Role of C- reactive protein as an inflammatory marker in sputum smear positive pulmonary tuberculosis patients

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Abstract

Background: Pulmonary tuberculosis is associated with local inflammation of the lung tissue andincreases the levels of the inflammatory markers. C – Reactive protein is an important inflammatory marker during pulmonarytuberculosis. The aims of our study were measuringserum CRP level in sputum smear-positive pulmonary tuberculosis patients at the start and end of the intensive phase of anti-tubercular therapy (ATT) along with correlation between sputum smear grading and serumCRP level at the start and end of intensive phase of ATT.

Methods: This was aprospective cohort study and60 patientswithsputum smear-positive pulmonary tuberculosiswere taken. Serum CRP level and sputum smear grading wasdone at the start and end of the intensive phase of ATT.

Results: SerumCRP level before the start and at end of intensive phase of ATT showed mean of 11.72 ± 5.53 mg/dl (males - 11.01 ± 5.25,   females - 12.77 ± 5.89) and 2.69 ± 1.81mg/dl(males -2.66 ± 1.87,   females - 2.72 ± 1.75), respectively. On statistical analysis, the p-value was <0.001, thus making it statically significant.There was no correlation found between sputum AFB grading and CRP levels.

Conclusion: Serum CRP levels in sputum positive pulmonary tuberculosis patients showed a downward trend at the end of the intensive phase of anti-tubercular therapy; explained that a decrease in the levels due to control in the inflammatory process with treatment. Serum CRP level can be used as a follow-up biomarker in pulmonary tuberculosis.

Keywords: Pulmonary tuberculosis,C - reactive protein,Anti-tubercular therapy,Intensive phase

Introduction

Tuberculosis is a communicable disease that is a major cause of ill health, and the leading cause of death from a single infectious agent.[1]C- reactive protein (CRP) is a protein found in the blood, which rises in response to inflammation. CRP rises to 50,000 fold in acute inflammation, and as its half-life is constant, its level is mainly determined by the rate of production and the severity of the precipitating cause. CRP is one of the biomarkers in the blood that exhibits macrophage activation in lung tuberculosis. CRP levels increase compared to baseline values in disease progression and decrease with successful treatment [2,3].CRP serum levels were increased in pulmonary TB patients with AFB smear-positive sputum. Their levels were significantly increased in pulmonary TB patients with more severe lung tissue damage.[4,5]Other studies showed that anti-tuberculosis drug treatment and sputum conversion resulted in a progressive decrease in CRP levels to normal levels indicating an adequate therapeutic response.[6–8]Thus, CRP examination is expected to evaluate response toanti-tubercular therapy and curing treatment simply and inexpensively.Furthermore, high baseline CRP levels have been shown to correlate with slow sputum culture conversion [9]. A raised CRP level after eight weeks of ATT is predictive of continued culture-positive status[10].We are conducting a study to measure CRP levels, inpatientswithsputum smear-positive pulmonary tuberculosis, at the start of anti-tubercular therapy and two months of tubercular treatment to know about CRP levels in pulmonary tuberculosis patients and their role in decreased disease activity.The aims of our study were measuring serum CRP level in sputum smear-positive pulmonary tuberculosis patients at the start and end of the intensive phase of anti-tubercular therapy (ATT) along with correlation between sputum smear grading and serum CRP level at the start and end of intensive phase of ATT.

Material and methods - This was a prospective cohort study done at the department of pulmonary medicine at tertiary care hospital in Patiala, Punjab. There were60 subjects were included in the study to measure serum levels of C- reactive protein inpatients ofsputum smear-positive pulmonary tuberculosis at the start and at the end of the intensive phase of anti-tubercular therapy. Anti-tubercular therapy has been given according to

NTEP.The study was performed under the institute's ethical committee considerations, and the consent of all the participants was taken before the start of the study. The patients were selected based on random sampling.

Inclusion criteria –
1. Sputum smear-positive pulmonary tuberculosis patients on anti-tubercular Treatment for the first time.
2. Patients with age more than 18 years

Exclusion criteria
1. Patient having co-morbidities – MDR tuberculosis, HIV infection Diabetes mellitus, Heart disease, Cancer disease, Systemic lupus erythematosus, rheumatoid arthritis, Acute pancreatitis, acute infection.

Results

Total 60 patients of sputum smear-positive pulmonary tuberculosis, of which60% weremenand 40%, were females. The average age was in the range of 26 – 40 years (58%). (Table 1)Mean serum CRP level in males and females before starting anti-tubercular therapywas 11.01 ± 5.25 and 12.77 ± 5.89. On statistical analysis, no correlation was found, p value<0.233. (Table 2) Serum CRP levels with sputum smear grading before the start of anti-tubercular therapy in which two patients had CRP levels between 1 - 4.9 mg/ dl (mean 2.41 ± 0.84), and 58 patients had CRP levels between 5 – 100 mg/dl (mean 11.97 ± 5.46). On statistical analysis p value <0.012, which was statically significant.(Table 3) Mean CRP levels in males and females at the end of intensive phase tubercular therapy was 2.66 ± 1.87and 2.72 ± 1.75. On statistical analysis, no correlation was found p <0.906. (Table 4)Serum CRP levels with sputum smear grading at the end of anti-tubercular therapy in which One patient had CRP level < 0.5 mg/dl, seven patients had CRP level in the range of 0.5 - 0.9 mg/dl, 45 patients had CRP level 1.-4.9 mg/dl(mean 2.41 ± 0.84) and seven patients had CRP level 5 - 100 mg/dl(mean 6.73 ± 1.43).On statistical analysis p-value was 0.694, making it non-significant.(Table 5)CRP levels before the start of ATT were 11±72 ± 5.53 mg/dland at the end of the intensive phase was2.69 ± 1.81. On statistical analysis, the P-value was < 0.001,statistically significant. (Table 6) There was no correlation found between sputum AFB grading and CRP levels before start and at end of intensive phase of ATT. (Table 7)

Table 1: Gender and Age distribution of patient in present study

Characteristics		
Male	36	60.0
Female	24	40.0
Age		
18 -25 years	4	6.7
26-40 years	35	58.3
41-55 years	21	35.0

Table 2: Serum CRP level based on gender and age before start of ATT.

Characteristics	Average of CRP ± S.D	P value
Male	11.01 ± 5.25	0.233
Female	12.77 ± 5.89	
Age		
18-25 years	13.28 ± 11.39	0.143
26-40 years	12.69 ± 5.65	
41-55 years	9.81 ± 3.27	

Table 3: AFB smear-positive sputum grading based on CRP level before ATT.

AFB Grading	CRP Serum Level					
	<0.5	0.5-0.9	1.-4.9	5-100	>100	Total
Negative	-	-	-	-	-	-
Scanty	0 (0.0)	0 (0.0)	2 (3.4)	5 (8.3)	0 (0.0)	7 (11.7)
1+	0 (0.0)	0 (0.0)	0 (0.0)	17 (28.3)	0 (0.0)	17 (28.3)
2+	0 (0.0)	0 (0.0)	0 (0.0)	21 (35.0)	0 (0.0)	21 (35.0)
3+	0 (0.0)	0 (0.0)	0 (0.0)	15 (25.0)	0 (0.0)	15 (25.0)
Total	0 (0.0)	0 (0.0)	2 (3.4)	58 (96.6)	0 (0.0)	60 (100.0)
Mean ± S.D	-	-	4.50 ± 0.42	11.97 ± 5.46	-	11.72 ± 5.53

Fisher Exact Test	7.223
P value	0.012
Significance	S

Table 4: Serum CRP level based on sex and age at end of intensive phase of ATT.

Characteristics	Average of CRP ± S.D	P value
Male	2.66 ± 1.87	0.906
Female	2.72 ± 1.75	
Age		
18-25 years	2.78 ± 3.23	0.943
26-40 years	2.74 ± 1.97	
41-55 years	2.58 ± 1.21	

Table 5: AFB smear-positive sputum grading based on serum CRP level at end of intensive phase of ATT.

AFB Grading	CRP Serum Level					
	<0.5	0.5-0.9	1.-4.9	5-100	>100	Total
-	1 (1.7)	7 (11.6)	42 (70.0)	6 (10.0)	0 (0.0)	56 (93.3)
Scanty	0 (0.0)	0 (0.0)	3 (5.0)	1 (1.7)	0 (0.0)	4 (6.7)
1+	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
2+	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
3+	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Total	1 (1.7)	7 (11.6)	45 (75.0)	7 (11.7)	0 (0.0)	60 (100.0)
Mean ± S.D	0.4 ± 0.0	0.73 ± 0.15	2.41 ± 0.84	6.73 ± 1.43	0 ± 0.0	2.69 ± 1.43
Fisher exact value	2.396					
P value	0.694					
Significance	NS					

Table 6: Comparison of CRP level before and after ATT

	Before ATT	At end of intensive phase	P value
CRP	11.72 ± 5.53	2.69 ± 1.81	<0.001

Table 7: Correlation of sputum AFB grading and CRP levels before start and at end of intensive phase of ATT

Sputum AFB	Negative	Scanty	1+	2+	3+
CRP	Mean ± S.D	Mean ± S.D	Mean ± S.D	Mean ± S.D	Mean ± S.D
Before Start ATT	-	6.97 ± 2.77	12.37 ± 5.73	12.73 ± 5.41	11.78 ± 5.75
At end of intensive phase	2.67 ± 1.79	2.88 ± 2.39	-	-	-

Discussion

In pulmonary tuberculosis, the patient those were not took anti-tubercular treatment , results damage to the lung tissue and due to local inflammatory changes causes in increases in the value of CRP[5].In the present study, serum CRP level were measured in sputum smear-positive pulmonary tuberculosis patients before the start and at the end of the intensive phase of ATT, in which mean serum CRP level were 11.72 ± 5.53 mg/dl and 2.69 ± 1.81 mg/dl, before the start and at the end intensive phase of ATT respectively.The risk of mycobacterial infection in the adult age group from 20 – 30 years is high due to the second peak of infection in this age

group[11]. In the present study, most of the patient's age was 26 to 40 years of age, as explained due to the increased risk of infection in this age group. There was not much difference in the CRP level in the different age groups; similar findings were seen in the other studies by Ünsal E et al.[12] and Ojo D et al.[13]In our study, before starting anti-tubercular treatment, 96% of the patients hada moderate increase in CRP value (5 -100mg/dl) with a mean value of 11.72 ± 5.53. Similar findings were obtained in the study done by Dar MY et al. , in which a CRP value of 21.71±6.73[14].In a study done by Brown J et al. on multi-ethnic people of sputum smear-positive pulmonary tuberculosis, baseline CRP level was 66 before starting anti-tubercular treatment, higher than the present study but was moderate in the range[15].After completing the intensive phase of anti-tubercular therapy, 70% of the patients had a mild increase in CRP level with a mean of 2.69 ± 1.81. A similar trend of decreasing CRP levels after anti-tubercular therapy was seen in studies done by Baynes R et al.,de Beer FC et al., and Bajaj G et al.[16–18]. Their study, F C de Beer et al., stated that C-reactive protein levels decreased rapidly after initiation of treatment in post-primary tuberculosis patients.[17]Bajaj G et al.noticed that the elevated CRP levels fell significantly after one month of treatment and that3 to 6 months of treatment had fallen to normal values[18].The CRP levels are raised in tuberculosis, and these levels fall and attain normal values by the end of treatment. But if the CRP values are consistently high despite treatment, then there is either resistance to drugs or the patient is not complying with the treatment[19].In the present study, there was no correlation found between sputum AFB grading and CRP levels, CRP levels of sputum smear +2 and + 3 showed no different value.. Finding in our study were consistent with Shameem Met al. and Saputera Damian D et al.[20,21]

Conclusion

The study shows that serum CRP levels in sputum positive pulmonary tuberculosis patients showed a downward trend at the end of the intensive phase of anti-tubercular therapy; explained that a decrease in the levels due to control in the inflammatory process with treatment. Serum CRP level can be used as a follow-up biomarker in pulmonary tuberculosis.

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