statistically insignificant calculated by test of chi square

Gender	Raised CRP		Total	P value
	Yes N=94	No N=92		
Male	92 (97.9%)	83 (90.2%)	175 (94.1%)	0.03*
Female	2 (2.1%)	9(9.8%)	11(5.9%)	

Table-X. Outcome of gender with CRP level N=186
*P Value is statistically significant calculated by Fisher's exact test of chi square

Educational Status	Raised CRP		Total	P Value
	Yes N=94	No N=92		
No Schooling	69 (73.4%)	20(21.7%)	89(47.8%)	< 0.00001*
Primary	15(16.0%)	40(43.5%)	55(29.6%)	
Secondary	8 (8.5%)	21(22.8%)	29 (15.6%)	
Graduation	2(2.1%)	11(12.0%)	13(7.0%)	

Table-XI. Outcome of educational status with CRP level N=186
*P Value is statistically highly significant calculated by Pearson's test chi square

Economical Status	Raised CRP		Total	P value
	Yes N=94	No N=92		
Poor (monthly income 10,000)	79 (84.0%)	25(27.2%)	104(55.9%)	0.0001
Middle (11 to 40,000)	10 (10.6%)	47 (51.1%)	57(30.6%)	
Upper (> 40,000)	5 (5.3%)	20(21.7%)	25(13.4%)	

Table-XII. Outcome of socio-economics status with CPR level N=186
*P value is statistically significant calculated by Pearson's test of chi square

Smoking Status	Raised CRP		Total	P value
	Yes N=94	No N=92		
Yes	92 (97.9%)	90(97.8%)	182(97.8%)	0.98*
No	2 (2.1%)	2 (2.2%)	4(2.2%)	

Table-XIII. Outcome of smoking habits with CRP level N=186
*P value is statistically insignificant calculated by Fisher's exact test of chi square

DISCUSSION

C-reactive protein (CRP) is an acute phase reactant secreted by liver in response to interleukin 6 (IL-6) stimulation. CRP elevated in most conditions associated with infection, inflammation or tissue damage, for which it is a sensitive marker.[11] COPD has been associated with excessive systemic inflammatory response as compared with control subjects and there is further up-regulation of systemic inflammation at time of exacerbation.[12,13]

The mean age of COPD patients in our study was 57.63±8.45 years. This is in comparison with study of Gupta et al[14] who found mean age of their patients 63.0±9.0 years. Another study by Aksu F et al[1] showed mean age of 60.6 years. The results of these studies were closer to our study. There were 175(94.08%) males and 11(5.92%) females with male to female ratio of 16:1 in our study. Broekhuizen R[7] showed that there were 69.60% males, while 30.39% females in their study. According to Aksu F et al[1], 86.51% males and 13.4% females patients. The results of these studies are similar to present study. Majority of our patients 182 (97.8%) had habit of smoking which is comparable by Pinto-Plata VM[8], who showed 60.2% smokers in their study.

In present study, mean CRP level ±SD in COPD patients was 1.26±0.79 (range 0.1-3.0 mg/dl). In a study by Subramanian et al[15], mean CRP level was higher (i.e 5.9 mg/dl) in 58 patients. This difference may be due to small sample size, sampling technique and duration in their study. Out of 186 patients, we observed raised CRP level (higher than 1.0 mg/dl) in 94(50.6%) of our patients. Study by Subramanian et al[15] showed raised CRP level (higher than 5 mg/dl) in 30(60%) of their patients. The relation of raised CRP levels with COPD has been shown in various population-based studies.[16,17] These observations and results

correlate well to our study. During this study, we found gender, educational and socio-economic statuses and habit of smoking to be significant factors for raised serum CRP levels in COPD patients (p-values 0.03, < 0.00001, 0.0001, 0.98 respectively).

A recent study by Danesh et al[18] has reported an association between cigarette smoking and raised CRP level (p-value 0.001). However, no such studies on educational and socio-economic statuses were found to be significantly associated with raised CRP levels nationally or internationally except to our study.

CONCLUSION

From this study we conclude that much higher frequency (50.6%) of raised C-reactive protein levels in our population which were commonly associated with gender, educational and socio-economic statuses and habit of smoking. CRP may be a systemic marker of inflammatory process that occur in COPD patients.

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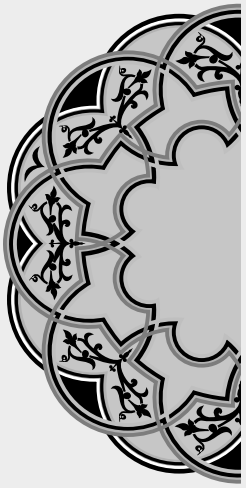

"Climb the mountain so you can see the world, not so the world can see you."

Unknown

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Dr. Atif Sitwat Haya	Concept and design of study and manuscript drafting	
2	Dr. Abdul Haque Khan	Manuscript typing and data collection	
3	Dr. Ghulam Nabi Pathan	Critical revision of article and statistical analysis	
4	Dr. M. Zubair Mushtaque	Data collection	