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Analysis of Hematological Examination Results in Pulmonary Tuberculosis (TB) Patients Undergoing Intensive Phase Anti-Tuberculosis Drug Therapy

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A B S T R A C T

The intensive phase of anti-tuberculosis (TB) drug therapy consists of a combination of antibiotics, including Isoniazid (INH), Rifampicin (RIF), Pyrazinamide (PZA), and Ethambutol (EMB). The primary goal of this therapy is to inhibit the growth and spread of Mycobacterium tuberculosis, preventing its migration from the lungs to other organs. However, intensive-phase therapy may result in both major and minor side effects. This study aims to analyze the hematological profiles of pulmonary TB patients undergoing intensive-phase anti-tuberculosis treatment. The respondents were pulmonary TB patients recruited from primary healthcare centers within the East Bekasi District, Bekasi City. Those who met the sample criteria underwent hematological examinations, including hemoglobin (Hb), hematocrit (HCT), red blood cell count, white blood cell count, and platelet count. The tests were conducted using the electrical impedance method with a hematology analyzer. The hematological examination revealed a trend of low hemoglobin levels, with the average Hb recorded at 11.98 ± 8.65 g/dL. Additionally, abnormal blood parameters were observed, with 33.3% of patients experiencing erythropenia, 57% showing thrombocytopenia, 33% presenting leukopenia, and 20% exhibiting leukocytosis. These findings confirm that intensive-phase anti-tuberculosis therapy affects the hematological profiles of pulmonary TB patients, highlighting the need for close monitoring during treatment.

INTRODUCTION

Tuberculosis (TB) is one of the serious global health problems. Southeast Asia contributes 39% of the total global TB incidents. An estimated 3.4 million new cases of TB occur in Southeast Asia every year, with the majority occurring in India, Bangladesh, Indonesia, Myanmar, and Thailand. TB is caused by the bacterial infection of Mycobacterium tuberculosis (M. TB) and mainly affects the lungs, known as pulmonary TB. Besides lung involvement, M. TB is reported to attack extrapulmonary organs (extrapulmonary TB), including the pleura, lymph nodes, abdomen, urinary tract, skin, joints, bones, and even the meninges (Khan et al., 2019; Rodriguez-Takeuchi et al., 2019).

TB management in Indonesia is conducted comprehensively involving the government from the central to regional levels with 6 main strategies: strengthening commitment and leadership of stakeholders, increasing access to services, optimizing promotion, prevention and infection control, utilizing research findings (screening technology, diagnosis, and management), enhancing the role of communities, partners, and other multisectoral entities, as well as strengthening program systems and management with the ultimate goal of achieving the TB elimination target by 2030 (Kemenkes RI, 2020).

The treatment of pulmonary TB consists of two phases, namely the intensive phase and the continuation phase. The therapy target in the intensive phase of treatment is to halt the growth and invasion of bacteria

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in the patient's body, primarily suppressing the invasion of Mycobacterium tuberculosis into extrapulmonary organs. The intensive phase comprises a 2-month treatment with a combination of antibiotics: isoniazid (INH), rifampicin (RIF), pyrazinamide (PZA), and ethambutol (EMB). Whereas in the continuation phase, a combination of isoniazid and rifampicin is administered for 4 months. The dosage of the treatment should follow the recommendations of the WHO (Kemenkes RI, 2018; Burhan et al., 2020; Sotgiu et al., 2015).

Intensive Phase Anti-Tuberculosis Drug Therapy (OAT) consists of a combination of antibiotics Isoniazid, Rifampicin, Pyrazinamide, and Ethambutol. The combination of antibiotics (isoniazid, rifampicin, pyrazinamide, and ethambutol) in intensive phase TB treatment has different pharmacological effects, but overall aims to inhibit the growth and spread of Mycobacterium tuberculosis, including inhibiting its migration from the lungs to other organs (extrapulmonary) (Pratama et al., 2021; Wallis et al., 2021). According to the Indonesian Ministry of Health's 2020 tuberculosis management guidelines, the use of OAT can cause side effects, both major and minor. In minor side effects, OAT treatment should continue with appropriate symptomatic therapy. However, if the patient experiences severe major side effects, OAT treatment should be discontinued, and the patient should preferably be referred to further healthcare facilities for appropriate management (Burhan et al., 2020).

Hematological examination (Hemoglobin, Hematocrit, Erythrocytes, Leukocytes, and Platelets) is a routine laboratory test performed at various levels of healthcare facilities, including primary healthcare facilities such as community health centers and primary clinics (Balepur & Schlossberg, 2017). Hematological examination plays an important role in monitoring and prognosis of a disease (Jamwal et al., 2020).

This study aimed to analyze the results of hematological examination (Hemoglobin, Hematocrit, Erythrocytes, Leukocytes, and Platelets) in TB patients undergoing intensive phase OAT treatment with the hope that this research can contribute to more effective monitoring and management of pulmonary TB patients, especially during the intensive phase.

METHOD

This research was conducted using a descriptive-analytic design with a cross-sectional approach. The population of this study was pulmonary TB patients in East Bekasi District, Bekasi City, West Java, Indonesia. Respondents were recruited from primary health centers in the working area of East Bekasi District, Bekasi City, Indonesia. Thirty respondents who met the research criteria underwent blood draw using an open system with a syringe and collected into vacuum tubes with EDTA anticoagulant, blood specimens underwent hematological examinations, including hemoglobin (Hb), hematocrit (HT),

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erythrocyte count, leukocyte count, and platelet count, conducted with the electrical impedance method using a hematology analyzer. Hematological parameters were interpreted based on normal values: Hb: 12-15 g/dL, HT: 13-17 g/dL, Erythrocytes: 3.80 - 5.20 x 10^6/µl, MCV=80-100 fL, Leukocytes: 3.5 - 10.5 x 10^3/µl, Platelets: 1.5 x 10^5 - 4.5 x 10^5/µl(Lasocki et al., 2020). The data were analyzed descriptively using the statistical analysis software SPSS version 25.

RESULT

Respondent characteristics

Respondent characteristics including age and gender obtained from medical record summarized in table 1

Table 1 Respondent Characteristics

Respondent characteristics	n (%)	Rerata±(SD)	Median (Min - Max)
Age (Years)	30	33,37 ±8,64	33,37 (21 – 45)
Gender			
Male	22 (73,3 %)	-	-
Female	8 (26,7 %)	-	-

Table 1 shows of 30 respondents consisting of 22 respondents (73.3%) men and 8 respondents (26.7%) women. Respondents' ages were in the range of 21 – 45 years, where 8 respondents (26.7%) were teenagers, 18 respondents (60%) were adults, and 4 respondents (13.3%) were elderly.

Hematological Examinations

Hematological examination including Hb, HT, erythrocyte count, leukocyte count, and platelet count using a hematology analyzer presented in table 2

Table 2. Mean, standard deviation (SD), median, & Min-Max of hematological examinations

Hematological Examinations	n	Mean ±(SD)	Median (Min - Max)
Hb (gr/dL)	30	11,98 ±8,65	11,07 (9,30 - 16,53)
RBC (10^6/µl)	30	3,94 ±0,74	3,63 (3,00 - 5,51)
HT (%)	30	36,79 ±6,01	35,72 (22,20 - 48,09)
MCV (fL)	30	93,23 ±8,19	97,85 (72,29 – 99,67)
MCH (pg)	30	30,00 ±0,00	30,00 (30,00 -30,00)
MCHC (%)	30	32,22 ±2,67	30,65 (30,09 - 37,84)
WBC (10^3/µl)	30	5,77 ±3,43	3,70 (3,05 – 12,05)
PLT (10^5/µl)	30	1,76 ±0,83	1,31 (1,00 – 3,58)

The mean, standard deviation (SD), median, and Min-Max of each hematological parameter in 30 respondents indicate a low trend in Hb, with a mean Hb of 11.98 ± 8.65 g/dL (Normal Hb values: female: 12-15 g/dL, male: 13-17 g/dL). The mean erythrocyte count is within the normal range; 3.94 ± 0.74 x 10^6/µl (Normal erythrocyte values: 3.80 - 5.20 x 10^6/µl). The mean hematocrit (HT) and erythrocyte indices (MCV, MCH, MCHC) are within the normal range with mean values of HT 36.79 ± 6.01% (Normal HT value 13-17 g/dL), MCV 93.23 ± 8.19 fL (Normal MCV values 80-100 fL), MCH 30.00 ± 0.00 pg (Normal MCH values 28-34 pg), and MCHC 32.22 ± 2.67% (Normal MCHC values 32-36%).

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The mean leukocyte count is within the normal range: 5.77 ± 3.43 x 10^3/µl (Normal leukocyte values 3.5 - 10.5 x 10^3/µl), and the mean platelet count is within the normal range; 1.76 ± 0.83 x 10^5/µl (Normal platelet values 1.5 - 4.5 x 10^5/µl).

Erythrocyte, leukocyte and platelet cell count

Interpretative erythrocyte, leukocyte, and platelet cell count of 30 respondents included in this study present in figure 1

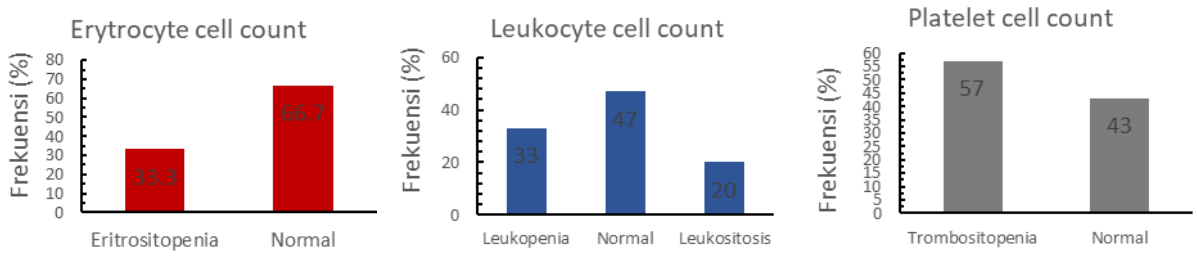

Figure 1 Abnormalities in the Number of Erythrocytes (a), Leukocytes (b), and Platelets (c)

Erythrocyte count (Figure 2a) shows that the proportion of normal erythrocyte count (3.80 - 5.20 x 10^6/µl) is more dominant (66.7%) compared to erythrocytopenia (erythrocytes < 3.80 x 10^6/µl), which is 33.3%. Leukocyte count (Figure 2b) shows that the proportion of normal leukocyte count (3.5 – 10.5 x 10^3/µl) is more dominant (47 %) compared to leukopenia (< 3.5 x 10^3/µl) which is 33 % and leukocytosis (>10.5 x 10^3/µl) which is 20 %. Platelet count (Figure 2c) shows that the proportion of thrombocytopenia (>1.5 x 10^5/µl) is more dominant at 57 % compared to normal (1.5 – 4.5 x 10^5/µl) which is 43 %, and no cases of thrombocytosis (>4.5 x 10^5/µl) were found.

Anemia

The proportion of anemia combined with non-anemia (normal) of 30 respondents included in this study and the type of anemia presented in figure 2

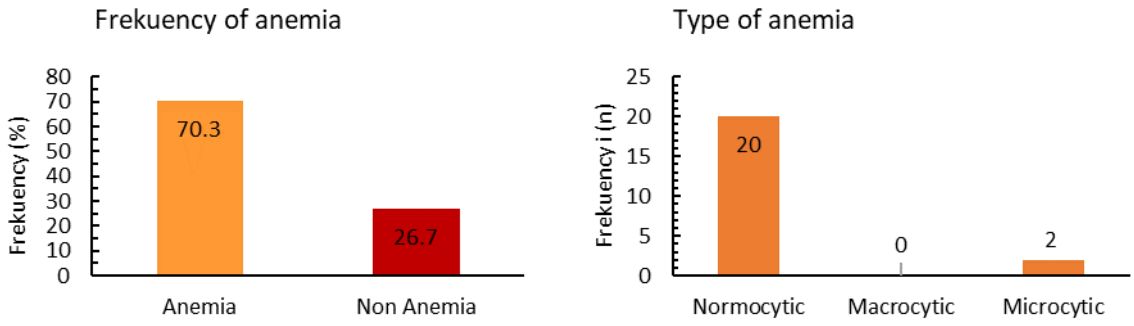

Figure 2 proportion of anemia and non-anemia (a) and type of anemia (b)

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Figure 2 shows the proportion of anemia (70.3%) compared to non-anemia (26.7%). Furthermore, most anemia cases are normocytic anemia (MCV=80-100 fL), with 20 respondents, while only 2 respondents have microcytic anemia (MCV<80 fL), and no cases of macrocytic anemia were found.

DISCUSSION

Tuberculosis (TB) remains a serious global health issue, with Southeast Asia contributing to 39% of the total global TB incidents. An estimated 3.4 million new cases of TB occur annually in Southeast Asia, with a majority concentrated in India, Bangladesh, Indonesia, Myanmar, and Thailand (1). This study analyzed hematological examination results in TB patients undergoing intensive phase OAT treatment in the East Bekasi District, covering 4 community health centers (Duren Jaya, Aren Jaya, Bekasi Jaya, and Karangkitri health centers). The study included 30 respondents, 73.8% male and 26.2% female.

Hematologic effect

Hematological disorders are common findings in TB patients undergoing OAT treatment phase I, clinically manifest as abnormalities in cell count, morphology, or substance of blood cells population. Hematological examination results reflect the hematopoiesis process in the bone marrow microenvironment and the interaction of cellular and plasma components in the periphery (Pinho & Frenette, 2019). The erythrocyte, leukocyte, and platelet counts (Figure 2) indicate that the proportion of normal erythrocyte count is greater at 66.7% compared to erythrocytopenia at 33.3%. The proportion of leukocyte count falls within the normal range at 47%, with 33% leukopenia and 20% leukocytosis. Thrombocyte count shows a predominance of thrombocytopenia at 57% compared to 43% normal counts, with no cases of thrombocytosis. Erythrocyte, leukocyte, and platelet counts are essential examinations in nearly all pathological conditions. In TB patients, hematological examination is crucial for monitoring prognosis and complications and providing clinical information on the effects of OAT therapy (Shah et al., 2022). Furthermore, OAT is known to have side effects such as thrombocytopenia, thrombocytosis, leukopenia, and leukocytosis (Balepur & Schlossberg, 2017). Intensive phase TB treatment involves the highest dose and duration of OAT exposure, combining INH, RIF, PZA, and EMB for 4 months allows for potential OAT side effects in patients; INH is reported to affect all hematopoiesis pathways, leading to erythrocyte abnormalities, thrombocytopenia, and neutropenia. RIF is known to cause megaloblastic anemia and thrombocytopenia. Thrombocytopenia due to RIF side effects is mediated by mechanisms involving decreased production and increased destruction of erythrocytes (Anemia Is a Strong Predictor of Wasting, Disease Severity, and Progression, in Clinical Tuberculosis (TB), 2022).

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Anemia

Anemia is defined as a condition characterized by low hemoglobin levels below normal value based on age and gender. It is a clinical manifestation of certain pathological conditions. Anemia can occur through various mechanisms depending on its etiology (Chaparro & Suchdev, 2019). Proportion and type of anemia (Figure 2) show a high proportion of anemia 70% compared to non-anemia at 30% with most of the anemia are normocytic anemia (MCV=80-100 fL), with 20 respondents, while only 2 respondents have microcytic anemia (MCV<80 fL), and no cases of macrocytic anemia were found. This study indicates that anemia is a common complication in TB, especially in patients undergoing intensive phase treatment. Additionally, 33.3% of respondents show a decrease in the number of erythrocytes, indicating inadequate hematopoiesis processes in producing erythrocytes or an acceleration of erythrocyte apoptosis (Zivot et al., 2018). This study demonstrates consistency with previous research conducted on 168 TB patients at the University of Gondar Hospital, Northwest Ethiopia, where hemoglobin, hematocrit, and platelet levels significantly decreased after patients completed the intensive phase of treatment compared to levels before starting treatment. Moreover, high Red Cell Distribution Width (RDW) and Platelet Distribution Width (PDW) during the second month of intensive phase treatment indicate variations in erythrocyte and platelet sizes (Kassa et al., 2016). Furthermore, this research aligns with a study conducted on 692 TB patients at the Pulmonary Disease Treatment Unit of West Kalimantan Province, Indonesia, where 76.4% of pulmonary TB patients experienced anemia. It was further reported that normocytic normochromic anemia is the most common type of anemia (Sadewo et al., 2016). A cohort study conducted by Dasaradhan et al (2022) indicates a strong correlation between anemia in tuberculosis (TB) and persistent inflammation. Furthermore, anemia from the early stages of infection to the development phase of Mycobacterium TB directly impacts treatment outcomes. This suggests that the condition of anemia serves as a significant predictor in the management of anemia therapy (Dasaradhan et al., 2022).

CONCLUSION

Hematological analysis of TB patients undergoing intensive treatment reveals that the most common complications and side effects are primarily linked to anemia, with normocytic normochromic anemia being the most frequently observed type. Additionally, thrombocytopenia is present in nearly half of the respondents, alongside cases of leukocytosis and leukopenia. Regular hematological examinations play a vital role in managing TB therapy by enabling early detection of treatment-related complications. These examinations provide essential clinical data that support informed decision-making, particularly in adjusting and optimizing therapeutic strategies for TB patients.

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