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Correlation between leukocyte, neutrophil, lymphocyte, and the neutrophil to lymphocyte ratio levels in *Mycobacterium tuberculosis* detection using rapid molecular tests

Correlación entre los niveles de leucocitos, neutrófilos, linfocitos y la relación neutrófilo a linfocito en la detección de *Mycobacterium tuberculosis* mediante pruebas moleculares rápidas

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SUMMARY

Pulmonary tuberculosis (TB) is a chronic inflammatory disease caused by Mycobacterium Tuberculosis (MTB). Rapid molecular testing (TCM) can detect MTB and simultaneously perform drug sensitization testing by identifying genetic material that represents resistance. One of the immune responses to TB is inflammation. Leukocytes, Neutrophils, Lymphocytes, and neutrophil-lymphocyte ratio (NLR) have become potential inflammatory markers to determine the presence of chronic inflammation that plays a role in the physiological immune response of TB infection.

Leukocytes circulate against various stress conditions during inflammation, characterized by increased neutrophil counts and decreased lymphocyte counts. This study aims to determine the relationship between the number of leukocytes, neutrophils, lymphocytes, and NLR as biomarkers of germ detection levels with TCM in TB patients.

This type of quantitative research uses analytical study methods with a cross-sectional approach, with total sampling in accordance with the exclusion and inclusion criteria with a total sample of 187 people consisting of 67 positive samples and 120 negative samples.

Results show the mean value of the number of leukocytes at the detection level was High 12.20 (7.30 -18.40), Medium 10.50 (470-19.90), Low 9.35 (5.20-17.60), and Negative 8.80 (3.30-19.80). Neutrophils at detection levels were High 77.00 (53.20 - 86.90), Medium 73.15

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(55.50 - 90.60), Low 71.70 (48.10 - 89.30), and Negative 65.05 (11.30 -88.80). Lymphocytes at detection levels were High at 11.40 (2.70 - 27.50), Medium at 14.55 (4.10 - 31.50), Low at 16.90 (5.00 - 44.70), and Negative at 22.05 (5.80 - 69.30). And NLR at detection levels of High 16.90 (2.27 - 21.26), Medium 5.22 (1.76 - 22.10), Low 4.30 (1.15 - 16.98), and Negative 2.90 (0.35 - 14.80). There was a significant association between leukocyte count (p=0.003), neutrophil (p=0.001), and NLR (p=0.001) with the germ detection rate using TCM.
Conclusion: *The number of leukocytes, neutrophils, lymphocytes, and NLR can be used as biomarkers to detect the level of germ count with TCM in TB.*

Keywords: *Pulmonary TB, TCM, leukocytes, neutrophils, lymphocytes, NLR*

RESUMEN

La tuberculosis pulmonar (TB) es una enfermedad inflamatoria crónica causada por Mycobacterium tuberculosis (MTB). Las pruebas moleculares rápidas (TCM) pueden detectar el MTB y, simultáneamente, llevar a cabo pruebas de sensibilidad a los medicamentos identificando material genético que representa resistencia. Una de las respuestas inmunitarias a la TB es la inflamación. Los leucocitos, los neutrófilos, los linfocitos y la relacion neutrofilos-linfocitos (RNL) se han convertido en marcadores inflamatorios potenciales para determinar la presencia de inflamación crónica que desempeña un papel en la respuesta inmunitaria fisiológica a la infección por TB. Los leucocitos circulan en diversas condiciones de estrés durante la inflamación, que se caracteriza por un aumento en el recuento de neutrófilos y una disminución en el recuento de linfocitos.
Este estudio tiene como objetivo determinar la relación entre el número de leucocitos, neutrófilos, linfocitos y la RNL como biomarcadores de los niveles de detección de gérmenes con TCM en pacientes con TB.
Esta investigación es un tipo de investigación cuantitativa que utiliza métodos de estudio analítico con un enfoque transversal, con un muestreo total como técnica de muestreo de acuerdo con los criterios de inclusión y exclusión, con un total de 187 personas, que consta de 67 muestras positivas y 120 muestras negativas.
Los resultados del estudio muestran que el valor promedio del número de leucocitos en el nivel de detección es alto, 12,20 (7,30 – 18,40), medio, 10,50 (4,70 – 19,90), bajo, 9,35 (5,20 – 17,60) y negativo, 8,80 (3,30 – 19,80). Los neutrófilos en los niveles de detección son altos, 77,00 (53,20 – 86,90), medios, 73,15 (55,50 – 90,60), bajos, 71,70 (48,10 – 89,30), y negativos, 65,05 (11,30 – 88,80). Los linfocitos en los niveles de detección son altos, 11,40 (2,70 – 27,50), medios, 14,55 (4,10 – 31,50), bajos, 16,90 (5,00 – 44,70), y negativos, 22,05 (5,80 – 69,30). Y la RNL en los niveles de detección es alto, 16,90 (2,27 – 21,26), medio, 5,22 (1,76 – 22,10), bajo, 4,30 (1,15 – 16,98), y negativo, 2,90 (0,35 – 14,80). Hubo una asociación significativa entre el recuento de leucocitos (p=0,003), los neutrófilos (p=0,001) y la RNL (p=0,001) con la tasa de detección de gérmenes utilizando TCM.
En conclusión, el número de leucocitos, neutrófilos, linfocitos y la RNL pueden utilizarse como uno de los biomarcadores para detectar el nivel de recuento de gérmenes con TCM en la TB.

Palabras clave: *TB pulmonar, TCM, leucocitos, neutrófilos, linfocitos, RNL.*

INTRODUCTION

Pulmonary tuberculosis (TB) is a chronic inflammatory disease caused by *Mycobacterium tuberculosis* (MTB), an infectious agent characterized by gram-positive, rod-shaped bacteria that thrive in an aerobic atmosphere and exhibit acid resistance. This bacterium primarily attacks the lungs (pulmonary TB), leading to airway disorders, but it can also affect other organs (extrapulmonary TB). It is generally transmitted through the air as droplets (1).

MTB ranks as the 13th leading cause of death and is the second leading cause of death from a single infectious agent following COVID-19. Globally, in 2020, an estimated 10 million people were afflicted with tuberculosis, including approximately 1.1 million children under 15. Of these, 226 100 children (comprising 205 000 HIV-negative children and 21,100 HIV-positive children) succumbed to MTB. Among the HIV-negative individuals who died from MTB, 53 % were male, 32 % were female, and 16 % were children under the age of 15. The higher proportion of children succumbing to tuberculosis compared to their estimated number of cases (11 %) indicates limited access to diagnosis and treatment (2).

In 2020, 30 high-burden countries accounted for 86 % of new TB cases. Two-thirds of these cases originated from eight countries, with India being the most significant contributor, followed by Indonesia, the Philippines, China, Pakistan, Nigeria, Bangladesh, and South Africa.

In Indonesia alone, it is estimated that there were 845 000 (ranging from 770 000 to 923 000) new cases of pulmonary TB in 2019, including 19 000 new cases of TB-HIV positivity. It is estimated that there were 92 000 deaths in TB-HIV-negative cases and 4,700 deaths in TB-HIV-positive patients (2). Data from the Palu City Health Office in 2020 identified 598 TB patients out of 3 389 suspected TB patients, with an increase in 2021, 776 TB patients were identified out of 2 959 suspected TB patients (3).

The Xpert®MTB/RIF test consists of an automated, semi-quantitative, real-time polymerase chain reaction (PCR) *in vitro* diagnostic assay that, in just two hours, allows the detection of *Mycobacterium tuberculosis* complex (MTB) DNA and mutations associated with resistance to rifampicin. This test has proven to be a valuable diagnostic tool in the battle against tuberculosis (4). TCM is a widely used molecular test that is easy to operate. In 2010, the World Health Organization (WHO) recommended the GeneXpert MTB/RIF test for diagnosing pulmonary tuberculosis in adult patients, and in 2013, it was recommended for diagnosing pediatric and extrapulmonary tuberculosis (5).

Leukocytes play a pivotal role in the systemic inflammatory response to infection. Following an infection, the number of circulating neutrophils increases while the number of lymphocytes decreases. The neutrophil-to-lymphocyte count ratio, a suitable indicator of inflammation, is a valuable biomarker for predicting bacteremia and the severity of certain infectious diseases, including tuberculosis. Combining both parameters, such as the Neutrophil-Lymphocyte Ratio (NLR), is also increasingly utilized as a clinical marker. NLR is extensively assessed as a marker of infection severity, including tuberculosis (6). Hematological examination is a routine procedure, but its role in diagnosing TB has been limited. Therefore, there is an increasing interest in evaluating the relationship between the number of leukocytes, neutrophils, lymphocytes, and the Neutrophil-Lymphocyte Ratio (NLR) as biomarkers for the level of germ detection using molecular rapid tests (TCM) in TB patients at Undata Palu Hospital.

METHODS

This study was conducted after it was declared to meet the ethical requirements to be carried out by the Health Research Ethics Commission of the Faculty of Medicine, Hasanuddin University Makassar (KEPK FKUH RSPTN Hasanuddin University-RSWS) with No. 148/UN4.6.4.5.31/PP36/2023, as well as with the permission of the Director of Undata Palu Hospital, in this case the medical records section, pulmonary clinic, and laboratory of Undata Hospital, hammer, with No. 11290/UN.4.20.1/PT.01.04/2023. This quantitative research uses an analytic study method with a cross-sectional approach. The sampling technique used total sampling, secondary data from medical records, and laboratory results in hematological examinations and rapid molecular tests of pulmonary TB patients at Undata Palu Hospital from January 2022 - December 2022. Data criteria in this study are inclusion, data on positive TB patients with TCM Rifampicin sensitive, with hematological data such as Leukocytes (WBC), Neutrophils, Lymphocytes, and Neutrophil to Lymphocyte Ratio (NLR). The NLR was obtained from the absolute neutrophil count divided by the absolute lymphocyte count. Exclusion criteria were TB patients with co-infectious diseases, HIV TB, MDR TB, XDR TB, and TB patients with incomplete hematological examination. Univariate data analysis was used to determine the characteristics of data on each variable studied, such as age, gender, contact with TB patients, smoking habits, and their relationship with the occurrence of TB, and Bivariate data analysis to determine the relationship between the number of Leukocytes (Wbc), Neutrophil, Lymphocytes, and Neutrophil Lymphocyte Ratio to the level of germ detection with TCM in TB patients which were then analyzed using the One-way ANOVA statistical test, if the data were normally distributed, and the Kruskal-Wallis H statistical test if the data were not normally distributed, using the SPSS version 26 program, and presented in tabulated form. Statistical test results were considered significant for a $p < 0.05$.

RESULTS

As shown in Table 1, of the 207 subjects of MTB patients, positive MTB results with rapid molecular tests (TCM) were obtained predominantly in the male gender, namely, 58 people (66.7 %), with 44 MTB patients with rifampicin-sensitive and 14 patients with rifampicin-resistant, with the Chi-Square test obtained a P-value of 0.022 which indicates that there is a relationship between gender and the incidence of Tuberculosis. The most MTB patients were found in patients who had a smoking habit, namely 52 people (59.8 %), where there were 38 MTB patients' rifampicin-sensitive and 14 rifampicin-resistant MTB patients, with the Chi-Square test obtained a P-value of 0.001 which indicates that there is an association between smoking habits and the incidence of tuberculosis.

Table. 1. Characteristics of study subjects based on gender, age, contact with TB patients, and smoking habits and the relationship with the incidence of tuberculosis.

		NEGATIVE	POSITIVE SENSITIVE	POSITIVE RESISTANT	N	P-VALUE
GENDER TYPE	MALE	57	44	14	115	**0.022
	WOMEN	63	23	6	92	
	TOTAL	120	67	20	207	
SMOKING HABIT	SMOKING	27	38	14	79	**0.001
	NO SMOKING	93	29	6	128	
	TOTAL	120	67	20	207	
CONTACT WITH MTB PATIENTS	CONTACT.	31	39	9	79	**0.001
	NO CONTACT	89	28	11	128	
	TOTAL	120	67	20	207	
AGE SCALE	17-25 YEARS	13	13	5	32	**0.021
	26-35 YEARS	21	18	1	40	
	36-45 YEARS	28	18	6	52	
	46 YEARS AND ABOVE	58	18	7	83	
	TOTAL	120	67	20	207	

**P-value obtained from Chi-Square Test

Based on contact status with MTB patients, positive MTB with TCM was mainly found in patients with a history of contact with MTB patients, as many as 48 people (55.2 %), consisting of 39 rifampicin-sensitive patients, and nine patients with rifampicin-resistant, with-Chi-Square test obtained a P-value of 0.001 which indicates that there is a relationship between contact status with MTB patients and the incidence of tuberculosis. As well as the age group, most were over 46 years, as many as 25 people (28.7 %), with 18 MTB patients with rifampicin sensitivity, and seven patients with rifampicin-resistant, with Chi-Square test obtained a P-value 0.021 which indicates there is a relationship between age group and the incidence of tuberculosis.

Table 2 and Figure 1 show the leukocyte count (Wbc) comparison test in TCM-positive, rifampicin-sensitive groups with high, medium, and low detection levels. Of the 187 TCM samples, the median leukocyte value at the High detection level was 12.20 (7.30 -18.40), Medium 10.50 (470-19.90), Low 9.35 (5.20-17.60), and Negative 8.80 (3.30-19.80). This result shows a significant value with a p-value of 0.003, indicating a significant mean difference in the number of Leukocytes (Wbc) between TCM detection levels: High, Medium, Low, and Negative.

The comparison test results of Neutrophil counts in TCM Positive, rifampicin-sensitive, with High, Medium, Low, and Negative detection level groups show that of the 187 TCM samples, the Median neutrophil value at the detection level was High 77.00 (53.20 - 86.90), Medium 73.15 (55.50 - 90.60), Low 71.70 (48.10 - 89.30), and Negative 65.05 (11.30 -88.80). These results indicate a p-value of 0.001, showing a significant mean difference in neutrophil counts between TCM High, Medium, Low, and Negative detection levels.

Table 2. Comparison of Leukocyte, Neutrophil, and Lymphocyte Counts in MTB Positive, Rifampicin Sensitive TCM testing with High, Medium Low, and Negative germ detection levels.

	Germ Detection with TCM	N	Median	Min	Max	P-Value
Leukocytes (x 10^3 uL)	HIGH	15	12.20	7.30	18.40	
	MEDIUM	32	10.50	4.70	19.90	
	LOW	20	9.35	5.20	17.60	**0.003
	NEGATIVE	120	8.80	3.30	19.80	
	Total	187				
Neutrophil (%)	HIGH	15	77.00	53.20	86.90	**0.001
	MEDIUM	32	73.15	55.50	90.60	
	LOW	20	71.70	48.10	89.30	
	NEGATIVE	120	65.05	11.30	88.80	
	Total	187				
Lymphocytes (%)	HIGH	15	11.40	2.70	27-50	**0.001
	MEDIUM	32	14.55	4.10	31.50	
	LOW	20	16.90	5.00	44.70	
	NEGATIVE	120	22.05	5.80	69.30	
	Total	187				
NLR (%)	HIGH	15	6.90	2.27	21.26	**0.001
	MEDIUM	32	5.22	1.76	22.10	
	LOW	20	4.30	1.15	16.98	
	NEGATIVE	120	2.90	0.35	14.80	
	Total	187				

**P-value obtained from Kruskal Wallis Test

Lymphocyte counts comparison test in TCM positive and rifampicin-sensitive, with high, medium, low, and negative detection level groups show that of the 187 TCM samples, the Median neutrophil value at the High detection level was 11.40 (2.70 - 27.50), Medium 14.55 (4.10 - 31.50), Low 16.90 (5.00 - 44.70), and Negative 22.05 (5.80 - 69.30). These results demonstrated a

p-value of 0.001, indicating a significant mean difference in lymphocyte counts between high, medium, low, and negative TCM detection levels.

In the results of the NLR count comparison test in TCM Positive, rifampicin-sensitive, with High, Medium, Low, and Negative detection level groups, of the 187 TCM samples, the Median Neutrophil value at the High detection level was 16.90 (2.27 - 21.26), Medium 5.22 (1.76 - 22.10), Low 4.30 (1.15 - 16.98), and Negative 2.90 (0.35 - 14.80). This result shows a p-value of 0.001, indicating a significant mean difference in the number of NLRs between TCM detection levels of High, Medium, Low, and Negative.

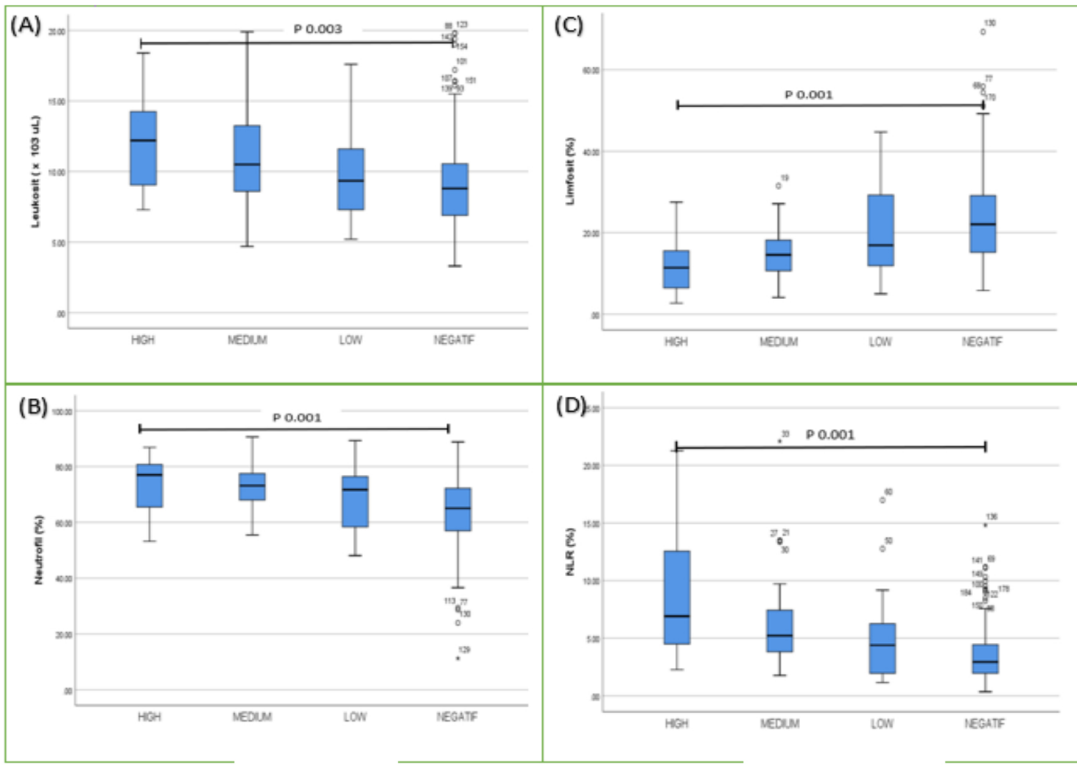

Figure 1. Comparison between Leukocyte (A), Neutrophil (B), Lymphocyte (C), and NLR (D) counts with germ detection levels (High, Medium, Low, and Negative) in the Molecular Rapid Test examination. The abscise axis shows germ detection levels with TCM.

DISCUSSION

In the distribution of sample results based on gender characteristics, it was found that the male gender had the highest number of people infected with MTB, namely 58 people; this is in line with Lamria et al., who stated that the number of TB cases in Indonesia in men is 1.5 times higher than that of women. Men have a risk of 2.07 times suffering from TB compared to women. This is largely attributed to the lifestyle and habits of men who have higher intensity and tend to smoke and consume alcohol. This causes the body's immunity to decrease easily, making it more susceptible to MTB infection (7).

This study involved people with an age limit of 17-50 years, classified as productive age; this age group is considered more active in moving and interacting and more vulnerable to MTB infection. The highest number of positive MTBs was found in the age group above 46 years, namely 25 people (28.7 %), with 18 MTB patients with rifampicin-sensitive and seven patients with rifampicin-resistant, with a p-value of 0.021, which indicates that there is a relationship between age group and the incidence of tuberculosis. The

risk of infection in the elderly, especially the risk of severe infection, increases with age and predisposes to reactivation of TB; the reason is that increased vulnerability in older adults includes immunosenescence, various anatomical and physiological changes associated with aging, and malnutrition and comorbidities (8). Advanced age contributes to systemic immune dysfunction. With age, systemic "inflammation," a basal chronic inflammation that occurs with natural aging, has been implicated as a direct contributor to the decreased innate immune response in elderly people (8,9). This is due to the loss of function of innate immune proteins due to reduced alveolar lining fluid (ALF), which has important antimicrobial and homeostatic effects and contributes to the increased susceptibility of elderly individuals to infectious diseases, including *Mtb* (9).

Contact intensity is when positive MTB patients interact with people around them (family and neighbors) daily. The length of interaction can be seen from the intensity of time used, such as chatting, watching TV, cooking, eating, sleeping, and doing homework together for an extended period of time without using a mask (10). In this study, the highest number of positive MTB was found in patients with a history of contact with positive MTB sufferers, as many as 48 people (55.2 %). Surakhmi Oktavia et al. explained that people who have been in contact with pulmonary MTB sufferers have a risk of 4.7 times greater lung MTB infection compared to people who have never been in contact with pulmonary MTB sufferers (11). A person who tests positive for MTB, with a high positivity rate, can potentially spread MTB disease. Each MTB-positive individual can infect 10 to 15 other people, resulting in a 17 % likelihood that each contact will contract MTB (12).

Based on smoking habits, the most positive MTB was found in someone with smoking habits, namely 52 people (59.8 %). Wahyuni Harahap et al. concluded that there is a significant relationship between a person's smoking degree and the incidence of tuberculosis. Particles present in cigarette smoke affect the performance of the respiratory system's vibrational hairs, which results in the cleansing of the mucociliary system. Cigarette smoke particles will settle on the mucus layer of the respiratory system, which causes irritation to the epithelium of the bronchial mucosa so that a person can easily get sick, especially tuberculosis (13). Smoking habit causes increased lung fluid production function in both normal and MTB-infected people. Smoking also causes cellular immunity changes, resulting in the function of macrophages and leukocytes (6).

Leukocyte count (Wbc) comparison test results in TCM Positive, Rifampicin Sensitive, with High, Medium, and Low detection level groups, show that of the 187 TCM samples, the median leukocyte value at the High detection level was 12.20 (7.30 -18.40), Medium 10.50 (470-19.90), Low 9.35 (5.20-17.60), and Negative 8.80 (3.30-19.80), with a p-value of 0.003, indicating a significant mean difference in the number of Leukocytes (Wbc) between TCM detection levels: High, Medium, Low, and Negative. Leukocytes (Wbc) have a normal value between 4.5 - 10 x $10^3/\mu$L; at the High and medium detection levels, there is an average increase in the number of leukocytes that exceeds normal limits, while at the Low and Negative detection levels have an average leukocytes that are still within normal limits. Thus, the higher the level of germ detection in the TCM examination, the higher the number of leukocytes.

An increase in leukocyte count or leukocytosis indicates the presence of an acute infectious or inflammatory process. Increased leukocyte counts play an important role in the systemic inflammatory response to tuberculosis infection. It is characterized by the number of circulating neutrophils increasing while the number of lymphocytes decreases (14).

However, a normal leukocyte count can also occur in this condition. This is because many inflammatory cells undergo apoptosis when fighting MTB, induced by the cells themselves and T lymphocyte cells. This could be the cause of the normal leukocyte count picture in TB patients (15).

Comparison test results of neutrophil counts in rifampicin-resistant positive TCM, with High, Medium, Low, and Negative detection level groups, indicate that of the 187 TCM samples, the Median Neutrophil value at the detection level was High 77.00 (53.20 - 86.90), Medium 73.15 (55.50 - 90.60), Low 71.70 (48.10 - 89.30), and Negative 65.05 (11.30 -88.80), with a p-value

of 0.001, indicating a significant difference in the mean number of neutrophils between TCM detection levels High, Medium, Low, and Negative. From the data, we can see that an increase in the detection of the number of germs in the molecular rapid test will increase the number of circulating neutrophils in the bloodstream.

The neutrophil is the major phagocyte and the final effector cell of innate immunity, with a primary role in the clearance of extracellular pathogens. Using the broad array of cytokines, extracellular traps, and effector molecules as the humoral arm, neutrophils play a crucial role in the host's defense against pathogen infections. Neutrophil reactions aim to attack MTB pathogens; neutrophils in circulation can move towards infected tissues such as lung parenchyma due to the influence of cytokines, which cause neutrophils to be activated and then phagocytose pathogens at the site of infection. Following migration to the site of infection and phagocytosis, neutrophils have a repertoire of antimicrobial arsenal to fulfill this function. Neutrophils utilize a combination of NADPH oxidase-derived reactive oxygen species (ROS), cytotoxic granule components, antimicrobial peptides, and neutrophil extracellular traps (NETs) to generate a highly lethal environment that is essential for efficient microbe killing and degradation. In addition, neutrophils also secrete a number of cytokines that lead to the recruitment and activation of other natural immune system cells so that neutrophils contribute to the cellular immune response to Mtb infection. This causes neutrophil levels to increase during examination. During infection, neutrophils with phagocytized bacteria secrete antimicrobial effectors from their granules and act as potent effector cells, mediating antimicrobial activity and immunopathology in humans. Antimicrobials secreted by neutrophils are elastase, collagenase, and myeloperoxidase enzymes, which can inhibit bacterial growth in infected macrophages. These enzymes from neutrophils help the apoptosis of infected macrophages, limiting the length of life of bacteria that grow in macrophages. However, these neutrophil enzymes can also cause damage to the lung fibers and can also cause an excessive inflammatory response (16).

Research evidence has shown the role of neutrophils from the first day of TB infection to granuloma formation. The neutrophil response to the presence of MTB germs is biphasic. The first increase occurs on the first day of infection; then, the value will drop. The neutrophil response will increase again after 8 - 15 days and then last until the end of the infection. These results show that neutrophils play an important role in the early phase of MTB infection (17).

Comparison test results of lymphocyte counts in rifampicin-sensitive positive TCM, with High, Medium, Low, and Negative detection level groups, indicate that of the 187 TCM samples, the Median Lymphocyte value at the High detection level was 11.40 (2.70 - 27.50), Medium 14.55 (4.10 - 31.50), Low 16.90 (5.00 - 44.70), and Negative 22.05 (5.80 - 69.30), with a p-value of 0.001, indicating a significant mean difference in lymphocyte counts between TCM detection levels of High, Medium, Low, and Negative. The higher the detection of germs will affect the decrease in the number of lymphocytes, and the less detection of germs, the more the number of lymphocytes will increase towards normal. The reduction of the number of lymphocytes in Tuberculosis is due to a decrease in the percentage of CD4+ and the absolute number in the peripheral blood of Mtb patients because there is an increase in the number of CD4+ in the infected tissue area compared to the circulating one. This is associated with the severity of tuberculosis disease, which returns to normal after anti-TB treatment (18). Low lymphocyte counts in tuberculosis are caused by aggregation of lymphocytes at the site of infection, altered hematopoiesis, or increased apoptosis. Low lymphocyte counts have also been reported to be associated with inflammation, atherosclerosis, and plaque progression (19).

The results of the NLR comparison test on rifampicin-sensitive positive TCM, with High, Medium, Low, and Negative detection level groups, indicate that of the 187 TCM samples, the Median Neutrophil value at the High detection level was 6.90 (2.27 - 21.26), Medium 5.22 (1.76 - 22.10), Low 4.30 (1.15 - 16.98), and Negative 2.90 (0.35 - 14.80), with a p-value of 0.001, indicating a significant mean difference in the number of NLRs between High, Medium, Low, and Negative TCM detection levels. This study shows that an increase in the number of germ detections in TCM examination will increase the number of NLR due to an increase in the number

of neutrophils and a decrease in the number of lymphocytes during Mtb infection.

NLR has a normal value of <5, and its increase is indicated as a marker of the severity of an infection or Systemic Inflammatory Response Syndrome (SIRS). This study found the number of NLRs with a mean of >5, where the highest median value at the high detection level was 6.90, indicating inflammation caused by MTB infection. High NLR in active MTB disease is associated with elevated neutrophil and low lymphocyte counts, further related to extensive lung damage and persistent infection (20).

The neutrophil-to-lymphocyte ratio is one of the laboratory tests used to evaluate or as a marker of inflammation. The neutrophil-lymphocyte ratio is a suitable parameter in predicting bacteremia (21). Yoon et al. stated that the NLR is a marker that distinguishes tuberculosis and pneumonia. The NLR value is obtained from the number of neutrophils divided by the number of lymphocytes (22).

NLR has been used as a potential indicator for reflecting inflammation, clinical diagnosis, and prognosis evaluation, including as a biomarker of TB disease severity. They found a significantly decreased NLR, indicating that the bacterial load decreased, was of lower value in patients, and cultures became negative. This may indicate the usefulness of this NLR evaluation before and after therapy in predicting clinical outcomes. In addition, lower NLR values in TB patients consistently correlated with lower absolute neutrophil counts and non-significantly higher absolute lymphocyte counts. These findings may reflect the effectiveness of anti-TB therapy (23).

CONCLUSION

Leukocyte, neutrophil, lymphocyte, and NLR counts are inflammatory indicators that can be used as biomarkers to detect the level of germ count by rapid molecular testing (TCM) in TB, especially for areas with limited health facilities. It is recommended that future researchers analyze the relationship between the level of germ detection on TCM and the examination of leukocytes, neutrophils, lymphocytes, and NLR in resistant TB and in a larger number of samples.

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