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VARIATIONS IN LEUKOCYTE COUNTS OF TUBERCULOSIS PATIENTS DURING THE TREATMENT PERIOD

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Abstract

Background*:** *Tuberculosis is one of the deadliest infectious diseases in the world. The disease is caused by Mycobacterium tuberculosis bacteria that spread in the air through the saliva of the patient. Infection from these bacteria causes an increase in leukocytes in the blood as a form of body resistance in the process of phagocytosis. Administration of anti-tuberculosis drugs during the first-line phase can kill bacteria and relieve symptoms arising from infection because these drugs have an effect on the work of the spinal cord in producing new blood cells.* ***Research Objective: *This study aims to determine the variation of leukocyte count of tuberculosis patients who are undergoing the first-line phase of treatment as an indication of cure rate.* ***Research Methods:*** *The research method used was analytic cross sectional, which was then analyzed by performing normality and homogeneity tests, then continued with the one way anova test.* ***Results:*** *The results of this study showed the average leukocyte value in the first month of treatment was 5,026 cells/mm3 blood, second month 9,415 cells/mm3 blood, third month 6,140 cells/mm3, fourth month 6,566 cells/mm3, fifth month 6,054 cells/mm3, and sixth month 6,667 cells/mm 3. With an average value of all 6,776 cells/mm3.* ***Conclusion:*** *From these results, it can be concluded that there is a significant difference in the variation of leukocyte counts between the six treatment duration groups with an overall mean value of 6,776 cells/mm3 blood. The significant difference in leukocyte count variation between the six treatment duration groups indicates that leukocytes can be used as a benchmark to determine indications of cure rate of tuberculosis patients who are undergoing the first line of treatment.*

Keywords: Leukocytes, Tuberculosis, Anti-tuberculosis Drugs, Treatment Phase

1. Introduction

Tuberculosis (TB) is a disease caused by infection with the Mycobacterium tuberculosis complex and is the second leading cause of death after HIV (Human Immunodeficiency Virus). According to the World Health Organization (WHO) Tuberculosis is the second deadliest infectious disease in the world after Covid-19 and ranks thirteenth as the leading cause of death worldwide. Data from 2021 showed that the incidence of tuberculosis increased by 3.6% compared to 2020, where 10.6 million people in the world contracted TB and 1.6 million of them died. Indonesia has the second highest number of TB cases after India (1). NTB Province is one of the areas that has a high prevalence rate. Riskesdas data states that the national prevalence of TB disease is 0.99%. This number is expected to continue to swell. The

increase in the number of TB patients is due to the lack of public knowledge about efforts to prevent disease transmission (2). Mataram City in 2021 managed to find as many as 739 TB cases then in 2022 there were 2,448 cases. From this data, Mataram City is called one of the top 4 cities with the highest TB sufferers in NTB (3). Mycobacterium tuberculosis (MTB) is a rod-shaped, acid-resistant bacterium (also known as Acid Resistant Bacteria) on Ziehl Neelsen staining. MTB bacteria can dormant in the body for several years before actively infecting body tissues. Mycobacterium Tuberculosis is an intracellular bacteria, the natural immune response to intracellular bacteria is phagocytosis. TB patients expel infected droplets when they talk. Varaine and Rich said that transmission usually occurs when infected droplets are inhaled. Bacteria entering the body mount an immune response to fight the bacteria (4) said that the cellular immunity mechanism in TB is played by T lymphocyte but the effector function to eliminate bacteria is played by macrophages activated by cytokines produced by T cells. Leukocytes are cells that protect the body from various diseases by phagocytizing and antibodies. Tuberculosis is classified as an airborne disease, transmitted by droplets in the air.

Tuberculosis first-line treatment is carried out for 6 months regularly, which is measured in 1 month, 2 months, 3 months, 4 months, 5 months and 6 months. Isoniazid, rifampicin, pyrazinamide and ethambutol are the most effective first-line anti-TB drugs. These drugs have been used for many years by the world population, even isoniazid has been used since the 1950s. All of these first-line drugs can be administered orally because they are lipophilic (5).

Leukocytes are cells that function to protect the body against various diseases by phagocytes and producing antibodies (6).

When viewed with a light microscope, white blood cells have specific granules (granulose) which when alive are in the form of semi-liquid droplets, have varying nuclear shapes and homogeneous cytoplasm (7).

Based on research results (8) reported in his research before treatment from 12 samples obtained an increased leukocyte count of 3 samples (25%), normal as many as 9 samples (75%), while after treatment for one intensive month the number of leukocytes increased by 3 samples (25%) and decreased by 1 sample (8%) and normal as many as 8 samples (67%). This study was conducted on samples who underwent a treatment period of 1 month and used 12 samples. The difference with previous studies, this study was conducted in the first line of the treatment period of 6 months to be able to see the variation of leukocyte counts which includes changes in the

number in the treatment period. Based on the above background, the researcher is interested in conducting research on "Leukocyte Count Variations in Patients in Line One of the Treatment Period Tuberculosis".

2. Research Methods

The research design used in this study is analytic cross sectional with the research procedure is that the researcher takes and examines directly the sample of respondents infected with tuberculosis based on data information from the health facility.

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page.122-129, https://ejournal.poltekkes-denpasar.ac.id/index.php/M

The sampling technique used in this study was Non Probability Sampling with purposive sampling method that is by not giving the respondents a chance to be infected with tuberculosis equal opportunity for each member of the population to be selected as a sample by determining the sample based on certain objectives and considerations made by the researcher based on the nature or characteristics of the population that is already known in advance (9). The sample criteria that will be used in this study are the following inclusion and exclusion criteria:

1. Inclusion criteria
   a. Willing to be a research subject
   b. Tb patients on treatment for 1 month, 2 months, 3 months, 4 months, 5 months and 6 months.
2. Exclusion Criteria
   a. New TB patients with Diabetes Mellitus
   b. TB Patient with Leukemia

In this study, data were analyzed using the data obtained, including the results of the examination of leukocyte count levels in the blood of Tuberculosis patients using the Hematology Analyzer tool. The effect of the length of tuberculosis treatment as an indication of the level of cure was analyzed using one way Anova. If the data is normally distributed and homogeneous, a parametric test will be used, but if the data is not normally distributed, a non-parametric test will be used.

3. Results and Discussion

From the research that has been conducted on tuberculosis patients in accordance with the criteria set by the researcher, namely sampling of patients who are in the first line of treatment period, namely 1 month, 2 months, 3 months, 4 months, 5 months and 6 months, the following results were obtained:

Table 1. Results of Leukocyte Count Examination in Tuberculosis Patients in the First Line of Treatment.

Sample Code	Age (Year)	Gender	Duration of Diagnosis/month	Leukocyte count of the previous month	Leukocyte Count X10^3
1	45	L	1	11.57	7.48
2	32	P	1	10.06	4.30
3	32	P	1	10.80	3.30
4	29	L	2	11.50	9.46
5	36	L	2	12.84	9.50
6	34	L	2	11.98	9.50
7	31	P	2	12.06	9.20
8	54	P	3	10.47	6.14
9	33	P	4	9.83	7.62
10	24	P	4	9.00	5.10
11	29	L	4	9.70	6.98
12	46	L	5	10.61	7.53
13	75	P	5	8.29	4.12
14	31	L	5	9.07	5.09
15	32	L	5	8.90	4.53
16	50	L	5	11.82	9.00
17	50	L	6	9.04	6.87
18	23	P	6	8.95	6.77
19	29	P	6	8.86	6.80
20	29	L	6	9.73	6.98
Total sample 20				**Average 10.25**	**Average 6.81**

Based on table 1, the results of the lowest leukocyte count of the respondents were found in the first month of drug consumption with a total of 3,300

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page.122-129, https://ejournal.poltekkes-denpasar.ac.id/index.php/M

cells/mm3 blood, then for the highest leukocyte value was in the second month of drug consumption, namely 9,500 cells/mm3 blood and for the results of the number of leukocytes from other respondent samples between 4,120 cells/mm3 - 9,460 cells/mm3 blood.

Table 2. Results of normality test for leukocyte counts

One-Sample Kolmogorov-Smirnov Test

		leukosit
N		20
Normal Parameters[a,b]	Mean	6.7760
	Std. Deviation	1.93798
Most Extreme Differences	Absolute	.124

a. Test distribution is Normal.

b. Calculated from data.

c. Lilliefors Significance Correction.

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

Based on the output above, the statistical value is 0.124 and sig is 0.200. Since the sig value of 0.200 is greater than 0.05, we accept H0. So the conclusion obtained is that the leukocyte count data is normally distributed at the 5% real level. This means that the normality assumption on the data has been met so that it can be continued with the one-way anova method.

Table 3. Homogeneity test results

Test of Homogeneity of Variances

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Levene Statistic	df1	df2	Sig.
7.823	4	14	.002

From table 3 above, the statistical value is 7.823 and sig is 0.002. Since the sig value of 0.002 is smaller than 0.05, we reject H0. So the conclusion obtained is that the leukocyte count data between treatment duration groups have different variances at the 5% real level. This means that the assumption of homogeneity of variance in the data has not been met but can still be continued with the one-way anova method.

Because the results of the normality test state that leukocytes are normally distributed so that the sample falls into the criteria in accordance with the requirements of one-way anova, then further data processing will continue with the one-way anova test.

Table 4. Results of one-way data analysis

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	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
					Lower Bound	Upper Bound		
1.00	3	5.0267	2.18269	1.26018	-.3954	10.4488	3.30	7.48
2.00		9.4150	.14457	.07228	9.1850	9.6450	9.20	9.50
3.00	1	6.1400	.	.	.	.	6.14	6.14
4.00	3	6.5667	1.30986	.75625	3.3128	9.8205	5.10	7.62
5.00	5	6.0540	2.11245	.94471	3.4311	8.6769	4.12	9.00
6.00	4	6.6675	.29466	.14733	6.1986	7.1364	6.23	6.87
Total	2 0	6.7760	1.93798	.43335	5.8690	7.6830	3.30	9.50

Table 5. One-way Anova analysis results

ANOVA

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	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	40.227	5	8.045	3.618	.026
Within Groups	31.133	14	2.224		
Total	71.360	19			

Based on tables 4 and 5 above, the calculated F value is 3.618 and sig is 0.026. The F table value is

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page.122-129, https://ejournal.poltekkes-denpasar.ac.id/index.php/M

$F(0.05,5,14)$ = 2,958 for alpha 5%. Since the F value of 3.618 is greater than the F table of 2.958 or the sig value of 0.026 is less than 0.05, we reject H0. So the conclusion obtained is that there is no significant difference in leukocyte counts between the six groups of treatment duration at the 5% real level.

The number of leukocytes based on the length of treatment each month has decreased in each blood of each respondent. This indicates that the longer the treatment, the lower the number of leukocytes in the patient.

In the first month of treatment, there were 3 respondents. In the first month of treatment, it was found that the number of leukocytes in the respondent's blood was still in the normal range with an average value of 5.026 cells/mm3. This happens because in new tuberculosis patients, leukocytes are still identifying microbes as an initial response so that the number of leukocytes has not increased significantly in accordance with the theory of (10) namely immunity or immunity is a system of mechanisms in organisms that protect the body against external biological influences, with the stage of identifying and then killing pathogens, this system detects various kinds of external biological influences to protect the body from infection .

In the second month of treatment, there were 4 respondents. At this stage of treatment, it was found that the patient's leukocytes decreased but there were several samples that increased with an average value of 9.415 cells/mm3 , this happens because patients do not consume drugs routinely in accordance with the direction of medical personnel so that leukocytes in the body increase, this is in line with the theor (11), explaining that treatment can cure a disease gradually, most BTA positive tuberculosis patients become BTA negative (conversion) within 2 months (at the end of intensive treatment), and if the way of using drugs is not appropriate, the bacteria or microbes in the body will not die completely and will return toactively attack the body.

In the third month of treatment, the patient amounted to 1 respondent. At this stage of treatment, it was found that the patient's leukocytes decreased to normal values with an average value of 6,140 cells/mm3 , this occurred because the patient had taken anti-tuberculosis drugs regularly and routinely during treatment, in accordance with the theory (12), namely the patient's leukocyte count will return to normal it is influenced by patient compliance who takes anti-tuberculosis drugs regularly.

In the fourth month of treatment the sample amounted to 3 respondents. At this stage of treatment, the results of the number of leukocytes in the patient's blood decreased to normal values with an average value of 6,566 cells/mm3. In accordance with the theory of (12), namely the number of leukocytes that returned to normal because the patient had taken anti-tuberculosis drugs routinely with a length of treatment of more than 2 months so that the number of leukocytes returned to normal.

In the fifth month of treatment the sample amounted to 5 respondents. In this phase, the results of the number of leukocytes in the respondent's blood decreased and had returned to normal values with an average value of 6,054 cells/mm3. Based on the theory (13) that the

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page.122-129, https://ejournal.poltekkes-denpasar.ac.id/index.php/M

number of leukocytes of tuberculosis patients after taking anti-tuberculosis drugs will decrease because anti-tuberculosis drugs can stop the development and kill bacteria so that there is a suppression of the work of the bone marrow in producing new blood cells.

In the sixth month of treatment the sample amounted to 4 respondents. At this stage of treatment, the results of leukocytes increased from the previous month but only by 0.08%, namely at an average value of 6,667 cells / mm3. The theory of Eni Purwaeti from the source (14) says that in general an increase in leukocytes occurs due to the body fighting infection, but if the increase is not too high then it is normal because leukocytes in the body are not always in the exact same range of numbers. Based on the results of research that has been conducted from samples that have been taken in accordance with the criteria determined by the researcher, the overall number of leukocytes in tuberculosis patients who are undergoing treatment for 1 month, 2 months, 3 months, 4 months, 5 months and 6 months is decreasing at each stage of treatment carried out at the first line of treatment with an average value of 6,776 cells/mm3 blood. In their theory, (15) said that tuberculosis treatment with anti- tuberculosis drugs can reduce the number of leukocytes and leukocyte counts that previously increased in number due to infection, leukocytes function to fight foreign objects that enter the body, these foreign objects can be viruses or bacteria. And also that tuberculosis treatment with anti-tuberculosis drugs can reduce the number of leukocytes that previously increased in number due to infection. A normal leukocyte count is obtained after several months of treatment.

4. Conclusion

The average number of leukocytes in the blood of patients with tuberculosis undergoing 1-month treatment was 5,026 cells/mm3 blood from 3 (15%) respondents, 2-month treatment was 9,415 cells/mm3 blood from 4 (20%) respondents, 3-month treatment was 6,140 cells/mm3 blood from 1 (5%) respondent, 4-month treatment was 6.566 cells/mm3 blood from 3 (15%) respondents, 5 months treatment was 6,054 cells/mm3 blood from 5 (25%) respondents, 6 months treatment was 6,667 cells/mm3 blood from 4 (20%) respondents, and the average number of leukocytes in tuberculosis patients who were undergoing treatment period of 1 month, 2 months, 3 months, 4 months, 5 months and 6 months was 6,776 cells/mm3 blood from 20 (100%) respondents. From these results, it can be concluded that there is a significant difference in the variation of leukocyte counts between the six groups of treatment duration, which indicates that leukocytes can be used as a benchmark to determine indications of the recovery rate of tuberculosis patients who are undergoing the first line of treatment.

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page.122-129, https://ejournal.poltekkes-denpasar.ac.id/index.php/M

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page.122-129, https://ejournal.poltekkes-denpasar.ac.id/index.php/M

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