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Relationship between Quantitative C-Reactive Protein (CRP) Levels and Leukocyte Counts in Pulmonary Tuberculosis Infection Patients at Arifin Achmad Regional Hospital

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Abstract

Pulmonary tuberculosis is a chronic infectious disease caused by Mycobacterium tuberculosis. C-reactive protein (CRP) and leukocyte count are indicators that can reflect the severity of infection in pulmonary TB patients. This study aims to analyze the relationship between quantitative CRP levels and leukocyte counts in pulmonary tuberculosis patients. This study is an observational analytical study with a cross-sectional approach conducted on 30 pulmonary TB patients at Arifin Achmad Hospital, Pekanbaru who met the inclusion and exclusion criteria. Data on CRP levels and leukocyte counts were obtained through laboratory examinations, while demographic data were taken from patient medical records. Normality and linearity tests were performed before correlation analysis using linear regression tests. The average CRP level of patients was 84.14 ± 91.59 mg/L, with the lowest level of 0.71 mg/L and the highest of 316.7 mg/L. The mean number of leukocytes was 10,481 ± 4,625.53 mm^3, with the lowest number of 3,190 mm^3 and the highest of 21,310 mm^3. The results of the bivariate analysis showed no significant relationship between CRP levels and leukocyte counts in pulmonary TB patients ($p = 0.378$). There was no significant correlation between quantitative CRP levels and leukocyte counts in pulmonary tuberculosis patients at Arifin Achmad Hospital Pekanbaru. Further research with larger samples and longitudinal designs is needed to further explore the relationship between these two variables and their implications in the management of pulmonary TB.

Keywords: C-Reactive Protein, Leukocytes, Pulmonary tuberculosis.

Introduction

Tuberculosis is an infectious disease caused by the Mycobacterium tuberculosis bacteria. There are several species of Mycobacterium, including Mycobacterium tuberculosis, Mycobacterium africanum, Mycobacterium bovis, Mycobacterium leprae, and others. Tuberculosis (TB) is one of the main infectious diseases and has become a public health concern worldwide (Ministry of Health, 2021)

The World Health Organization (WHO) estimates that there were around 10.6 million cases of TB in 2021, equivalent to 134 cases per 100,000 population. Most TB cases recorded in 2021 were in Southeast Asia (45%), Africa (23%) and the Western Pacific (18%), with smaller percentages in the Eastern Mediterranean (8.1%), America (2.9%) and Europe (2.2%) (WHO, 2022). For Riau Province, from the TB Incident Estimate set at 31,899 cases, 13,011 TB cases were found consisting of 12,866 SO TB and 145 RO TB cases. The percentage of TB Treatment Coverage is 40.78%, and the achievement in 2022 is also the highest record achievement since TB was declared a national priority program and the total number of suspected TB in Pekanbaru City in 2022 was 32,755 cases (P2P Profile, 2022)

In general, every tuberculosis sufferer will experience general symptoms in the form of coughing up phlegm for more than two weeks, coughing up blood, weakness, weight loss, increased body temperature, and frequent night sweats (Hasnawati, 2018).

In efforts to treat TB, a fast and accurate diagnosis is crucial to reduce the impact of this disease. Laboratory examinations, especially measuring C-Reactive Protein (CRP) levels and Leukocyte Counts, have become an important part of the TB diagnostic process. C-Reactive Protein (CRP) is a biomarker that is useful for monitoring disease progression. C-Reactive Protein (CRP) is useful for monitoring disease progression.

The concentration of C-Reactive Protein (CRP) is related to the severity of the disease. A rapid decrease in the concentration of C-Reactive Protein (CRP) is considered to be associated with a good response to early antimicrobial treatment (Purwanto and Astrawinata, 2019).

Leukocytes are one of the blood components that play an important role in fighting infections in the body. These infections can be caused by many things such as viruses, bacteria, or metabolic processes of toxins. In bacterial infections, the number of leukocytes can increase or leukocytosis (Dicky & Ahmad, 2019).

Mycobacterium tuberculosis that enters the body can cause inflammation. Inflammation is a body mechanism caused by the presence of foreign objects entering. In the process, these cells will release pro-inflammatory cytokines including IL-6, then IL-6 will induce liver cells to synthesize active phase proteins such as C-Reactive Protein (CRP) and fibrinogen which function as extracellular proteins that induce phagocytes to phagocytosis bacteria. Measurement of cytokines and acute phase proteins can be used as indicators of inflammation. CRP levels in the body will increase when the body experiences inflammation (Ustiawaty et al., 2020).

Leukocytes are white blood cells that are part of the bone marrow of human blood cells that have a major role in the immune system or protect the body's defenses from infection (Geni L, Panjaitan LMR., 2019). The number of leukocytes in normal conditions is 4000/mm2. If the number of leukocytes is above 10,000/mm2 this condition is called leukocytosis and if the number of leukocytes is less than 4000/mm2 it is called leukopenia (Geni L, Panjaitan LMR, 2019).

Tuberculosis causes an increase in the number of leukocytes related to its function as a defense, so that blood sedimentation accelerates due to the increase in the number of

blood cells (Tahumurin et al., 2017). Based on previous studies, it was found that there were very diverse changes in hematology examination results, both in the number of leukocytes, erythrocytes, platelets and LED (Sundari et al., 2017).

Arifin Achmad Regional General Hospital (RSUD) Pekanbaru, as one of the main health institutions that is a reference for handling TB disease. Based on laboratory data, the request for CRP examination and the number of leukocytes increased in pulmonary TB patients who were controlled at this hospital,

Based on the explanation above, researchers have conducted research on "The Relationship between Quantitative C-Reactive Protein (CRP) Levels and Leukocyte Counts in Patients with Pulmonary Tuberculosis Infection at Arifin Achmad Hospital". This study is expected to provide a better understanding of the role of C-Reactive Protein (CRP) and leukocyte count in the diagnosis and management of Pulmonary TB, so that it can help improve the quality of health services provided to patients and optimize TB control efforts at the hospital level.

Method

The design used for this study is analytical research using a cross-sectional approach, namely measuring the variables at the same time and at the same time and once observed. Then the comparative analysis in this study was to determine the relationship between quantitative CRP levels and the number of leukocytes in patients with tuberculosis (TB) infection at Arifin Achmad Hospital. Population is the total number of objects or subjects that have certain characteristics determined by researchers to be studied and then conclusions drawn. (Sujarweni, 2014). The population in this study were TB infection patients who were controlled at Arifin Achmad Hospital from May 2024 to June 2024, totaling around 30 people. The sample in this study was all samples of pulmonary TB infection patients who were treated at Arifin Achmad Hospital from May 2024 to June 2024, totaling 30 samples the sampling technique used was total sampling, the total sampling technique is a sampling determination technique where the

entire population is used as a sample. The samples used are those that meet the inclusion and exclusion criteria. The research procedure began with blood sampling, then a quantitative CRP level examination was carried out using the Architect c4000 automatic tool and a leukocyte count examination using the XN Xysmex 1000 tool. The data obtained were processed using SPSS and continued with univariate analysis.

Results

Characteristics of Research Subjects

Table1
Characteristics of Research Subjects

Variable	f (%)	Average	SD	Median (Min-Max)
Gender				
Male	21 (70)			
Female	9 (30)			
Age		42,4	16,75	44,5 (15-65)
Male		45,2	16,30	49 (18-68)
Female		35,8	16,88	29 (15-65)

Based on Table 1, it is known that the majority of respondents are male, 21 people (70%), while female respondents are 9 people (30%). The age characteristics of the subjects of this study are the youngest age is 15 years, female gender, and the oldest is 65 years, female gender.

Univariate Analysis

Average of CRP Levels

Table 2
CRP Levels

Variable	f (%)	Average	SD	Median (Min-Max)
CRP Levels (mg/L)		84,14	91,59	57,77 (0,71-316,7)

Based on Table 2, the Characteristics of Quantitative CRP levels in the research subjects showed that the average Quantitative CRP level was 84.14 ± 91.59 mg/L. The lowest Quantitative CRP level was 0.71 mg/L in female respondents aged 49 years, while the highest Quantitative CRP level was 316.7 mg/L in male respondents aged 49 years.

Average leukocyte count

Table 3
Leukocyte count

Variable	f (%)	Average	SD	Median (Min-Max)
Leukocyte count (mm³)		10.481	4.625,53	10.450 (3.190 -21.310)

From Table 3, it can be explained that the characteristics of the number of leukocytes in the research subjects obtained an average number of leukocytes of 10,481 ± 4,625.53 mm³. The lowest number of leukocytes was 3,190 mm³ in male respondents aged 23 years, while the highest number of leukocytes was 21,310 mm³ in male respondents aged 38 years.

Bivariate Analysis

Data Normality and Linearity Test

1. CRP Outcome Variable

Normality Test

Table 4
Results of the CRP Variable Normality Test

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
CRP Outcome	.200	30	.004	.833	30	.000

Lilliefors Significance Correction

The results of the normality test of the CRP outcome variable are not normally distributed because the significance value of Shapiro Wilk is 0.878 greater than alpha 5% or 0.05.

Linearity Test

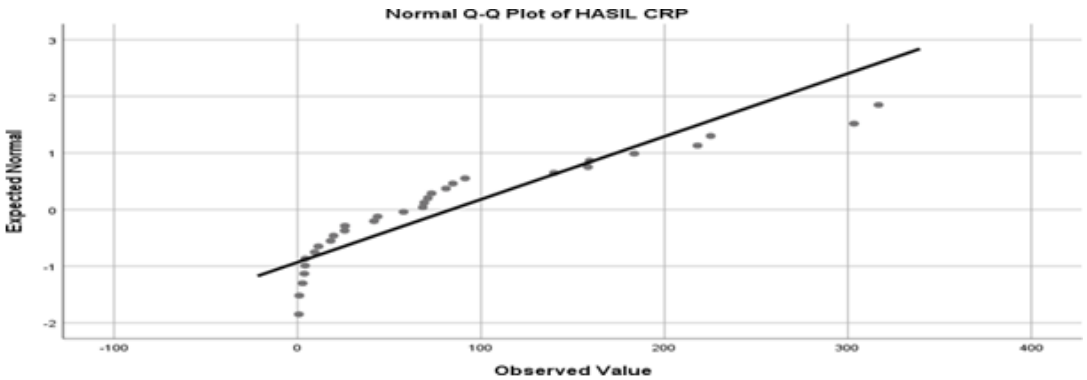

Figure 1 Results of Linearity Test of CRP Result Variables

The results of the linearity test of the CRP result variables are not linear because the

plot does not follow the linear line in the graph.

2. Leukocyte Result Variable

Normality Test

Table 5
Leukocyte Variable

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
RESULT LEUKOCYTE 1	.077	30	.200*	.982	30	.878

*. This is a lower bound of the true significance.

Lilliefors Significance Correction

The results of the normality test of the leukocyte result variable are normally distributed because the significance value of Shapiro Wilk is 0.878, greater than alpha 5% or 0.05.

Linearity Test

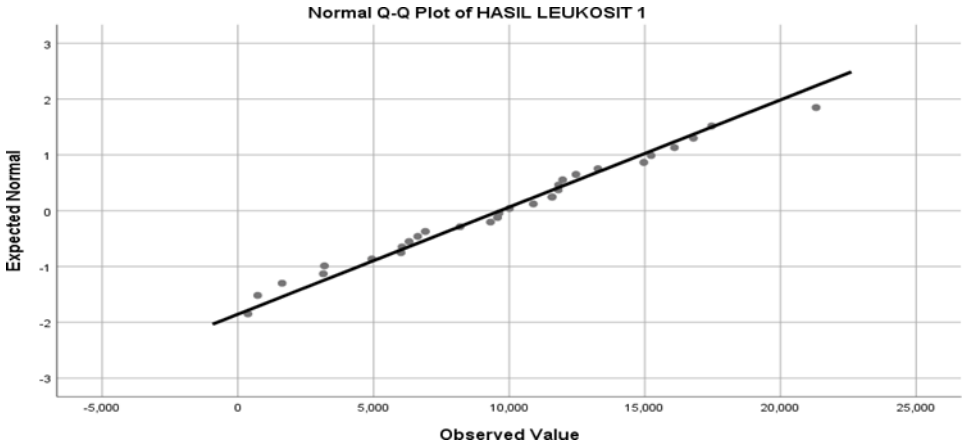

Figure 2 Results of Linearity Test of Leukocyte Result Variables

The results of the linearity test of the leukocyte result variables are linear because the plot follows the linear line in the graph.

Results of Data Homogeneity Test

Table 6
Homogeneity Test Results

Coefficients						
		Unstandardized Coefficients		Standardized Coefficients		
Model		B	Std. Error	Beta	t	Sig.
1	(Constant)	4552.115	784.784		5.800	.000
	HASIL CRP	-6.552	6.442	-.189	-1.017	.318

a. Dependent Variable: ABS_RES

The results of the heteroscedasticity test using the Glejser Test show that the

significance value is 0.318 greater than 0.05, so there are no symptoms of heteroscedasticity in the data or the data is homogeneous.

Linear Regression Analysis Results

Coefficients

Table 7
Results of Linear Regression Analysis

Model		Unstandardized Coefficients		Standardized Coefficients		
		B	Std. Error	Beta	t	Sig.
1	(Constant)	8853.160	1312.649		6.744	.000
	HASIL CRP	9.659	10.775	.167	.896	.378

a. Dependent Variable: LEUKOCYTE RESULTS 1

Hypothesis Ho: There is no influence between Leukocyte Levels and CRP

Based on Table 7, the results of multiple linear regression show that quantitative CRP levels and the number of leukocytes in patients with pulmonary tuberculosis infection obtained a significance value of 0.378, greater than alpha 5% or 0.05, which means there is no influence between quantitative CRP levels and the number of leukocytes in patients with pulmonary tuberculosis infection.

Discussion

Univariate Analysis

Based on the results of research conducted at the Arifin Achmad Hospital, Riau Province, the results of the analysis showed that the Characteristics of the Research Subjects, most of the respondents with Pulmonary TB who met the inclusion and exclusion criteria were male, 21 people (70%) and some were female, 9 people (30%). This shows that men suffer from Pulmonary TB more than women. This is by research conducted by (Ergiana et al., 2022) that men suffer from Pulmonary TB more than women, namely 16 men (53.5%) and 14 women (46.5%).

This is because TB sufferers are more in men than women. After all, in men there are several factors including the habit of smoking and consuming alcoholic beverages which can reduce the immune system so that it is easier to be infected with the bacteria M. tuberculosis (Ergiana et al., 2022).

The researcher's assumption, the results of the study show that TB sufferers tend to be more male than female, this is in line with research by (Sutrisna and Elsi

Rahmadani, 2022) and (Lestari et al., 2022). Smoking and alcohol consumption factors are common causes but can also be caused by outside interaction activities in men compared to women in the population studied, which contributes to the higher prevalence of Pulmonary TB in men.

Average Quantitative CRP Levels

Quantitative CRP levels in the study subjects obtained an average Quantitative CRP level of 84.1431 ± 91.59206 mg / L. The lowest Quantitative CRP level was 0.71 mg / L in female respondents aged 49 years, while the highest Quantitative CRP level was 316.7 mg / L in male respondents aged 49 years.

C- Reactive Protein is an acute-phase protein produced by the liver in response to increased levels of inflammatory cytokines, especially interleukin 6 (IL-6) and tumor necrosis factor-alpha (TNF-α). C-Reactive Protein levels are known to increase in response to tissue damage, infection, and inflammation and its concentration will increase in circulation during inflammatory events. C-Reactive Protein is not only a marker of inflammation but also plays an active role in the inflammation process (sproston and Ashworth, 2018).

The results of Shameem et al's study (2017), a history of smoking in TB patients is one of the supporting factors causing high CRP levels in serum.

The researcher's assumption, From the study it was found that high CRP levels were obtained from a 49-year-old male patient, where from the results of the search on the medical record it turned out that there were complications suffered by the patient, namely Diabetes Mellitus, HIV, and a history of long-term smoking, and taking certain drugs such as narcotics. This can be associated with inflammation due to mycobacterium Tuberculosis infection which causes severe lung damage, due to lifestyle such as smoking, free social life, alcohol, etc. This is evident from the highest CRP results found in male respondents who have a history of complications such as HIV and diabetes mellitus. Which can contribute to high CRP levels, because there is damage to the lungs.

Average Leukocyte Count

The number of leukocytes in the study subjects obtained an average of leukocytes of 10,481 ± 4,625.536 mm^3. The lowest number of leukocytes was 3,190 mm^3 in male respondents aged 23 years, while the highest number of leukocytes was

21,310 mm³ in female respondents aged 15 years.

Based on the results of the study, the number of leukocytes varied, where the highest number of leukocytes was found in female patients aged 15 years. From the search for medical records, it was found that this patient had not consumed OAT drugs. Meanwhile, the lowest leukocyte count was obtained in a 23-year-old male patient who had undergone intensive treatment for 6 months. The researcher assumes that OAT therapy can affect the number of leukocytes and suppress the growth of mycobacterium Tuberculosis bacteria, but an increase in the number of leukocytes during therapy indicates an active infection or has not been completely resolved.

Bivariate Analysis

The normality test results of the CRP result variable are not normally distributed because the significance value of Shapiro Wilk is 0.878 greater than alpha 5% or 0.05. The results of the normality test of the leukocyte result variable are normally distributed because the significance value of Shapiro Wilk is 0.878 greater than alpha 5% or 0.05. Based on Table 7, the results of multiple linear regression, quantitative CRP levels with the number of leukocytes in patients with pulmonary tuberculosis infection obtained a significance value of 0.378 greater than alpha 5% or 0.05, which means that there is no influence or no relationship between quantitative CRP levels and the number of leukocytes in patients with pulmonary tuberculosis infection. Meanwhile, this study found that there was no correlation between quantitative CRP levels and the number of leukocytes in tuberculosis patients due to infection or other factors such as at the time of sampling and when the sample was examined, causing no relationship between quantitative CRP levels and the number of leukocytes. This is similar to the results of research conducted by (Magdalena Kase, 2023), stating that there is no significant relationship between CRP and the number of leukocytes. Research conducted by (Bastian, 2023) also found that there was no correlation between the number of leukocytes and CRP levels in patients with pulmonary tuberculosis. In examination of tuberculosis patients, CRP binds directly to microorganisms as opsonins for the complement, activates neutrophils, and inhibits platelet aggregation. The greater the stimulation in the body, the higher the CRP levels will last. After the stimulation is removed, the CRP value will drop rapidly and

immediately return to normal (Mega. J., Sari D. (2019).

Examination of the total number of leukocytes in TB patients before treatment above normal by 25%. Examination of the number of leukocytes shows resistance from the human body to fight mycobacterium tuberculosis germs. Neutrophils are the first line of defense against bacterial infections by lysing and phagocytosing bacteria (Khasanah, 2016).

The researcher's assumption is that the results of the study obtained have no relationship between CRP levels and the number of leukocytes in patients with pulmonary TB infection. This is because the increase in CRP levels is influenced by inflammation or stimulation in the body, namely damage to the lungs. Changes in CRP levels are greatly influenced by the reaction of drug therapy carried out and depend on the success of the treatment. If the drug given is successful, the CRP level will gradually decrease. The number of leukocytes is influenced by the reaction of the drug given which is useful for killing Mycobacterium Tuberculosis bacteria. Leukocytes function as the body's defense during infection, and the number of leukocytes increases if the body is infected with bacteria. And if the number of leukocytes returns to normal, it means that the bacterial infection has subsided (Giyartika, F., & Keman, S., 2020).

Conclusion

Based on the results of data processing and analysis, the following conclusions can be drawn:

1. The average quantitative CRP level in tuberculosis infection patients at Arifin Achmad Hospital was 84.14 mg/L.
2. The average number of leukocytes in tuberculosis infection patients at Arifin Achmad Hospital was 10,481 mm^3.
3. From the results of multiple linear regression, the quantitative CRP level with the number of leukocytes in pulmonary tuberculosis infection patients obtained a significance value of 0.378 greater than alpha 5% or 0.05, which means there is no influence or no relationship between quantitative CRP levels and the number of leukocytes in pulmonary tuberculosis infection patients at Arifin Achmad Hospital.

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