https://doi.org/10.48047/AFJBS.6.15.2024.11133-11146

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

"Serial C-Reactive Protein Monitoring as a Biomarker of Treatment Response in Tuberculosis"

1.* Dr. Surabhi Vaidya, PG Resident 3rd Year, Department of Pulmonary Medicine, People's College of Medical Sciences & Research Centre, Bhopal.
2. **Dr. Sanjay Tandon, Professor and Head, Department of Pulmonary Medicine, People's College of Medical Sciences & Research Centre, Bhopal.
Correspondence author: Dr. Surabhi Vaidya, PG Resident 3rd Year, Department of Pulmonary Medicine, People's College of Medical Sciences & Research Centre, Bhopal.

Volume 6, Issue 15, Oct 2024

Received: 15 Aug 2024

Accepted: 25 Sep 2024

Published: 21 Oct 2024

doi: 10.48047/AFJBS.6.15.2024.11133-11146

ABSTRACT

***Background*:** Tuberculosis (TB) treatment efficacy is traditionally assessed through clinical and microbiological evaluations. This study investigates the utility of serial C-reactive protein (CRP) measurements as a biomarker for monitoring treatment response in TB patients.

***Methods*:** In this prospective observational study, 204 newly diagnosed TB patients were enrolled from a tertiary care hospital in central India between November 2022 and April 2024. Serum CRP levels were assessed at baseline, 6 months, and treatment completion.

***Results*:** A significant decrease in median CRP levels (IQR) was observed in both PTB 32 mg/L (20.25 - 52.75) to 3mg/L (2.275 - 4), $p < 0.05$ and EPTB patients 30mg/L (14-55) to 3mg/L (2.2-4), $p < 0.05$ during treatment. Notably, 30% of PTB and 61.7% of EPTB patients required extended treatment beyond 6 months, with median CRP levels remaining elevated (>5 mg/L) at 6 months.

***Conclusion*:** Serial CRP measurements demonstrate potential as a biomarker for monitoring TB treatment response, with declining levels correlating with effective treatment. This biomarker may aid in guiding end-of-therapy decisions and optimizing treatment duration.

Keywords-CRP, inflammation, tuberculosis, extended duration, pulmonary TB, EPTB, response

INTRODUCTION

Tuberculosis is characterized by systemic inflammation, marked by increased acute phase reactants, including C-reactive protein (CRP), haptoglobin, alpha-2 macroglobulin, and serum amyloid P [1]. Although serum CRP is a non-specific inflammation marker, serial measurements can guide TB treatment in conjunction with clinicoradiological and laboratory findings.

Previous studies have demonstrated CRP's utility in pulmonary tuberculosis screening but have neglected to assess its role in extrapulmonary patients [2]. High baseline CRP levels are associated with delayed sputum culture conversion and poor treatment outcomes [3, 4].

In clinical practice, treatment response is primarily evaluated based on symptomatic relief, microbiological improvement, and radiological findings. However, some patients exhibit improvement despite persistent symptoms. Moreover, the current treatment duration guidelines may not ensure complete cure for all patients, particularly those with extrapulmonary TB.

A significant concern is the recurrence of TB, with a reported 27.1% recurrence rate among cured PTB and EPTB patients [5]. This underscores the need for reliable biomarkers to monitor treatment response and guide end-of-therapy decisions.

This study aims to:

1. Determine baseline serum CRP levels in pulmonary and extrapulmonary TB patients.

2. Evaluate treatment response based on declining CRP trends.

3. Assess CRP's role in guiding end-of-therapy decisions.

METHODS

Study Design and Setting

This prospective observational study was conducted at a tertiary care Medical College hospital in Central India from November 2022 to April 2024.

Inclusion and Exclusion Criteria

Newly diagnosed tuberculosis patients >16 years old were included. Patients with immunodeficiency diseases, autoimmune diseases, cancer, liver diseases, MDR/XDR TB, and those unwilling to participate were excluded.

Sample Size Calculation

The sample size was calculated using the formula

$N=Z_{(1-\alpha)}^2 pq/d^2$

Where, $Z_{(1-\alpha)}$= 1.96 at 95% CI

P=prevalence of TB, according to WHO TB reports, South-East Asia contribute to overall 45% of global TB burden.[5]

Q=1-p=55%

D= allowable error =10%

Based upon the formula, sample size was estimated to be 95.

Keeping 10% attrition rate, the sample size was estimated to be 105.

Patient Enrolment

All pulmonary and extrapulmonary TB patients initiated on anti-tubercular treatment (ATT) and fulfilling inclusion criteria were enrolled.

Diagnostic Criteria

Pulmonary TB was diagnosed based on:

- Classical TB symptoms
- Microbiology
- Molecular test results
- Cytology
- Radiology

Extrapulmonary TB was diagnosed based on:

- Clinical symptoms
- Microbiology
- Molecular test results
- Fluid analysis (routine microscopy, ADA level, cytology)
- Lymph node FNAC
- Histopathology-
- Clinico-radiological findings

Data Collection

Patient weight, serum CRP levels, sputum AFB smear, chest X-ray, CBNAAT, and LPA findings (for pulmonary TB) were documented. Extrapulmonary TB data included site, diagnostic basis, and clinicoradiological findings.

Follow-up

CRP levels and clinicoradiological findings were assessed at 6 months and/or end of therapy. Median follow up duration was 8 months (8 to 12 months).

ATT Regimen

The standard ATT regimen for pulmonary TB consisted of 6 months of 2HRZE/4HRE. Fixed-dose combination (FDC) tablets were used over separate drug formulations in treatment of patients with drug-susceptible TB.[6]

The duration of therapy in drug sensitive extra pulmonary TB was as per the INDEX-TB guidelines on extrapulmonary tuberculosis for India. [7]

Site of Disease	Initial Regimen (IP + CP)	Duration
Ocular TB	(2)HRZE + (4-7)HRE	6-9 Months
CNS TB	(2)HRZ+E/S + (10)HRE	6-12 Months
Tuberculous Otitis Media	(2)HRZE + (7)HRE	9 Months
Ear, Nose and Throat TB (Others)	(2)HRZE + (4-7)HRE	6-9 Months
Lymph node TB	(2)HRZE + (4-7)HRE	6-9 Months
Pleural TB	(2)HRZE + (4)HRE	6 Months
Pericardial TB	(2)HRZE + (4)HRE	6 Months
*Hepatobiliary TB	(2)HRZE+(4-7)HRE	6-9 Months
Intestinal TB	(2)HRZE + (4)HRE	6 Months
Urinary TB	(2)HRZE + (4)HRE	6 Months
Genital TB (Male or Female)	(2)HRZE + (4)HRE	6 Months
Spinal TB	(2)HRZE + (10-16)HRE	12-18 Months
Bone and Joint TB (others)	(2)HRZE + (10)HRE	12 Months
Cutaneous TB	(2)HRZE + (4)HRE	6 Months

Adverse Event Monitoring

Adverse events were monitored and recorded throughout the study.

Data Quality Control

To ensure data accuracy and reliability, rigorous quality control measures were implemented throughout the study. Source data verification (SDV) was conducted for 20% of patient records to validate data entry accuracy. Data cleaning and normalization were performed regularly to handle missing or duplicate values.

The CRP assay results were validated against quality control samples, and coefficient of variation (CV) was calculated to ensure assay precision (CV < 5%). Furthermore, data validation checks were performed to ensure consistency across multiple data sources, including patient medical records and laboratory reports.

Missing Data Management

Patients lost to follow up or patients with incomplete data were excluded from the follow up analysis.

Statistical Analysis

Data was compiled using MS Excel and analyzed using IBM SPSS software version 20.

- Categorical variables: frequency and proportion

- Continuous variables: mean ± SD (normally distributed) or median and interquartile range (non-normally distributed)

- CRP level comparison: Friedman test

- Median comparison: Mann-Whitney U test

- Statistical significance: $p < 0.05$

Ethics Approval

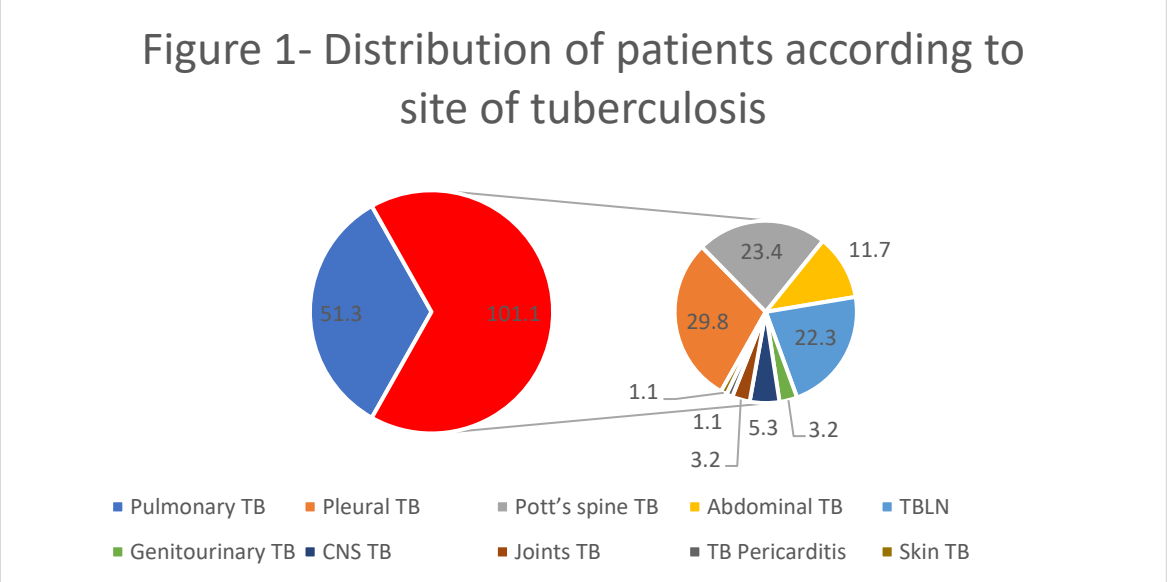
This study was approved by the Institutional Ethics Committee (Approval No.IEC-2022/103)

Informed Consent

Written informed consent was obtained from all participants.

RESULTS

Study Population



A total of 204 patients were enrolled, consisting of 105 (51.5%) pulmonary tuberculosis (PTB) patients and 99 (48.5%) extrapulmonary tuberculosis (EPTB) patients (Figure 1). Ten patients were lost to follow-up and excluded from further analysis.

Baseline Characteristics

Table 1- Distribution of patients with tuberculosis according to baseline variables

Baseline variables		Pulmonary TB (n=105)	Extrapulmonary TB (n=99)	Total (n=204)
		n (%)	n (%)	n (%)
Age (years)	≤20	25 (23.8%)	11 (11.1%)	36 (17.6%)
	21-30	25 (23.8%)	38 (38.4%)	63 (30.9%)
	31-40	15 (14.3%)	15 (15.2%)	30 (14.7%)
	41-50	12 (11.4%)	14 (14.1%)	26 (12.7%)
	51-60	13 (12.4%)	14 (14.1%)	27 (13.2%)
	>60	15 (14.3%)	7 (7.1%)	22 (10.8%)
	Mean±SD	36.66±17.63	36.20±15.64	36.44±16.65
Sex	Male	57 (54.3%)	51 (51.5%)	108 (52.9%)
	Female	48 (45.7%)	48 (48.5%)	96 (47.1%)
Comorbidities	Diabetes	16 (15.2%)	20 (20.2%)	36 (17.6%)
	Hypertension	7 (6.7%)	9 (9.1%)	16 (7.8%)
	HIV reactive	0 (0%)	0 (0%)	0 (0%)
Addiction	Tobacco smoking	20 (19.0%)	12 (12.1%)	32 (15.7%)
	Alcohol	12 (11.4%)	10 (10.1%)	22 (10.8%)
	Tobacco chewing	14 (13.3%)	8 (8.1%)	22 (10.8%)

The mean age of patients with tuberculosis was 36.44 ± 16.65 years. The majority of patients (30.9%) belonged to the 21-30 years age group. A slight male predominance was observed, with a male-to-female ratio of 1.13:1 (1.2:1 for PTB and 1.1:1 for EPTB). Diabetes and hypertension were present in 17.6% and 7.8% of patients, respectively. Overall, 37.3% of TB patients had a history of addictions (smoking, alcohol, tobacco chewing) (Table 1).

Baseline serum CRP levels

Table 2- Baseline CRP levels at the start of ATT in PTB and EPTB patients.

	Baseline serum CRP in PTB Patients (mg/L)	**Baseline serum CRP in EPTB Patients (mg/L)**

Median	32	30
IQR	20.25-52.75	14-55
Range	2.6-126	2.14-255

Median baseline CRP level in patients with pulmonary tuberculosis was 32 (IQR-20.25-52.75) mg/L.

In EPTB patient, median CRP level was 30 (IQR 14 to 55)mg/L .

CRP Levels During Treatment

Table 3- Comparison of median CRP levels in patients at the beginning of ATT, end of 6 months of therapy and at end of therapy

CRP levels (mg/L)		**At beginning**	**At 6 months**	**At end of treatment**	**P value**
PTB	Median (IQR)	32 (20.25-52.75)	5.25 (3-9)	3 (2.275-4)	**0.001**
EPTB	Median (IQR)	30 (14-55)	6 (3-9)	3 (2.2-4)	**0.001**
Pleural TB	Median (IQR)	52 (33.75-73)	7.8 (6.6-10)	3 (2.8-4)	**0.001**
Pott's spine TB	Median (IQR)	40 (18.5-56.5)	8.4 (7-10.5)	3 (2-3.65)	**0.001**
Abdominal TB	Median (IQR)	19 (1149)	6 (5.7-11)	4 (4-6)	**0.017**
TBLN	Median (IQR)	12 (6.5-17.5)	6 (5.6-19)	2.8 (2-3.2)	**0.001**
Genitourinary TB	Median (IQR)	13 (2.65-18.5)	8 (2.14-16)	3.5 (2.075-4.275)	**0.018**
CNS TB	Median	54 (26.5-	5.65(4.2-	4.5 (2.25-6.5)	**0.001**

	(IQR)	122)	7.78)		
Joint TB	Median (IQR)	22 (2.9-44)	5.6 (1.6-5.6)	3.5 (3-5.5)	**0.001**
TB Pericarditis	Median (IQR)	82 (82-82)	11 (11-11)	4 (4-4)	**0.001**
Skin TB	Median (IQR)	55 (55-55)	7 (7-7)	2.2 (2.2-2.2)	**0.001**

A significant serial decrease in median CRP levels was observed with effective anti-tubercular treatment (ATT) in TB patients, regardless of site ($p < 0.05$) (Table 3).

CRP Normalization

Table 4 - Distribution of PTB and EPTB patients according to normalization of CRP (<5mg/L) at 6 months and at the end of ATT

CRP normalized (<5 mg/L)		**Pulmonary TB (n=100)**	**Extrapulmonary TB (n=94)**	**Total (n=194)**	**P value**
		n (%)	**n (%)**	**n (%)**	
at 6 months of ATT	No	30 (30.0%)	58 (61.7%)	88(45.3%)	**0.0001**
	Yes	70 (70.0%)	36 (38.2%)	106 (54.6%)	
	Patients cured	70 (70.0%)	36 (38.2%)	106 (54.6%)	
At end of treatment	No	10 (10%)	8 (8.5%)	18 (9.2%)	0.703
	Yes	90 (90.0%)	86 (91.4%)	176 (90.7%)	
	Patients cured	100 (100%)	94(100%)	194(100%)	

Seventy percent PTB and 38.2% EPTB patients showed CRP normalization and were declared cured at 6 months of ATT. Ninety percent of PTB and 91.6% of EPTB patients had normalisation of serum CRP at the end of treatment. Even though , all PTB and EPTB patients were declared cured at the end of therapy. (Table 4).

		At the start of therapy (n=105)	At the end of therapy (n=100)	Patient declared cured	Lost to follow up

Duration of Therapy

Table 5- Duration of therapy in PTB and various types of EPTB patients with respect to CRP levels at 6 months of ATT.

		CRP >5 mg/L at 6 months of ATT		**CRP <5 mg/L at 6 months of ATT**	
	Recommended duration of ATT as per NTEP guideline (Months)	**Mean±SD Duration (Months)**	**Median (IQR) Duration (Months)**	**Mean±SD Duration (Months)**	**Median (IQR) Duration (Months)**
PTB	6 (24 weeks)	8.46±1.79	9(7-9)	6 ± 0	6 (6-6)
Pleural TB	6 (24 weeks)	9.16±0	9 (8-10)	6.11±1.71	6 (6-6)
Pott's spine TB	12-18	20.42±0	18 (18-24)	11±4.89	12 (9-12)
Abdominal TB	6 (24 weeks)	10±0	9 (9-9)	6±2.02	6 (6-6)
TBLN	6 – 9	10.44±1.73	9 (9-12)	6.67±2.94	6 (6-6)
Genitourinary TB	6 (24 weeks)	-	-	6±0	6 (6-6)
CNS TB	6 – 12	21±6	24 (15-24)	-	-
Joint TB	12	13.5±2.12	13.5 (9-13.5)	6±0	6 (6-6)
TB Pericarditis	6 (24 weeks)	10±0	10 (10-10)	-	-
Skin TB	6 (24 weeks)	8±0	8 (8-8)	-	-

Patients whose treatment ended at 6 months and were declared cured had normalized CRP levels at 6 months of ATT. In contrast, patients with continued treatment beyond 6 months had non-normalized CRP levels at 6 months (Table 5).

Diagnostic Methods

Table 6 – Response to treatment in PTB patients on the bases of sputum smear test, chest radiology improvement, symptomatic relief

Sputum/ BAL examination	MTB positive	91 (86.6%)	0	100 (95.2%)	5 (4.7%)
	MTB negative	14 (13.3%)	100 (100%)		
Chest radiological findings S/o	Active PTB	105 (100%)	0	100 (95.2%)	5 (4.7%)
	Improved	0	99 (99%)		
	Stable	0	1 (1%)		
	Worsening	0	0		
Symptoms S/o PTB(fever, cough, sputum, weight loss, night	Present	105 (100%)	0	100 (95.2%)	5 (4.7%)
	Absent	0	100 (100%)		
Median CRP level	>5 mg/L	105 (100%)	10(10%)	100 (95.2%)	5 (4.7%)
	< 5 mg/L	0	90 (90%)		

Most PTB patients were diagnosed using sputum/BAL MTB CBNAAT. Remaining patients were diagnosed based on clinicoradiological findings. MTB CBNAAT was not used for follow-up or to determine end of therapy. At the end of therapy, patients were declared cured based on clinicoradiological findings and median CRP levels (IQR) decreased to normal range in majority of patients [32 (20.25-52.75) to 3 (2.275-4)] (Table 6)

Extrapulmonary Tuberculosis

Table 7- Response to treatment in EPTB patients on the bases clinicoradiological improvement

		At the start of therapy (n=99)	**At the end of therapy (n=94)**	**Patient declared cured**	**Lost to follow up**
Clinicoradiological findings/ Imaging specific to site of TB	Present	99 (100%)	0	94(94.9%)	5(4.7%)
	Absent	0	94(100%)		
Median CRP levels	>5 mg/L	95(95.9%)	8(8.5%)	94(94.9%)	5(4.7%)

	< 5 mg/L	4 (4%)	86(91.4%)		

All 99 EPTB patients with diverse manifestations showed clinicoradiological improvement and median CRP level(IQR) decrease to normal range [30 (14-55) to 3 (2.2-4)] after completing therapy in majority of the patients (Table 7).

Weight Gain

Table 8- Weight of patients with pulmonary and extrapulmonary TB at various follow up

Weight (Kg)	Pulmonary TB	Extrapulmonary TB	P value
	Median (IQR)	Median (IQR)	
At start	44 (41-50)	50 (42-57)	**0.001**
At 6 months	48 (45-55)	52 (48-60)	**0.001**
At end of treatment	50 (4656)	55 (50-65)	**0.02**
P value	**0.001**	**0.001**	

A significant serial increase in weight was observed in patients with pulmonary and extrapulmonary tuberculosis at 6 months and end of treatment from baseline weight ($p < 0.05$).

CRP Non-Normalization

Table 9- Association of not normalization of CRP at the end of therapy with Comorbidities and addiction

Comorbidities and addiction	**CRP**	
	>5 mg/L (10 PTB + 8 EPTB n= 18)	**<5mg/L (n=176)**
	n (%)	**n (%)**
Diabetes n =32	6 (18.75%)	26 (81.25%)
Hypertension n =15	4 (26.7%)	11 (73.3%)
Smoking n=29	4 (13.8%)	25 (86.2%)
Alcohol	3 (16.7%)	15 (83.3%)

n =18		
Tobacco n=20	2 (10%)	18 (90%)
Allergic Rhinitis n=1	1 (100%)	0 (0%)
Arthritis n=1	1 (100%)	0 (0%)
COPD (Chronic obstructive pulmonary disease) n=5	2 (40%)	3 (60%)
GERD (Gastro esophageal reflux disorder) n=4	0 (0%)	4 (100%)
IBD (Inflammatory bowel disease0 n=1	1 (100%)	0 (0%)
OSA(obstructive sleep apnea) n=1	0 (0%)	1 (100%)
PCOD (Poly cystic ovarian disease) n=1	0 (0%)	1 (100%)
PID(Pelvic inflammatory disease) n=1	0 (0%)	1 (100%)
URI(Upper respiratory tract infection) n=4	2 (50%)	2 (50%)
UTI(Urinary tract infection) n=4	4 (100%)	0 (0%)
Radiologically not cured n=1	0 (0%)	1 (100%)

Eighteen (9.2%) patients had non-normalized CRP levels at the end of therapy due to comorbidities, addictions, and inflammatory conditions (Table 9).

DISSCUSSION

In this prospective observational study, we investigated the utility of serial C-reactive protein (CRP) monitoring as a biomarker for treatment response in tuberculosis (TB) patients. Our findings demonstrate that CRP levels decrease significantly during effective treatment, normalizing in most patients by the end of therapy.

At the beginning of anti-tuberculosis treatment (ATT), baseline median CRP level (mg/L) was elevated in all TB patients, reflecting active disease and inflammation. In PTB patients, median CRP level was 32 (IQR 20.25-52.75) mg/L, and in EPTB patients, median CRP level was 30 (IQR 14-55). This finding is consistent with previous studies [9, 10], which reported elevated CRP levels in active TB patients.

We observed a sequential decrease in median CRP levels in both PTB and EPTB patients over the course of successful treatment, irrespective of the site of infection ($p < 0.05$). At six months of therapy, there was a significant reduction in CRP levels, indicating decreased inflammation. Patients who were cured at six months had normalized CRP levels (<5 mg/L) by six months.

Those who were not declared cured at six months had raised CRP at six months. In 30 (30%) PTB and 58 (61.7%) EPTB patients, ATT continued beyond six months (according to NTEP guidelines or those not declared cured at six months). Their CRP did not normalize at six months.

Our results are consistent with previous studies [8, 9], which reported decreased CRP levels following effective TB treatment. Pansey et al. documented that patients who had almost completed treatment had a mean CRP level of 4.78±4.34, while defaulters and treatment failures had raised CRP [8]. Similarly, Arya et al. found that mean CRP levels dropped from 53.55±6.11 to 4.63±1.33 in patients who completed treatment [9].

The decline in CRP levels correlated with symptom relief, clinicoradiological improvement, and sputum smear negativity in PTB patients. Elevated CRP levels at the end of therapy warrant further investigation for underlying conditions.

Notably, patients with comorbidities (e.g., diabetes, hypertension), addictions (e.g., smoking, alcohol), or adverse drug reactions (ADRs) had elevated CRP levels at six months, indicating residual inflammation or ongoing infection. These findings highlight the importance of managing comorbidities and ADRs to optimize treatment outcomes.

Median CRP level (IQR) decreased to normal range from the beginning of treatment 32 (20.25-52.75) to 3 (2.275-4) in PTB and 30 (14-55) to 3 (2.2-4) in EPTB patients at the end of therapy.

Three out of 10 patients who were lost to follow-up at six months did not show clinical improvement or decrease in CRP level at two months of ATT.

The decision to provide treatment more than six months by clinicians was based on clinical, radiological, and microbiological evaluation and as per National Tuberculosis Elimination Program (NTEP) guidelines [6, 7].

Limitations

Our study had certain limitations:

1. Small sample size in the EPTB subset.

2. Exclusion of drug-resistant TB patients.

3. Loss to follow-up of three patients.

CONCLUSION

In conclusion, serial CRP monitoring is a valuable tool for assessing treatment response in TB patients. Elevated CRP levels decline and normalize with effective treatment. Serum CRP may serve as a biomarker for monitoring TB treatment and guiding clinicians in deciding end-of-therapy.

Future Directions

1. Investigate CRP levels in CNS TB.

2. Explore early relapse detection using serial CRP levels.

REFERENCES

1. Singh J, Meena K, Singh SP, Singh H, Singh A. Role of C-reactive protein as an inflammatory marker in sputum smear positive pulmonary tuberculosis patients. Journal of cardiovascular disease research 2021;12;293-97.
2. Saripalli A, Ramapuram J. C-reactive protein as a screening test for tuberculosis in people living with HIV in southern India: a cross-sectional, observational study. Journal of Clinical Medicine. 2022 Jun 21;11(13):3566.
3. Djoba Siawaya JF, Chegou NN, van den Heuvel MM, Diacon AH, Beyers N, van Helden P, Walzl G. Differential cytokine/chemokines and KL-6 profiles in patients with different forms of tuberculosis. Cytokine. 2009;47(2):132–6.
4. Huang CT, Lee LN, Ho CC, Shu CC, Ruan SY, Tsai YJ, Wang JY, Yu CJ. High serum levels of procalcitonin and soluble TREM-1 correlated with poor prognosis in pulmonary tuberculosis. J Infect. 2014;68(5):440–7.

5. Giridharan P, Selvaraju S, Rao R, Rade K, Thiruvengadam K, Asthana S, Balachandar R, Dipak Bangar S, Bansal AK, Bhat J, Chakraborty D. Recurrence of pulmonary tuberculosis in India: Findings from the 2019–2021 nationwide community-based TB prevalence survey. Plos one. 2023 Dec 21;18(12):e0294254.
6. *National TB Elimination Programme, Central TB Division. Training modules for programme managers & Medical officers. Ministry of Health and Family Welfare, Government of India accessed at https://tbcindia.gov.in/index1.php?lang=1&level=1&sublinkid=5465&lid=3540 on 24 February, 2022.*

7. *INDEX-TB GUIDELINES - Guidelines on extra-pulmonary tuberculosis for India. 2016. Available from https://tbcindia.gov.in/WriteReadData/l892s/5585665076IndexTB%20Guidelines.pdf Last accessed on 14th February 2024.*.

8. Pansey P, Shukla S, Acharya S. Serum C-reactive protien (CRP)-a dependent prognostic marker in pulmonary tuberculosis. International Journal of Contemporary Medical Research. 2017; 4(10):2111-4.
9. Arya AK, Srivastava A,Mishra A, Mishra P. To evaluate the level of CRP in the serum as a potential biomarker of the disease activity in pulmonary TB. European Journal of Molecular & Clinical Medicine. 2023; 10 (3): 919-22.