

Hematology Profile of Tuberculosis Lymphadenitis Patients at Siti Rahmah Hospital, Padang, Indonesia

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ABSTRACT

Tuberculosis (TB) is a progressive granulomatous infectious disease caused by Gram-positive acid-resistant bacilli classified in the genus *Mycobacterium*. Tuberculosis in humans is caused by *Mycobacterium tuberculosis* (MTB) and it mainly infects the lungs, although it can also infect intestines, meninges, bones, lymph nodes, skin that cause extra-pulmonary TB. Tuberculous lymphadenitis is an inflammatory process in lymph nodes as a result of MTB activity. The inflammatory process caused by MTB activity is often associated with anemia as the most common complication. Anemia in TB is caused by an inflammatory process associated with bone marrow suppression due to pro-inflammatory cytokines, thus inhibiting the proliferation and differentiation of erythroid progenitor cells. This chronic TB infection also affects iron hemostasis, thus further affecting the hematological profile of TB patients. This study aimed to determine the hematology profile of TB lymphadenitis patients in the Siti Rahmah Hospital, Padang, Indonesia. This was a descriptive study, with a population of patients diagnosed with TB lymphadenitis based on the results of a fine needle biopsy in the Colli region. The samples of this study consisted of 24 patients who have tested the hematology profile. Tuberculosis lymphadenitis patients in females were higher than males, the mean age was 26.75 ± 19.53 years old dominated by an adult (54%). The mean of hemoglobin levels was 11.8 ± 1.522 g/dL, with 62.5% anemia patients. The mean leukocyte count was $10400 \pm 3018.926/\text{mm}^3$, with 54.2% of patients had normal levels of leukocyte. The mean of thrombocyte count was $334750 \pm 74440.668/\text{mm}^3$, with 83.3% in normal levels and the mean of Erythrocyte Sedimentation Rate (ESR) was 35.25 ± 31.489 mm/h, with 54.2% patients in high ESR. Hematology profile in TB lymphadenitis patient was anemia, normal levels of leukocytes, thrombocyte, and increased levels of ESR.

Keywords: Anemia, erythrocyte sedimentation rate, hematology profile, tuberculosis lymphadenitis

INTRODUCTION

Tuberculosis (TB) is a progressive granulomatous infectious disease caused by Gram-positive acid-resistant bacilli classified in the genus *Mycobacterium*. Tuberculosis in humans is caused by *Mycobacterium tuberculosis* (MTB) and it mainly infects the lungs, although it can also infect the intestines, meninges, bones, joints, lymph nodes, skin, and other tissues of the body that cause extra-pulmonary TB.^{1,2} Tuberculosis is ranked second in death (1.5 million cases) caused by infectious diseases worldwide after Human Immunodeficiency Virus (HIV) infection. Indonesia ranks 5th with the largest TB incidence in the world after India, China, Nigeria, Pakistan. The prevalence of tuberculosis based on diagnosis in Indonesia in 2013 was 0.4% of the population.³ Tuberculous lymphadenitis, also known as scrofula (Evil King), was first described 3,000 years ago and is one of the common types of extrapulmonary TB.^{4,5}

Tuberculous lymphadenitis consists of 30-50% of extrapulmonary TB cases in the US.⁴ In Indonesia, especially in Padang, 53% of extrapulmonary TB cases have been reported, and TB lymphadenitis is the second disease with the highest case (11.6%) after TB meningitis.⁶ Tuberculous lymphadenitis is an inflammatory process in lymph nodes as a result of MTB activity. Some of the factors that cause extrapulmonary tuberculosis include factors sociodemographic, history of contact with tuberculosis patients, history of Bacillus Calmette immunization Guérin (BCG) immunization, and previous history of pulmonary or extrapulmonary TB. The inflammatory process caused by MTB activity is often associated with anemia as the most common complication of TB patients. Anemia in TB is caused by the inflammatory process associated with bone marrow suppression due to pro-inflammatory cytokines, thus inhibiting the proliferation and differentiation of erythroid progenitor cells. This

chronic TB infection also affects iron hemostasis, thus further affecting the hematological profile of TB patients.⁵⁻⁸

The prevalence of pulmonary TB in West Sumatra in 2014 was 0.11%, and it had increased to 0.15% in 2016 with the Case Detection Rate (CDR) reaching 42.8% in 2018.⁶ Padang City has an area of 694.96 km² with a population of 950871 people. It has 11 districts and Koto Tengah district is the largest district (232.25 km²). The largest population in Padang City is also located in Koto Tengah District with a total of 197005 inhabitants. This research was conducted at Siti Rahmah Hospital because it is the only type C hospital in Aia Pacah village, Koto Tengah district.⁶ In addition, the prevalence of pulmonary TB in the Aia Pacah village is 14 patients of a total of 8343 residents. However, only several studies have reported the hematological features in TB lymphadenitis patients. The current study was expected to give a better understanding and become baseline data on the incidence of anemia, diagnosis, in TB lymphadenitis in type C hospitals.

METHODS

This research was a descriptive study with 37 patients with tuberculous lymphadenitis as the population. The sample of this study consisted of 24 patients diagnosed with TB lymphadenitis based on the results of a fine needle biopsy in the Colli region. The inclusion criteria were patients with complete laboratory data based on the diagnosis coding system in the medical records. The study protocol was approved by the Ethics Commission of Clinical Research Center, Faculty of Medicine, Baiturrahmah University with number 039/ETIK-FKUNBRAH/03/08/2020.

Inclusion criteria in this study were all patients with TB Lymphadenitis diagnosed in 2019 based on the diagnosis coding system in the medical records. This study used data from patient medical records diagnosed with TB lymphadenitis and performed hematology profile tests consisting of hemoglobin levels, leukocyte count, platelet count by using an automatic analyzer and ESR with the Westergren method. Standard laboratory test results were adjusted to normal values based on World Health Organization (WHO) criteria.

Data were analyzed using SPSS Version 25 (SPSS Inc., Chicago, IL, USA). Quantitative variables were reported as mean \pm SD and qualitative variables were reported as numbers (percentage), tables, and diagrams.

RESULTS AND DISCUSSIONS

The medical records of patients with TB Lymphadenitis in 2019 were investigated in this study. The samples of this study consisted of 24 patients, with inclusion criteria were patients with TB lymphadenitis based on the results of a fine needle biopsy and also performed hematology profile examination consisting of 16 females (67%) and 8 males (33%) (Fig. 1).

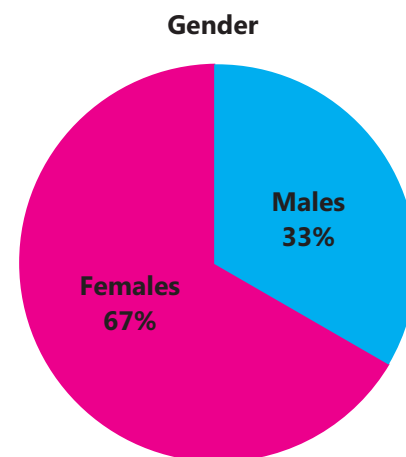


Figure 1. The proportion of tuberculosis lymphadenitis patients by gender

This study showed that the mean age of patients with TB lymphadenitis was 26.75 \pm 19.53 years old, with a minimum age of one year and a maximum age of 69 years. The patients with TB lymphadenitis were divided by age into three groups as follows: children, which age younger than 18 years, adults aged 19-59 years, and elderly over 60 years. The results showed that there were 10 children (42%), 13 adults (54%), and 1 elderly (4%) (Fig. 2).

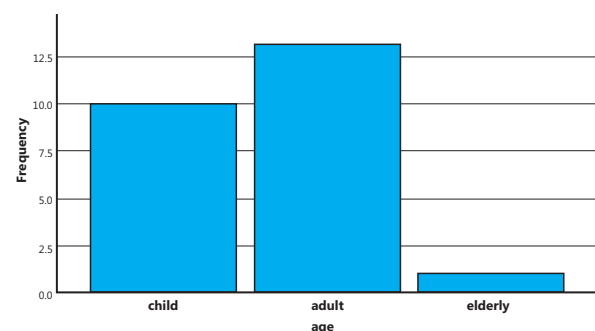


Figure 2. The proportion of tuberculous lymphadenitis patients by age

The hematology profile of each patient was obtained from medical records and it was examined by using an automatic analyzer and 2 mL blood with EDTA anticoagulant. The mean hemoglobin levels in all TB lymphadenitis patients in the Siti Rahmah Hospital, Padang, West Sumatera was 11.8 ± 1.522 g/dL, with mean hemoglobin levels in females were 11.69 ± 2.001 g/dL, and males were 12.24 ± 1.686 g/dL. Hemoglobin levels in children were classified by age based on WHO criteria, and found 62.5% (15 people) with anemia in this study, consisting of 6 subjects from the children group, 5 subjects from the female's group, and 4 subjects from the male's group (Table 1).

The mean leukocyte count in TB lymphadenitis patients was $10400 \pm 3018.926/\text{mm}^3$, with a minimum level of $5600/\text{mm}^3$ and a maximum level of

$16400/\text{mm}^3$. In this study that was found 45.8% leukocytosis and 54.2% normal leukocyte count. The mean thrombocyte count in TB lymphadenitis patients was $334750 \pm 74440.668/\text{mm}^3$, with a minimum level of $199000/\text{mm}^3$ and a maximum level of $480000/\text{mm}^3$. In addition, 16.7% thrombocytosis and 83.3 % normal thrombocyte count were found in this study (Table 2). The total number of leukocytes and thrombocytes based on WHO criteria are $5000-10000/\text{mm}^3$ and $150.000-400.000/\text{mm}^3$, respectively.⁷

The mean ESR in TB lymphadenitis patients increased in this study after measured by using the Westergren method. The mean ESR in females was 38.44 ± 35.911 mm/h, in males was 28.88 ± 20.615 mm/h, and 54.2% (13) patients with high ESR were found in this study, consisting of 11 females and 2 males (Table 3).

Table 1. Hemoglobin level in tuberculous lymphadenitis patients

Parameter	n	Mean \pm SD	Normal Range (WHO)
Hemoglobin (g/dL)	24	11.8 ± 1.522	based on age and gender
Hemoglobin female (g/dL)	10	11.69 ± 2.001	> 12
Anemia in female	5	(50%)	
Hemoglobin male (g/dL)	5	12.24 ± 1.686	> 13
Anemia in Male	4	(80%)	
Hb children (g/dL)	10		
< 5 years old	2	11.35 ± 0.354	> 11
5-11 years old	5	11.58 ± 0.887	> 11.5
12-18 years old	3	11.80 ± 0.656	> 12
Anemia in children	6	(60%)	

Table 2. Leukocyte and thrombocyte count in tuberculous lymphadenitis patients

Parameter	Level	Minimum Level	Maximum Level
Leukocyte count (mm^3)			
Mean \pm SD	10400 ± 3018.926	5600	16400
Leukocytosis	11 (45.8%)		
Normal	13 (54.2%)		
Leukopenia	0		
Thrombocyte count (mm^3)		199000	480000
Mean \pm SD	334750 ± 74440.668		
Thrombocytosis	4 (16.7%)		
Normal	20 (83.3%)		
Thrombocytopenia	0		

Table 3. Erythrocyte sedimentation rate in tuberculous lymphadenitis patients

Parameter	Mean \pm SD	Total (n)	Min-Max Level
ESR (mm/h)	35.25 ± 31.489	24	4-131
Total high ESR		13 (54.2%)	
ESR female (mm/h)	38.44 ± 35.911	16	4-131
High ESR		11 (68.8%)	
ESR male (mm/h)	28.88 ± 20.615	8	10-75
High ESR		2 (25%)	

In this study, the diagnosis of patients with TB lymphadenitis was based on the results of a fine needle biopsy and hematology profile test, resulting in 16 females (67%), 8 males (33%). The results of this study were in line with a study by Angelia in Bandung, which stated that extra-pulmonary tuberculosis was found in 63.88% females and 36.12% males.⁹ An epidemiological study conducted in Malaysia reported that out of 1,548 tuberculosis cases, 7% were TB lymphadenitis, with 53.2% males and 46.8% females. This study showed that the mean of age patients with TB lymphadenitis was 26.75 ± 19.53 years old. The results in this study showed 10 children (42%), 13 adults (54%), and 1 elderly (4%).

The source of TB transmission is positive Acid-Resistant Bacteria (BTA) from TB patients, which is spread into the air in droplet nuclei through coughing or sneezing. *Mycobacterium tuberculosis* in sputum splashes can last for several hours in dark and humid conditions but can be killed by direct sunlight. However, in some cases, some of these MTBs do not immediately phagocytose alveolar macrophages, because the immune response to MTB is not completely effective in eliminating MTB. This is not influenced by age and gender, but rather by host resistance and pathogenicity of inhaled MTB.^{10,11}

Anemia in this study was diagnosed based on WHO criteria. Anemia is a condition of hemoglobin level less than 13 g/dL in males and less than 12 g/dL in females. Anemia is the most common complication of pulmonary tuberculosis and its prevalence ranges from 16-94% in several studies. Anemia is a condition in which the red blood cell count or oxygen-carrying capacity is lower than the body's physiological requirements.¹²

Anemia is an indicator of poor nutrition and poor health. Anemia in TB is caused by the suppression of erythropoiesis by inflammatory mediators is the most common pathogenesis of anemia in TB. IL-6, IL-1 β , and Interferon- γ affect to decrease erythroid progenitor.^{7,12} This decrease in erythroid progenitor directly inhibits erythrocyte differentiation and proliferation. Retention of iron in the reticuloendothelial system is one of the body's defense mechanisms. Disruption of iron hemostasis results in the transfer of iron from the circulation to the reticuloendothelial system storage area and is followed by a limited supply of iron for progenitor erythroid cells. This causes the limitation of the erythrocyte formation process.^{13,14}

The mean leukocyte count in TB lymphadenitis patients was $10400 \pm 3018.926/\text{mm}^3$. However,

normal leukocyte count in this study was found in 54.2%. The mean thrombocyte count in TB lymphadenitis patients was $334750 \pm 74440.668/\text{mm}^3$, and normal in this study was found in 83.3 % of subjects.

The mean ESR in females was $38.44 \pm 35.911\text{mm/h}$, and males were $28.88 \pm 20.615\text{mm/h}$. This study showed 54.2% (13 people) patients with high ESR. Inflammation by *M.tuberculosis* causes dysregulation of proinflammatory cytokines such as TNF- α , IL-6, interferon- γ , and IL-1 β . Dysregulation of cytokines such as IL-6 and TNF- α will induce protein synthesis of the reactant phase, inhibiting the production of serum albumin and shifts in plasma concentrations of essential micronutrients. Therefore, the ESR test with the Westergren method showed an increased ESR value.¹³

CONCLUSIONS AND SUGGESTIONS

Hematology profile in TB lymphadenitis patient was anemia, normal leukocytes count, thrombocyte, and increased ESR level. Further research is needed that will discuss the type of anemia in TB patients because it will affect the therapy and prognosis of the disease.

REFERENCES

1. Khan MK, Islam MM, Ferdous J, Alam MM. An overview on epidemiology of tuberculosis. *Mymensingh Med J*. 2019; 28(1): 259-266.
2. Rachmayanti N, Kusmiati T. Diagnostic value of encode TB IgG and IgM rapid test to support pulmonary tuberculosis diagnosis. *Indones J Clin Pathol Med Lab*, 2020; 26(2): 138-41.
3. Susanto J, Nugraha J, Soedarsono S. IL-4 level in rifampicin-sensitive and rifampicin-resistant lung tuberculosis patients. *Indones J Clin Pathol Med Lab*, 2020; 27(1): 46-50.
4. WHO. Guidelines on tuberculosis infection prevention and control. WHO, 2019; 91: 1689-99.
5. de Martino M, Lodi L, Galli L, Chiappini E. Immune response to *Mycobacterium tuberculosis*: A narrative review. *Front Pediatr*, 2019; 7: 1-8.
6. Indonesia Health Profile 2018] [Internet]. 2019; 207. Available from: http://www.depkes.go.id/resources/download/pusdatin/profil-kesehatan-indonesia/Data-dan-Informasi_Profil-Kesehatan-Indonesia-2018 (accessed 9 Sept, 2020).
7. Zhai W, Wu F, Zhang Y, Fu Y, Liu Z. The immune escape mechanisms of *Mycobacterium tuberculosis*. *Int. J. Mol. Sci*, 2019; 20: 340.
8. Howard NC, Khader SA. Immunometabolism during *Mycobacterium tuberculosis* infection. *Trends Microbiol* [Internet]. 2020; 28(10): 832-50. Available from: <https://doi.org/10.1016/j.tim.2020.04.010>

- (accessed 8 August, 2020).
9. Angelia E. Angka kejadian tuberkulosis paru dan ekstra paru pasien rawat jalan di Rumah Sakit Immanuel. Bandung, 2016; 1-52. (Thesis).
 10. Peddireddy V, Doddam SN, Ahmed N. Mycobacterial dormancy systems and host responses in tuberculosis. *Front Immunol*, 2017; 8: 1-19.
 11. Jee B. Understanding the host immune response against *Mycobacterium tuberculosis* infection. *Centr Eur J Immunol*, 2020; 45 (1): 99-103.
 12. Gothi D, Spalgais S. Review article lymph node tuberculosis. *EC Pulmonol Respir Med*, 2016; 2: 194-211.
 13. Nasution SD. Malnutrisi dan anemia pada penderita tuberkulosis paru malnutrition and anemia in tuberculosis patient. *J Majority*, 2015; 4: 29-36.
 14. Sharma D, Sarkar D. Pathophysiology of tuberculosis: An update review. *Pharmatutor*, 2018; 6(2): 15.