

## C-Reactive Protein in Patients with Pulmonary Tuberculosis

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**Abstract:** The present study was conducted to evaluate the C-reactive protein (CRP) in patients with pulmonary tuberculosis at Liaquat University Hospital, Hyderabad, Pakistan. All patients with pulmonary tuberculosis > 12 years of age, of either gender were evaluated for their serum CRP level. During twelve months study period, 127 patients with pulmonary tuberculosis were evaluated for CRP level, of which 76 (60%) were males and 51 (40%) were females. The observed symptoms were cough and expectoration 115 (91%), weakness and constant fatigue 92(72%), weight loss 110 (86%), fever 90(71%), night sweats 85(67%), chest pain 95(75%), coughing up blood 98(77%), loss of appetite 88(69%), headache 102(80%) and combined / mixed symptoms 100(79%). The overall mean CRP in patients with TB was  $9.87 \pm 4.83$  where as it was  $11.21 \pm 3.32$  and  $13.82 \pm 4.63$  in male and female subjects respectively. The mean $\pm$ SD of normal and raised serum CRP was  $2.76 \pm 1.34$  and  $13.26 \pm 4.42$  ( $p \leq 0.01$ ). The complications observed in patients with raised serum CRP were pneumothorax 04(4.7%), fibrosis 08(9.3%), miliary TB 06(7%), empyema 10(11.6%), fungal colonization within tuberculous cavity 09(10.5%), bronchiectasis 11(12.8%), more than 01 complication 11(12.8%) and Nil 19(22.1%). The present study detected elevation of CRP in pulmonary tuberculosis and a high CRP is clearly associated with more severe disease.

**Key words:** Tuberculosis • Pulmonary • C-Reactive Protein

### INTRODUCTION

Tuberculosis, MTB, or TB (short for tubercle bacillus) is a common and in many cases lethal, infectious disease caused by various strains of mycobacteria, usually *Mycobacterium tuberculosis* [1]. One third of the world's population is infected with *Mycobacterium tuberculosis*; the proportion of people in the general population who become sick with tuberculosis each year is stable or falling worldwide but, because of population growth, the absolute number of new cases is still increasing [2]. It is the second leading cause of adult death in impoverished communities of Pakistan [3]. Globally, Pakistan ranks 8th in terms of estimated number of cases by WHO, with an incidence of 175/100,000 persons [3]. Pakistan alone accounts for 44% of total TB burden in the Eastern Mediterranean Region of the WHO comprising 23 countries [3]. In India, approximately 4.8 million people are suffering from TB infection of which 2.2

million are smear positive; the annual risk of infection is 1 to 2% and the case fatality rate is 24% [4]. It is also a major cause of illness and death worldwide especially in Africa and Asia, in Nigeria, a prevalence of 460,000 has been reported [5]. The WHO in its report of 2007 estimated that globally 8.8 million people were infected with TB and 1.6 million people died of TB in 2005 and the majority of the infected people i.e. 7.4 million (84%) belonged to Asia and Sub-Saharan Africa [6]. The association between TB and malnutrition is well recognized; TB can lead to malnutrition and malnutrition may predispose to tuberculosis [7].

CRP is an established marker of acute inflammation and its serum concentration is frequently determined to assess the grade of systemic inflammation [8], e.g., in rheumatic or intestinal diseases, or to verify bacterial etiology of inflammation such as pneumonia and tuberculosis in adults. Recently, the immunoturbidimetric method on latex particles has been used to determine very

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low CRP concentrations thus enabling the use of CRP concentration as a prognostic marker of chronic inflammation in patients with cardiovascular disease, diabetes mellitus [9, 10], chronic infections and asthma [11, 12]. The objective of the present study was to assess changes in the concentration of CRP in patients with pulmonary tuberculosis infection. The CRP can serve as a sensitive indicator of activity of the disease and its proper evaluation indicates a good therapeutic response.

## MATERIALS AND METHODS

This descriptive case series study was conducted at Liaquat University Hospital from January 2011 to December 2011. All patients of > 12 years of age, of either gender with cough and expectoration for more than 15 days, weakness and constant fatigue, weight loss, fever, night sweats, chest pain, coughing up blood and loss of appetite came through outdoor patient department (OPD) or indoor patients or casualty outdoor department (COD) were enrolled and evaluated with detail history, relevant examination and specific investigations i.e. chest radiograph and early morning sputum for acid fast bacilli (AFB) for three consecutive days. The evidence of apical cavitations on chest radiographs and any one positive smear of sputum for AFB were considered as cases of pulmonary tuberculosis. CT scan of chest and pleural fluid (if present) were also evaluated as having pulmonary tuberculosis. All the patients were taken consecutively and an informed consent was taken from every patient or from next to the kin after full explanation of procedure. After planning the management protocol 3 ml sample of venous blood in a disposable syringe was taken for the evaluation of serum C-reactive protein and sent to laboratory for analysis. The value for serum C- reactive protein  $\geq 0.6$  mg/L (cut off) was considered as to be raised. Patients with rheumatic fever, myocardial infarction, leprosy, congestive heart failure, different infectious diseases (meningitis, poliomyelitis, infectious mononucleosis and syphilis), malignancy, rheumatoid and septic arthritis and the postoperative and puerperal periods and on antibiotic therapy were considered in exclusion criteria. The enrolled patients were also followed for the period of nine months to observe therapeutic response at the end of treatment and also for the evaluation of any complication of pulmonary tuberculosis during the treatment. The data was collected and analyzed in SPSS version 10.00. The frequency and percentage (%) was calculated for raised serum CRP level in patients with pulmonary tuberculosis and gender distribution. The

mean and standard deviation (SD) was calculated for age and CRP. The stratification was done for age, gender, C-reactive protein (CRP) in patients with pulmonary tuberculosis. The independent - samples t-test was applied between categorical variables, chi-square was applied to determine the statistical difference in gender and the p-value  $\leq 0.05$  was considered as statistically significant. The mentioned statistical tests were applied at 95% confidence interval (CI).

## RESULTS

During one year study period, 127 patients with pulmonary tuberculosis were studied for CRP, of which 76 (60%) were males and 51 (40%) were females. The observed symptoms were cough and expectoration 115 (91%), weakness and constant fatigue 92 (72%), weight loss 110 (86%), fever 90 (71%), night sweats 85 (67%), chest pain 95 (75%), coughing up blood 98 (77%), loss of appetite 88(69%), headache 102(80%) and combined / mixed symptoms 100(79%). The mean age  $\pm$  SD of overall subjects was  $45.86 \pm 7.52$  whereas the mean age  $\pm$  SD of male as well as female subjects was  $52.92 \pm 7.52$  and  $48.76 \pm 8.74$  respectively. The mean age  $\pm$  SD of males and females with raised CRP was  $51.88 \pm 10.54$  and  $52.86 \pm 9.34$ . The overall mean CRP in tuberculosis patients was  $9.87 \pm 4.83$  where as it was  $11.21 \pm 3.32$  and  $13.82 \pm 4.63$  in male and female subjects with tuberculosis respectively. The mean CRP in patients with tuberculosis in relation to its status is shown in Table 1. Ninety two (72%) patients belonged to rural area whereas thirty five (28%) were from urban areas of the Sindh province. The frequency of CRP in patients with pulmonary tuberculosis in relation to gender and complications observed in raised CRP pulmonary TB patients are shown in Tables 2 and 3.

## DISCUSSION

C-reactive protein (CRP) is a non-specific acute phase serum protein and a useful biomarker for the detection of inflammation and various active infections [13-14]. It has been shown to be beneficial in the clinical evaluation of respiratory tract infections in adults [15-18] as well as fever in children [19-21]. Additionally, an elevated CRP has been used as an indication to initiate antibiotic therapy [20].

In present study we evaluated the serum C-reactive protein in patients with pulmonary tuberculosis and found that CRP was raised in 86 (67.7%) patients of pulmonary TB cases which are consistent with the studies by

Table 1: C-reactive protein in patients with pulmonary tuberculosis

CRP	n = 127	Mean ± SD ( $\mu\text{g}/\text{dl}$ )	t-value	P-value
Raised	86	13.26±4.42	14.8	<0.01*
Normal	41	2.76±1.34		

\* P-value is statistically significant

Table 2: C-reactive protein in relation to gender

CRP	Gender		Total	P-value
	Male	Female		
Raised	57 (75%)	29 (56.9%)	86 (67.7%)	0.02*
Normal	19 (25%)	22 (43.1%)	41 (32.3%)	
Total	76 (100%)	51 (100%)	127 (100.0%)	

\*P value is statistically significant

$\chi^2$  value = 4.59; df = 1

Table 3: Complications observed in patients with raised serum C-reactive protein

Complication	Gender		Total	P-value
	Male	Female		
Pneumothorax	03 (5.3%)	01 (3.4%)	04 (4.7%)	0.06*
Fibrosis	05 (8.8%)	03 (10.3%)	08 (9.3%)	
Miliary TB	05 (8.8%)	01 (3.4%)	06 (7%)	
Empyema	08 (14%)	02 (6.9%)	10 (11.6%)	
Pleurisy	07 (12.3%)	01 (3.4%)	08 (9.3%)	
Fungal colonization within tuberculous cavity	07 (12.3%)	02 (6.9%)	09 (10.5%)	
Bronchiectasis	07 (12.3%)	04 (13.8%)	11 (12.8%)	
> 01 complication	05 (8.8%)	06 (10.7%)	11 (12.8%)	
No any	10 (17.5%)	09 (31%)	19 (22.1%)	
Total	57 (100%)	29 (100%)	86 (100%)	

\*P value is statistically non significant

$\chi^2$  value = 5.70; df = 4

Maasilta and Kostiala [22] and Choi *et al.* [23]. Sukhesh *et al.* [24] observed that serum CRP levels may have a role in identifying the advanced and extensive disease thereby indirectly helping the health workers to pick up delayed converters/potential defaulters, so as to guide them to put in extra efforts on such groups in tuberculosis control programs.

In our series the mean age of the overall population was  $45.86 \pm 7.52$  and majority of the subjects were from rural population, these findings are consistent with the study by Sukhesh *et al.* [24]. C-reactive protein is an indication of pathology and disappearance of C-reactive protein is concomitant with effectiveness of drugs used in treatment [25]. The study on C-reactive protein revealed that C-reactive protein turned to be negative in those who had inactive lesions (99 patients) and also in 32 cases that were in the process of improvement, it showed weak reaction, but in 26 cases with active lesions and resistant

mycobacterium, C-reactive protein was strongly positive. [25]. It is very interesting to note that sputum conversion and x-ray findings improvement is concomitant with negative C-reactive protein reaction.

The changes in serum CRP concentration during treatment with regimen of anti-tuberculous therapy were also studied and it was observed that there was a marked decrease in the CRP level with treatment. The mean serum CRP concentration at the time of diagnosis and at the end of treatment was 9.86 and 2.21 respectively. It has been suggested that the magnitude of the increase of serum CRP concentration over normal level reflect the extent of the tissue injury and may predict the course of ensuing illness and the determination of the CRP has been employed as an aid to diagnosis and for management.

The patients with extensive pulmonary destruction and high serum CRP levels remaining after sputum has become negative for *M. tuberculosis* may need broad

spectrum antibiotics and active physiotherapy in an attempt to reduce these levels [24]. This might prevent the development of incurable reactive systemic complications of pulmonary tuberculosis.

It is concluded that CRP can serve as a sensitive indicator of activity of the disease and the return to normal values of initially elevated CRP levels may indicate a good therapeutic response.

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