

## COMPARISON OF MEAN C- REACTIVE PROTEIN LEVELS IN SMEAR POSITIVE AND SMEAR NEGATIVE PULMONARY TUBERCULOSIS

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### ABSTRACT

**Objective:** To compare the mean C - reactive protein levels in clinically diagnosed adult patients with smear positive and smear negative pulmonary tuberculosis.

**Study Design:** Cross sectional study.

**Place and Duration of Study:** The study was conducted at the Department of General Medicine Military Hospital Rawalpindi from 21 May to 25 Sep 2011.

**Material and Methods:** In this study 150 patients of clinically diagnosed pulmonary TB from either sex, age between 15 to 60 years who fulfilled the inclusion criteria were studied. They were divided in two groups, smear positive (sputum for AFB positive) and smear negative (sputum for AFB negative). Serum CRP sample was measured before antituberculosis treatment (ATT) was given. All data were analyzed using SPSS Version 17.0. Qualitative variables X-ray chest findings and gender have been presented as frequency percentage. Mean and standard deviation (mean  $\pm$  SD) have been calculated for quantitative variables i.e. age, CRP levels in both groups. Mann Whitney - U test used to compare mean CRP levels in smear positive and smear negative cases of pulmonary TB. A *p*-value of  $<0.05$  was considered significant.

**Results:** The mean CRP levels were significantly higher in smear positive pulmonary tuberculosis  $49.92 \pm 10.25$  mg/dl as compared to smear negative pulmonary TB  $18.28 \pm 6.18$  mg/dl mean difference of 31.64mg/dl, *p*-value  $<0.0001$ . Mann Whitney - U test was used to compare the mean CRP levels of both groups.

**Conclusion:** Serum CRP levels can be used as add-on with other investigations in pulmonary tuberculosis. Patients of smear positive tuberculosis have significantly higher serum CRP levels as compared to smear negative patients.

**Keywords:** C-reactive protein, Pulmonary tuberculosis, Smear negative tuberculosis, Smear positive tuberculosis.

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### INTRODUCTION

Tuberculosis causes a great deal of ill health and an enormous burden on the population of Pakistan<sup>1</sup>. As per WHO estimates, about 410000 new cases of tuberculosis develop in Pakistan every year with prevalence of 373 cases per 100000 population and incidence of 231 per 100000 population and majority of cases are in productive age group. Tuberculosis causes 38 deaths per 100000<sup>1</sup>.

C-reactive protein (CRP) is an acute phase protein which can be helpful to diagnose and

monitor this grave disease. The sensitivity and the negative predictive value of CRP for tuberculosis is 93.3% and 90.0% respectively<sup>2</sup>. The CRP levels are higher in smear positive patients and extensive disease. An international study has found CRP levels among smear positive cases to be  $37.598 \pm 23.195$  and among smear negative patients to be  $5.40 \pm 1.88$  mg/dl respectively<sup>3</sup>. The serum concentration of CRP in the normal human population has a median of 0.8mg/l (interquartile rang 0.3-1.7mg/l) and is below 10mg/l in 99% of normal samples<sup>4,5</sup>. Levels above 10mg/l are abnormal and indicate the presence of a disease process<sup>6</sup>. ESR is conventionally used as an inflammatory marker in tuberculosis however it has number of disadvantages. The ESR is only an indirect measurement of serum acute phase

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protein concentration. Moreover as a patient's condition worsens or improves, the ESR changes relatively slowly and its values are higher in females<sup>7</sup>. CRP is an acute phase protein that is produced predominantly by the hepatocytes under the influence of cytokines such as Interleukin-6 and tumor necrosis factor- $\alpha$ . It is minimally affected by non-inflammatory conditions and rapidly changes in response to patient's condition<sup>8</sup>. Serum CRP levels are helpful in tuberculosis patients to assess the degree of intoxication, presence and rate of bacterial discharge, the absence or presence of disease and monitoring the response to the treatment<sup>9</sup>.

The exact CRP levels in smear positive and smear negative pulmonary tuberculosis in Pakistan are not documented. This study has been designed to document CRP levels in patients of T.B in local population. Serum CRP levels may have a role in identifying the advanced and extensive disease in patients of pulmonary TB thereby indirectly helping the health workers to pick up delayed converters/potential defaulters, so as to guide them to put in extra efforts on these groups. In tuberculosis control programs CRP levels may be used with other investigations and helpful in early diagnosis and management of tuberculosis.

## MATERIAL AND METHODS

This cross sectional study was conducted at the department of Medicine in collaboration with department of Pathology Military Hospital Rawalpindi. From 21<sup>st</sup> May to 25<sup>th</sup> September 2011. The aim of the study was "to compare the

pulmonary tuberculosis, with 15 to 60 years of age from either sex were included in the study. Individuals with any other respiratory disease, past history of treated pulmonary TB and any other illness were excluded from the study. Calculated sample size was 150 patients. Sampling was done through consecutive non probability. Clinically diagnosed cases of pulmonary TB undergoing sputum smear examination, Mantoux test and X-ray chest were included in the study. They were divided into smear negative pulmonary tuberculosis defined as (any person who presented with productive cough for more than 2 weeks which may be accompanied by other respiratory symptoms like shortness of breathing, haemoptysis and constitutional like symptoms weight loss, fever, night sweats, fatigue radiographic abnormalities consistent with active pulmonary TB<sup>10</sup> and sputum negative for acid-fast bacilli (AFB) by microscopy).

Smear positive pulmonary tuberculosis defined as patient with at least two sputum specimens positive for acid-fast bacilli (AFB) by microscopy, or radiographic abnormalities consistent with pulmonary tuberculosis with one sputum specimen positive for AFB<sup>11</sup>.

Sputum for AFB was performed and diagnosis of TB was confirmed by culture or by biopsy. Serum CRP sample was measured before ATT was given. Informed written consent was taken from all the patients. The serum CRP level was measured by using high sensitivity enzyme immunoassay kit<sup>11</sup> manufactured by Life

**Table-I: Serum CRP levels in the patients of smear positive and smear negative pulmonary TB.**

	Mean	SD	Median	Mod
Smear Negative (n=75)	18.28	6.18	18	20
Smear positive (n=75)	49.92	10.25	46	38

*p* value <0.0001

mean C-reactive protein levels in clinically diagnosed patients with smear positive and smear negative pulmonary tuberculosis". Approval from hospital ethical committee was obtained. Clinically diagnosed patients of

Diagnostics, inc, Catalog Number: 2210. The principle of the assay was based on a solid phase enzyme-linked immunosorbent assay. CRP level was recorded in mg/dl. CRP levels were observed by the Pathologist of Military Hospital,

Rawalpindi to rule out any possibility of observer bias.

All data were analyzed using SPSS version 17.0. Qualitative variables like X-ray chest findings and gender have been presented as frequency and percentages. Mean and standard deviation (mean ± SD) have been calculated for quantitative variables i.e. age, CRP levels in both groups. Mann Whitney U- test was applied to compare mean CRP levels in smear positive and negative cases. A p-value of <0.05 was considered as significant.

**RESULTS**

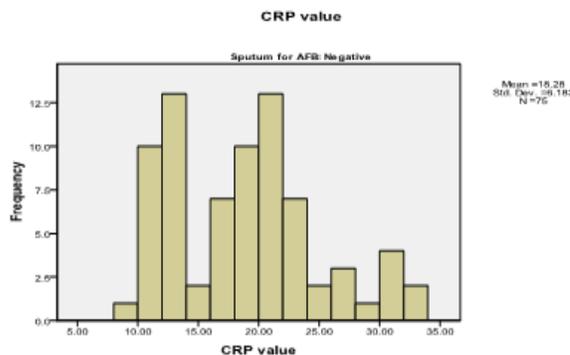
The mean CRP levels were significantly higher in smear positive pulmonary tuberculosis 49.92 ± 10.25 mg/dl as compared to smear negative pulmonary TB 18.28 ± 6.18 mg/dl mean difference of 31.64mg/dl, p value <0.0001. Mann Whitney - U test was applied to compare the mean CRP levels of both groups.

Smear positive patients had mean age of 33.51 years SD ± 13.23. Smear positive group comprises of 47 (62.7%) male and 28 (37.3%) female patients. X-ray chest findings consisted of consolidation 17.4% (13), collapse 13.3% (10), pleural effusion 4% (3), cavitations 22.7% (17), follicular nodular shadows 29.3% (22), miliary shadows 12% (9), and hilar lymphadenopathy in 1.3% (1) cases.

Smear negative patients had mean age of 32.16 years SD ± 13.10 and consisted of 53 (70.7%) male and 22 (29.3%) female patients.

X-ray chest finding consisted of

consolidation in 9.3% (7), collapse 16% (12), pleural effusion 24% (18) cavitations 2.7% (2), follicular nodular shadows 36% (27) and hilar lymphadenopathy in 12% (9).



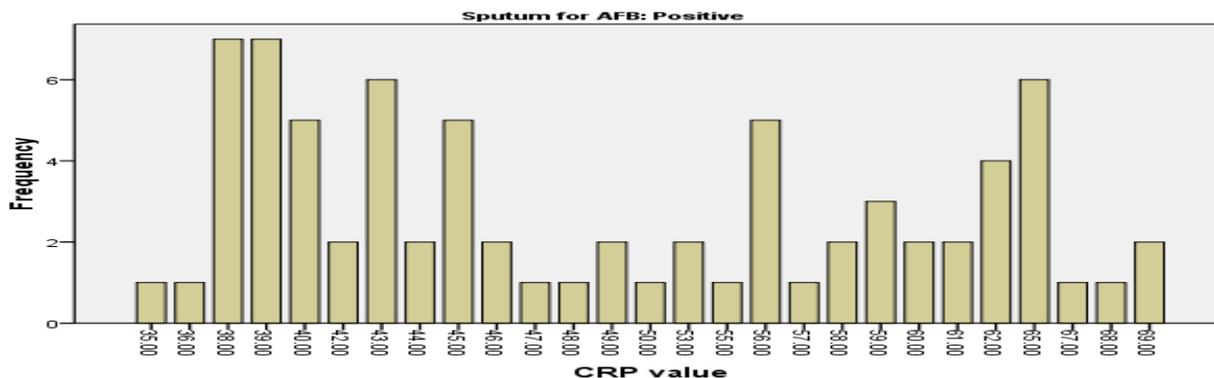
**Figure-1: Serum CRP levels in patients with smear negative pulmonary TB.**

High serum CRP levels were associated with extended lung damage.

**DISCUSSION**

Pakistan ranks seventh among the 22 high-burden tuberculosis countries worldwide<sup>12</sup>. In the current study the primary end point was to compare mean serum CRP levels in smear positive and smear negative cases of clinically diagnosed pulmonary TB. We have reported the serum CRP responses in patients with pulmonary TB according to data obtained from a hospital based study that includes all spectra of the disease.

The increased serum CRP levels in pulmonary TB are in agreement with the findings of other studies and suggest its use in aiding the



**Figure-2: Serum CRP levels in the patients with smear positive pulmonary TB.**

presumptive diagnosis of pulmonary TB together with clinical and epidemiological history even in individuals with negative sputum smear microscopy results<sup>13</sup>.

The results of our study are in agreement with the previous literature in several ways and confirmed the significantly higher mean serum CRP levels in smear positive pulmonary TB as compared to smear negative pulmonary TB<sup>3</sup>. The mean CRP levels in smear positive patients was  $49.92 \pm 10.25$  mg/d and  $18.28 \pm 6.18$  in smear negative pulmonary TB. Mean CRP levels in smear negative pulmonary TB were below 10 mg/dl in previous studies by Rao, Sukesh<sup>3</sup>, and Kang YA<sup>14</sup>.

The mean CRP was on higher side in consolidation and cavitations in both groups which is in agreement with previous studies by Caner, Koksai<sup>15</sup>.

Our study have certain limitations, it was a single center experience, hence long term outcomes need to be explored by multi-center randomized control trails. The sample size in our study was small so the results obtained may not represent the overall trend and X-ray chest findings correlation with serum CRP levels may not be definitive as well.

Our study recommended that, large sample size study for comparison of serum CRP levels in smear positive and negative Pulmonary TB is recommended for making guidelines.

Multi-center collaborated studies would give us more fruitful results with regards to standardization. Studies can be performed to find out serum CRP levels that can be used to find out non-responders to treatment and correlation between serum CRP levels in MDR TB.

## CONCLUSION

CRP levels are mildly increased in smear negative TB and considerable increased in smear

positive pulmonary TB.

CRP levels can be used in tuberculosis patients to add on with other investigations and helpful in early diagnosis and management of tuberculosis.

## CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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