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STUDY ON SERUM PROCALCITONIN AND SERUM C-REACTIVE PROTEIN IN PULMONARY TUBERCULOSIS PATIENTS, AND ITS ASSOCIATION IN A TERTIARY CARE HOSPITAL, ODISHA: A CROSS-SECTIONAL STUDY.

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ABSTRACT.

Background:
Pulmonary tuberculosis, a highly contagious bacterial lung infection, remains a significant global health issue. Given its prevalence and impact, this study seeks to analyze the baseline characteristics and distribution of Serum C-reactive protein (Sr. CRP) and Serum Procalcitonin (Sr. PCT) in individuals diagnosed with pulmonary tuberculosis (TB). Additionally, the research aims to elucidate the relationship between Sr. CRP and Sr. PCT levels in individuals with pulmonary TB.

Methods:
The research consisted of 50 adult individuals diagnosed with pulmonary tuberculosis, with 80% being male and 20% female. The study employed a hospital-based descriptive and cross-sectional study design to evaluate the baseline characteristics and distribution of Serum CRP and Serum PCT levels among the participants. Participation in the study was voluntary, and individuals were required to provide informed consent before being included in the research.

Results:
Among participants, females had a mean age of 29.70 years (±6.75, range: 21-40 years), while males had a mean age of 43.20 years (±11.88, range: 24-61 years). Sputum microscopy showed most cases at 2+ (50%). Hemoglobin, leukocyte count, CRP, Erythrocyte Sedimentation Rate, and Sr. PCT were significantly associated with Pulmonary Tuberculosis ($p<0.001$). Neutrophils peaked at 70 (26% of cases), and lymphocytes at 28 (18% of cases). CRP correlated positively with sputum microscopy ($p=0.004$) and Sr. PCT ($p=0.001$).

Conclusion:
The study findings indicate that the concentrations of Serum CRP and Serum PCT among the clinically diagnosed groups of study subjects showed a highly significant association. Moreover, there is evidence of a positive correlation between CRP and Sr. PCT levels, as well as between CRP and sputum microscopy results, in the context of pulmonary tuberculosis.

Recommendations:
Implement routine screening for serum CRP and PCT levels in diagnosed pulmonary TB patients, enhance TB awareness, and explore CRP and PCT as treatment biomarkers.

Keywords: *Pulmonary Tuberculosis, Serum C-reactive protein, Serum Procalcitonin*
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INTRODUCTION.

Tuberculosis which involves the lungs is the leading cause of death worldwide [1]. According to statistics pulmonary tuberculosis has claimed 10 million lives [2]. Therefore, the concern of pulmonary tuberculosis patients is on the rise.
As per the statistics of 2007, it was found that there were around 9 million cases of pulmonary tuberculosis, and around 1.3 million deaths [3]. The serum levels of

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procalcitonin can guide the treatment plan like the C-reactive protein levels in the case of pulmonary tuberculosis [3] procalcitonin levels serve as a marker for detecting the presence of pulmonary tuberculosis.

The general protocol for diagnosis of tuberculosis includes chest radiography, skin tuberculin test, and microbial examination of the causative agent. A smear test to culture mycobacterium bacilli and examine it confirms the presence of tuberculosis. Procalcitonin consists of 116 amino acids, and it is a marker of inflammation due to infection [4]

Earlier a study investigated C-reactive protein and procalcitonin as a marker of bacterial infection. C-reactive protein and Procalcitonin have been used as diagnostic markers of bacterial sepsis [5-7]. Although the C-reactive protein has been studied widely as a marker for tuberculosis, this is the first study that takes procalcitonin as the marker of tuberculosis

C-reactive protein marks the presence of bacilli. In the case of tuberculosis after therapy with anti-TB drugs if the bacilli count does not decrease the C-reactive protein is present [8] Under normal conditions, procalcitonin is secreted in response to hypercalcemia [9]. In a bacterial infection the levels of procalcitonin increase however during a severe bacterial infection it increases up to 200ng/ml which is substantially higher than the normal level [10]. Therefore, the present study aims to analyze the viability and their correlation among parameters like CRP as a diagnostic aid for tuberculosis.

Objectives.

To compare the characteristics of tuberculosis and the levels of serum procalcitonin and levels of C-reactive protein

Determine the correlation of serum C-reactive protein and Procalcitonin with pulmonary tuberculosis

MATERIAL AND METHODOLOGY.

Study design.

Hospital-based Descriptive and Cross-sectional study.

Study setting.

The study was conducted O.P.D. and I.P.D. in the P.G. Department of Pulmonary, Hitech Medical College and Hospital, Bhubaneswar served as the site of this study between January 2023 and July 2023.

Study Population.

A total of 78 individuals were admitted to the hospital during the study period.

Sample Size.

Fifty cases of Pulmonary Tuberculosis with standard protocols were followed.

Inclusion Criteria.

- Individuals presenting clinical symptoms and signs indicative of pulmonary TB.
- Biochemical and pathological reports indicating levels of Sr. CRP and Sr. PCT.
- Positive identification of acid-fast bacilli upon examining sputum using the Ziehl–Neelsen stain technique on three separate occasions.

Exclusion Criteria.

- Individuals diagnosed with bacterial lung infections other than pulmonary tuberculosis.
- Cases of secondary tuberculosis.
- Any instances of accompanying inflammatory diseases.

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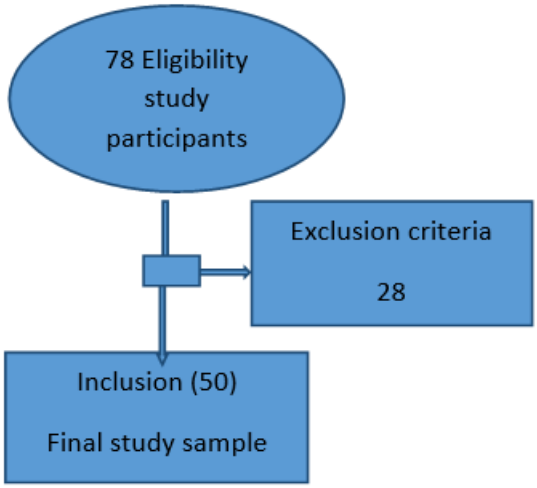

Figure 1: Flow chart of participants selection.

Bias.

There was a chance that bias would arise when the study first started, but it was avoided by giving all participants identical information and hiding the group allocation from the nurses who collected the data.
Statistical Analysis: SPSS version 22.0 was used for all statistical analysis. Data were presented as means, medians, standard deviations, and percentages. We compared group means using the Student's t-test, and proportions using the Fisher Exact test. P values below 0.05 were regarded as significant.

Ethical consideration.

Ethical permission has been taken from the Ethical Committee of Hitech Medical College and Hospital, Bhubaneswar. All patients provided their free, prior informed consent.

RESULTS.

Table 1: Age and sex-wise distribution of study participants.

Age group	Female	Male
20-30	5	6
30-40	4	8
40-50	1	12
50-60	0	9
above 61	0	5
Total	10	40

A total of 78 cases were admitted to the pulmonary department, and 50 were selected for the study. The incidence of age ranged from 20 to 30 years, with the highest occurrence observed in the 20-30 age group, constituting 50% of females and 30% of males among the 50 study participants. Additionally, among these participants, the maximum incidence was observed in the 40-50 age range among males, with 12 individuals representing this demographic.

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Table 2: Descriptive statistics.

Descriptive Statistics						
SEX		N	Minimum	Maximum	Mean	Std. Deviation
Female	AGE	10	21	40	29.70	6.75
Male	AGE	40	24	61	43.20	11.88

The descriptive statistics table reveals data from 50 study participants, illustrating notable findings regarding age distribution. Among the participants, the mean age for females was calculated at 29.70 years (± 6.75), and a range spanning from 21 to 40 years. In contrast, males exhibited a higher mean age of 43.20 years (± 11.88), and a wider age range from 24 to 61 years.

Table 3: Distribution of Sputum Microscopy.

Sputum microscopy	Frequency	Percent
1+	13	26.0
2+	25	50.0
3+	12	24.0

The data distribution of sputum microscopy was also done among the 50 study participants. Among them, the highest number of cases, constituting 50%, were categorized as 2+, followed by 26% classified as 1+, while the remaining 24% were categorized as 3+. This distribution highlights the varying degrees of severity observed among the study participants, indicating the prevalence of different levels of pulmonary tuberculosis within the sample population.

Table 4: Descriptive statistics of different parameters.

	N	Minimum	Maximum	Mean	Std. Deviation
Hb (g/dl)	50	6.60	12.40	9.49	1.63
TLC	50	1378	13780	7108.12	3137.84
CRP (mg/L)	50	10.00	353.00	94.34	89.43
Serum Procalcitonin	50	.02	14.00	2.54	4.28

Based on the descriptive statistics, which encompasses data from a total of 50 study participants, notable findings include a mean hemoglobin (Hb) level of 9.49 ± 1.63 g/dL, ranging from 6.60 to 12.40 g/dL, and a mean total leukocyte count (TLC) of 7108.12 ± 3137.84 cells/mm³, with a range spanning from 1378 to 13780 cells/mm³. Additionally, the mean CRP concentration was calculated at 94.34 ± 89.43 mg/L, varying between 10 and 353 mg/L, while the mean Serum Procalcitonin level stood at 2.54 ± 4.28 ng/mL, with a range extending from 0.02 to 14.00 ng/mL.

Table 5: Descriptive statistics of Sputum microscopy.

Descriptive Statistics						
Sputum microscopy		N	Minimum	Maximum	Mean	Std. Deviation
1+	CRP	13	10.00	85.00	37.23	33.79
	Sr. Procalcitonin	13	.02	5.60	0.52	1.53
2+	CRP	25	10.00	353.00	103.87	68.29
	Sr. Procalcitonin	25	.04	14.00	3.30	4.75
3+	CRP	12	18.00	353.00	136.35	134.99
	Sr. Procalcitonin	12	.02	11.20	3.14	4.83

The descriptive statistics of sputum microscopy highlight the variations in CRP and Sr. PCT levels across different grades of sputum microscopy. For sputum microscopy grade 1+, the mean CRP level was 37.23 ± 33.79 mg/L, with a range of 10-85, while the mean Sr. Procalcitonin level was 0.52 ± 1.53, ranging from 0.02 to 5.60. In contrast, sputum

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microscopy grade 2+ exhibited higher mean CRP levels at 103.87 ± 68.29 mg/L, with a broader range of 10-353, and higher mean Sr. Procalcitonin levels at 3.30 ± 4.75, ranging from 0.04 to 14.0. The most elevated mean CRP levels were observed in sputum microscopy grade 3+, reaching 136.35 ± 134.99 mg/L, with a range of 18-353, while Sr. Procalcitonin levels averaged 3.14 ± 4.83, with a range of 0.02-11.20.

Table 6: Distribution of Neutrophils.

NEUTROPHIL	Frequency	Percent
N58	4	8.0
N60	4	8.0
N63	3	6.0
N70	13	26.0
N72	2	4.0
N74	3	6.0
N84	6	12.0
N88	4	8.0
N90	4	8.0
N94	7	14.0
Total	50	100.0

The distribution of neutrophils highlights notable findings regarding neutrophil counts. Specifically, the maximum number of cases showed Neutrophil count at 70, with 13 instances, constituting 26% of the total. Additionally, significant occurrences were noted at Neutrophil counts of 94, with 7 cases (14%), and at counts of 84, with 6 cases (12%). Other observations encompassed Neutrophil counts of 58, 60, 88, and 90, each accounting for 8% of the total. Conversely, the fewest instances were recorded at a Neutrophil count of 72, with only 2 cases, representing a minimal 4% of the total.

Table 7: Distribution of Lymphocyte.

LYMPHOCYTE	Frequency	Percent
L12	6	12.0
L19	3	6.0
L2	7	14.0
L21	4	8.0
L26	2	4.0
L28	9	18.0
L29	3	6.0
L30	4	8.0
L34	4	8.0
L6	4	8.0
L7	4	8.0
Total	50	100.0

Lymphocyte distribution analysis was also achieved for the 50 participants. The maximum number of lymphocytes, totaling 28 cases, accounted for 18% of the observations. Among these, L2 and L12 showed the next highest frequencies, with 7 cases (14%) and 6 cases (12%), respectively. Additionally, categories such as L21, L30, L34, L6, and L7 collectively constituted 8% of the total cases. Conversely, the least number of cases were observed in L26, with only 2 instances (4%), followed closely by L29, which comprised 3 cases (6%).

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Table 8: Descriptive statistics of ESR and Sputum microscopy.

Descriptive Statistics						
Sputum microscopy		N	Minimum	Maximum	Mean	Std. Deviation
1+	ESR	13	30	39	33.23	3.14
2+	ESR	25	42	60	51.40	5.12
3+	ESR	12	60	95	76.58	11.14

The descriptive statistics reveal distinct patterns in Sputum microscopy readings categorized by ESR levels. For Sputum microscopy 1+, the mean and standard deviation of ESR is 33.23 ± 3.14, with a narrow range of 30-39. Conversely, Sputum microscopy 2+ exhibits a higher mean and standard deviation of ESR at 51.40 ± 5.12, reflecting a wider range of 42-60. Notably, for Sputum microscopy 3+, the mean and standard deviation of ESR further increase to 76.58 ± 11.14, with the widest range observed between 60 and 95.

Table 9: Correlation Between Serum Procalcitonin Levels, Sputum Microscopy, and C-reactive protein (CRP) Concentrations in Patients.

Correlations				
		Sputum microscopy	Sr. Procalcitonin	CRP
Sputum microscopy	Pearson Correlation	1	.224	.398
	Sig. (2-tailed)		.119	.004
	N	50	50	50
Sr. Procalcitonin	Pearson Correlation	.224	1	.597
	Sig. (2-tailed)	.119		.001
	N	50	50	50
CRP	Pearson Correlation	.398	.597	1
	Sig. (2-tailed)	.004	.001	
	N	50	50	50

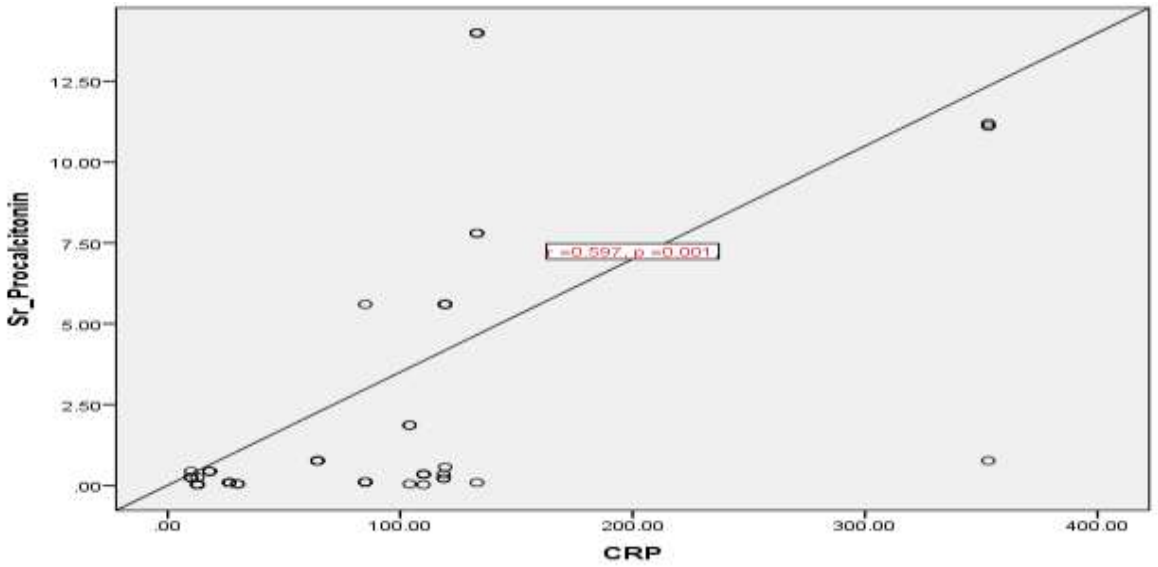

Figure 2: Correlation Between Serum Procalcitonin Levels and C-reactive protein (CRP) Concentrations in Patients.

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Original Article

The Pearson Correlation analysis revealed significant findings regarding the relationship between CRP levels and both sputum microscopy and Sr. PCT. For CRP and sputum microscopy, a correlation coefficient of 39.8% with a p-value of 0.004 indicates a moderate positive linear relationship, providing statistical evidence for this association. Similarly, the correlation coefficient between CRP and Sr. PCT was notably higher at 59.7%, with a p-value of 0.001, suggesting a stronger positive linear relationship between these variables.

DISCUSSION.

The current study, encompassing 50 participants, revealed a predominant age range of 20-30 years, with the highest incidence observed in this group among females (50%) and in the 40-50 age range among males (30%). Descriptive statistics indicated a mean age of 29.70 ± 6.75 among females and 43.20 ± 11.88 among males.

Notably, sputum microscopy revealed varying levels of tuberculosis bacilli, with the most prevalent being 2+ (50%), followed by 1+ (26%), and a minority at 3+ (24%). Descriptive statistics of sputum microscopy categorized by bacilli levels revealed corresponding increases in both CRP and Sr. PCT concentrations, suggesting a potential association. Furthermore, mean values for hemoglobin, total leukocyte count, and inflammatory markers such as CRP and Sr. PCT were documented. Analysis of neutrophil and lymphocyte counts demonstrated significant findings.

Additionally, correlations between CRP and both sputum microscopy and Sr. Procalcitonin were statistically significant, further indicating a linear relationship among these variables. These results underscore the potential utility of CRP and Sr. PCT as biomarkers for assessing tuberculosis severity and treatment response.

In recent studies, sixty-seven patients, comprising 41 males and 26 females with ages ranging from 23 to 61 years, were included to investigate active spinal tuberculosis [11, 12]. Sputum samples from another study were processed using the Kubica method and inoculated onto the Lowenstein-Jensen medium, with mycobacterial loads graded according to WHO recommendations [13].

Additionally, a separate study demonstrated decreased levels of Iron, Hb, Transferrin, and Transferrin Saturation (TS%), alongside increased levels of Total Iron Binding Capacity (TIBC), Ferritin, and CRP in Pulmonary Tuberculosis [14]. Furthermore, among various systemic inflammatory markers including ESR and Fibrinogen, CRP emerged as the most sensitive indicator in defining the severity of PTB [15].

Moreover, in another study, both CRP and PCT levels were found to be positively correlated with the TB score, confirming the TB score's ability to assess the degree of disease activity in pulmonary TB [16].

CONCLUSION.

From the study, it is found that serum procalcitonin levels and serum C-reactive protein are high in the subjects admitted for pulmonary tuberculosis. There is a high degree of association between serum levels of calcitonin, and C-reactive protein with the occurrence of Pulmonary tuberculosis.

LIMITATION.

The study population size was small. Such studies are required to be done on a large population size.

RECOMMENDATIONS.

Based on the findings of the study, it is recommended to implement routine screening protocols for serum CRP and serum PCT levels in individuals clinically diagnosed with pulmonary TB to aid in the diagnosis and monitoring of disease progression. Additionally, enhancing awareness campaigns to educate healthcare professionals and the general population about the importance of early detection and prompt treatment of TB is crucial to reduce its burden on public health. Moreover, further research is warranted to explore the potential utility of CRP and PCT levels as biomarkers for assessing treatment response and guiding therapeutic interventions in pulmonary TB patients.

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LIST OF ABBREVIATIONS.

TB: Tuberculosis
CRP: C-Reactive Protein
PCT: Procalcitonin
Sr: Serum
CAP: Community-Acquired Pneumonia
COPD: Chronic Obstructive Pulmonary Disease
Hb: Hemoglobin
TLC: Total Leukocyte Count
ESR: Erythrocyte Sedimentation Rate
TIBC: Total Iron Binding Capacity

DECLARATION OF COMPETING INTEREST.

The authors declare that there is no conflict of interest regarding the publication of this paper.

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