Nutritional Status of Hospitalized Tuberculosis Patients in South Kalimantan: A Cross-Sectional Study

Mohammad Isa[1], Ira Nurrasyidah[1], Elok Hikmatun Nikmah[1], Desi Rahmawaty[2]*, Ali Assagaf[1], Haryati[1], Erna Kusumawardhani[1]

[1]Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Universitas Lambung Mangkurat, South Kalimantan, Indonesia

[2]Faculty of Medicine, Universitas Lambung Mangkurat, South Kalimantan, Indonesia

Abstract: The burden of tuberculosis (TB) infection is significant in Indonesia. There is likely a substantial link between TB and malnutrition. Anemia, which is linked to TB patient outcomes and length of hospital stay, is another issue that might aggravate the disease. This study aims to identify how common undernutrition and anemia are among tuberculosis patients at the Ulin Regional Hospital in Banjarmasin. A cross-sectional observational study was conducted using medical record data from 31 hospitalized tuberculosis patients from September to December 2021. Data of weight, height, body mass index (BMI), Hemoglobin (Hb) and blood albumin level at admission were analyzed. The result showed that tuberculosis cases were mostly found in males (61.3%) aged 20-60 years (83.9%). There were 42% of patients with undernutrition (BMI <18.5), 93.5% with anemia, and 71% with hypoalbuminemia. Rifampicin resistance was found in 38.7% of all patients, with 58.3% malnutrition, 100% anemia, and 50% hypoalbuminemia. Thus, there was a possible link between tuberculosis and undernutrition condition. Screening, early diagnosis, and treatment for undernutrition, anemia, and hypoalbuminemia should be encouraged in patients with tuberculosis, whether they are susceptible or resistant to rifampicin, to lower the burden of the disease.

Keywords: albumin; anemia; Indonesia; tuberculosis; undernutrition

INTRODUCTION

Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis* (Mtb), transmitted through droplets. Tuberculosis can infect all body organs but is most commonly found in the lungs. A report by the World Health Organization in 2021 shows that 5.8 million people are newly diagnosed with TB. There were 1.3 million TB deaths among HIV-negative people and 214,000 among HIV-positive people.[1] The burden of TB infection is high in Indonesia. Based on the Dashboard of the Ministry of Health of the Republic of Indonesia, it is estimated that the number of people with TB in 2021 will be 824,000 resulting in 13,110 deaths.[2] The Indonesian Ministry of Health aims to reduce the incidence of tuberculosis to 190 cases per 100,000 population, while the most recent data on TB incidence in 2019 showed that it is still 210 cases per 100,000 population.[3,4]

The World Health Organization (WHO) stated there is a strong association between the TB incidence rate and the prevalence of undernutrition.[5] The link between TB and undernutrition has long been known. Undernutrition increases the risk of developing TB. At the same time, individuals with TB are more susceptible to undernutrition than the general population and can develop conditions such as anorexia, cachexia, and weakness caused by decreased appetite. TB also worsens undernutrition, weakening immunity and increasing the risk of activating latent TB. According to earlier studies, the prevalence of low body weight in TB cases in Ethiopia is 39.7% of total TB cases. Low body weight TB patients account for 35.5% of all TB patients in Taiwan. Meanwhile, in Indonesia, low body weight is found in 42.4% - 61.1% of tuberculosis patients.[1,6–8]

Pulmonary TB has several complications, either worsening pulmonary TB, spreading the infection to other organs, or systemic complications. Anemia is one of the most common complications. Anemia is linked to difficulties in recovering from TB. Anemia is also associated with TB patient outcomes and length of hospital stay.[9] These findings indicated the importance of nutritional support in treating pulmonary TB. Estimating the prevalence of undernutrition among TB patients is critical for formulating suitable strategies, policies, and implementation initiatives to improve care quality. In South Kalimantan, no studies show the burden of undernutrition and anemia among TB patients. As a result, this study aimed to describe the prevalence of undernutrition among tuberculosis patients hospitalized at Ulin Hospital from September to December 2021.

MATERIAL AND METHOD

This study is a descriptive study with a cross-sectional approach in hospitalized tuberculosis patients. The data on this study was obtained from medical record data from hospitalized tuberculosis patients at Ulin Regional Hospital Banjarmasin. The inclusion criteria were TB patients hospitalized from September to December 2021, with complete medical records of weight, height, Body Mass Index (BMI), hemoglobin (Hb) at admission, and blood albumin level at admission. This study's exclusion criteria were patients who received Anti Tuberculosis Drugs (ATD) before admission and patients with chronic diseases such as HIV, heart failure, diabetes mellitus, infectious hepatitis, and kidney disorders.

Determination of tuberculosis patients included in this study was the patient showing positive infection of *Mycobacterium tuberculosis* using GeneXpert, clinically symptoms and chest X-Rays. Anemia is classified according to WHO as mild anemia (Hb 11.0 - 12.9 g/dL for males, 11.0 - 11.9 g/dL for females), moderate (8.0 - 10.9 g/dL for males and females), and severe anemia (<8.0 g/dL for male and female).[10] Nutritional status is classified according to WHO as obesity level II (BMI ≥ 30 kg/m^2), obesity level I (BMI 25 - 29.9 kg/m^2), overweight (BMI 23-24.9 kg/m^2), normal weight (BMI 18.5-24.9 kg/m^2), and underweight (BMI <18.5 kg/m^2).[11] The classification of albuminemia is based on these 4 categories, such as Normal (3.5-4.5 g/dL), mild hypoalbuminemia (3.2 - 3.5 g/dL), moderate hypoalbuminemia (2.8 - 3.2 g/dL) and severe hypoalbuminemia (<2.8 g/dL).

Descriptive statistics with IBM SPSS 25.0 were used in this study to summarize data and results reported in mean where appropriate. Categorical variables were summarized as counts and percentages. This research has been approved by the Research Ethics Committee of Ulin Hospital Banjarmasin with registration number 37/IV-Reg Riset/RSUDU/22.
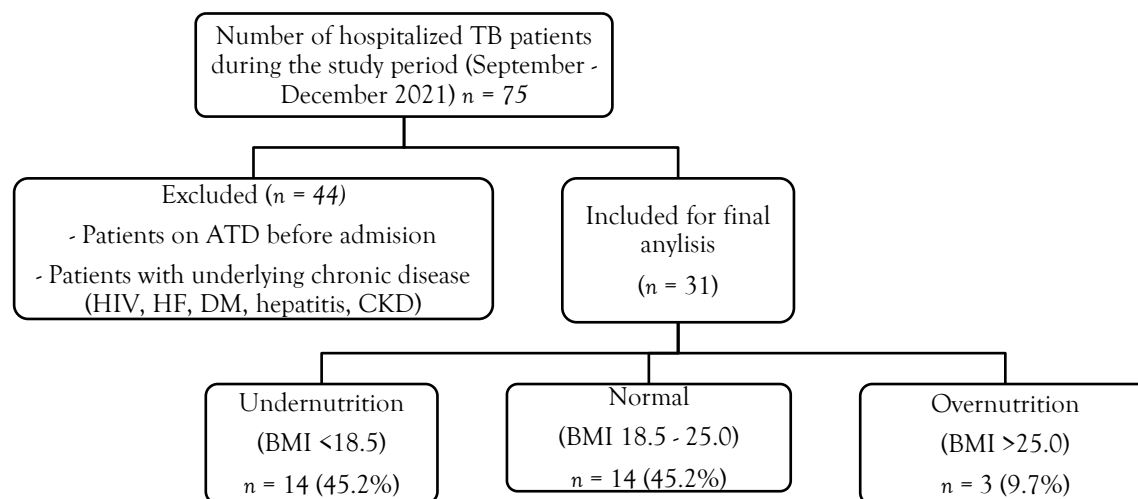

Figure 1. The flow of participants in the study

RESULT

Based on this study, we found a total of 75 TB patients who were hospitalized at Ulin Hospital Banjarmasin during the study period of September - December 2021. After excluding 44 patients, we included 31 patients who have no history of prior ATD and without another underlying chronic disease for the final

analysis. Patients' nutritional status was classified by Body Mass Index (BMI), and we found that 45.2% of patients had undernutrition, 45.2 had normal BMI, and only 9.7% had overnutrition (Figure 1).

The characteristics of hospitalized TB patients at Ulin Regional Hospital are shown in Table 1. The male gender predominated in this study, as did the productive age range of 20-60 years and the diagnosis of pulmonary tuberculosis. The percentage of nutritional status did not differ significantly between male and female patients. Patients aged 20-60 years were dominated by undernutrition, while patients with normal nutritional status dominated those aged >60 years. There were only three patients with overnutrition, and they were all male patients aged 20 to 60. Patients with undernutrition slightly outnumbered those with pulmonary TB; however, most extra-pulmonary TB patients had normal nutritional status.

Table 1. Clinical characteristics of hospitalized tuberculosis patients at Ulin Regional Hospital

Characteristics	Total (n = 31)		Undernutrition (n = 14)		Normal (n = 14)		Overnutrition (n = 3)	
	n	%	n	%	n	%	n	%
Gender								
Male	19	61.3	8	42.1	8	42.1	3	15.8
Female	12	38.7	6	50.0	6	50.0	0	0.0
Age, in years (mean = 46.7)								
20 – 60	25	80.6	12	48.0	10	40.0	3	12.0
>60	6	19.4	2	33.3	4	66.7	0	0.0
Type of TB								
Pulmonary	28	90.3	14	50.0	12	42.9	2	7.1
Extra-pulmonary	3	9.7	0	0.0	2	66.7	1	33.3
GeneXpert								
Bacteriologically positive	21	67.7	10	47.6	9	42.9	2	9.5
Bacteriologic		0.0						
Low	5	16.1	1	20.0	3	60.0	1	20.0
Medium	13	41.9	8	61.5	4	30.8	1	7.7
High	3	9.7	1	33.3	2	66.7	0	0.0
Resistance		0.0						
Rifampicin sensitive	9	29.0	3	33.3	6	66.7	1	11.1
Rifampicin resistant	12	38.7	7	58.3	4	33.3	1	8.3
Bacteriologically negative	10	32.3	4	40.0	5	50.0	1	10.0
Albumin								
Normal	9	29.0	3	33.3	4	44.4	2	22.2
Hypoalbuminemia	22	71.0	11	50.0	10	45.5	1	4.5
Mild	6	19.4	4	66.7	2	33.3	0	0.0
Moderate	6	19.4	1	16.7	4	66.7	1	16.7
Severe	10	32.3	6	60.0	4	40.0	0	0.0
Hb								
Normal	2	6.5	0	0.0	1	50.0	1	50.0
Anemia	29	93.5	14	48.3	13	44.8	2	6.9
Mild	11	35.5	4	36.4	5	45.5	2	18.2
Moderate	15	48.4	8	53.3	7	46.7	0	0.0
Severe	3	9.7	2	66.7	1	33.3	0	0.0

These patients were tested using GeneXpert to see if they had MTB bacteria and were resistant to rifampicin. In this study, 21 patients (67.7%) out of a total of 31 patients showed positive bacteriological results, while 10 patients (32.3%) did not have MTB and were classified as bacteriologically negative. Based on the number of bacteria found in bacteriologically positive patients, most were patients with medium MTB detected with undernutrition. Bacteriologically positive patients can also be tested for rifampicin resistance, and the majority of bacteriologically positive patients in this study were rifampicin-resistant and malnourished. In patients with negative bacteriological results, the majority had normal nutritional status. We found evidence of a possible link between tuberculosis and undernutrition, with most patients in this study having anemia and hypoalbuminemia. The majority of patients exhibited severe hypoalbuminemia with

undernutrition. Almost all patients were anemic, and the majority had moderate anemia. Most patients with mild anemia had normal nutritional status. Meanwhile, those with moderate to severe anemia were mostly malnourished.

The nutritional characteristics of TB patients with Rifampicin-resistant (RR) can be seen in Table 2. Similar traits were seen in patients with rifampicin resistance. More than half of these patients had undernutrition. Furthermore, all rifampicin-resistant patients were anemic, and at least half had hypoalbuminemia.

Table 2. Nutritional characteristics of hospitalized tuberculosis patients based on rifampicin resistance

Characteristics	Rifampicin resistant (n=12)	
	n	%
Nutritional status		
Undernutrition	7	58.3
Normal	4	33.3
Overnutrition	1	8.3
Hb		
Normal	0	0.0
Anemia	12	100.0
Mild	6	50.0
Moderate	4	33.3
Severe	2	16.7
Albumin		
Normal	6	50.0
Hypoalbumin	6	50.0
Mild	5	41.7
Moderate	0	0.0
Severe	1	8.3

DISCUSSION

In this investigation, 75 people were hospitalized for tuberculosis between September and December 2021. Thirty-one patients with no history of prior ATD and without other underlying chronic diseases were included in this study. According to research by Aljohaney *et al.*, medical comorbidities for TB patients (such as diabetes mellitus, congestive heart failure, renal failure, chronic lung disease, and hepatitis B virus infection) were shown to be significantly greater in the deceased group.[12]

This study's patients were male in 61.3% of cases. These results indicated a male predominance of TB, which is in line with a study conducted in New Jersey. The study found that men were found to be 79% more likely than women to have tuberculosis. It is linked to a history of drinking, specific immunological roles, and different iron metabolism in men that were considered a risk factor for tuberculosis. In terms of epidemiology, men consume more alcohol than women, lowering lung immunity and making it easier for tuberculosis to spread.[13,14] Smoking prevalence which was higher among men (38.8%) than among women (3.9%), was also a significant risk factor for the development of TB. Tobacco smoking was found to be responsible for 19.6% of all tuberculosis cases. Mucociliary dysfunction, decreased alveolar macrophage activity, immunosuppression of pulmonary lymphocytes, inactivated natural killer cells, and nonfunctional pulmonary dendritic cells are some of the possible mechanisms behind this effect on TB infection in response to cigarette smoke.[15]

An experimental study was conducted on mice to compare the susceptibility of male and female subjects to TB infection. According to the findings, male rats exhibited more bacilli in their lungs than female rats. It demonstrated that the immunological mechanism plays a role in the association with the presence of infection. Testosterone inhibits the immune system and influences innate and adaptive immune responses in the aftermath of *M. tuberculosis* infection. It contributes to disease pathogenesis by increasing neutrophil flow to the site of infection. Meanwhile, estrogen generated by women produces medroxyprogesterone acetate, which reduces women's susceptibility to infection, particularly tuberculosis.[13,16,17]

In this study, 45.2% of TB patients treated at Ulin Hospital Banjarmasin were underweight. This prevalence is higher than in studies conducted in Ethiopia (39.7%) and Peru (21%); the discrepancy between the two nations is related to socioeconomic inequalities. A study conducted in Ghana showed that undernutrition was prevalent in 51% of TB patients. This study included patients who had never been diagnosed with TB before and had not received treatment.[7,9] Our study also found that 58.3% of RR TB patients were malnourished

(Table 2), which was higher than the results of a study conducted at Dr. Soetomo, which revealed that 51.5% of RR TB patients were malnourished.[18] These findings showed that in South Kalimantan, specifically in Ulin Hospital, poor nutritional status is still a challenge in managing tuberculosis.

Undernutrition in tuberculosis is caused by a loss of appetite or other causes that induce irregular metabolism, absorption, and fever. A study by Gurung *et al.* revealed that about one-fifth of TB patients did not consume sufficient calories based on the recommended daily allowance.[19] Undernutrition compromises an individual's innate and adaptive immunity, making them vulnerable to various infections. As the two main processes for eliminating harmful organisms from the body, the functions of phagocytosis and the complement cascade are both weakened. Undernutrition has also been linked to the development of tuberculosis. A previous study by Lai *et al.* reported that being underweight (BMI less than 18.5 kg/m2) was related to a higher risk of all-cause death and a higher risk of early mortality within the first 8 weeks of starting treatment.[8] According to other studies, increasing BMI lowered the incidence of tuberculosis by 14%. Low BMI individuals had lower amounts of pro-inflammatory cytokines (IFN-γ, TNF-α, IL-22, IL-1α, IL-1β, and IL-6) but higher levels of cytokines (IL-10, TGF-β, IL-5, IL-13). These findings point to a protective mechanism against tuberculosis infection in those with a normal BMI.[19,20]

Hypoalbuminemia was identified in 71% of TB patients hospitalized in our research. This result is higher than Ganesan et al.'s study, which found hypoalbuminemia in 60% of hospitalized tuberculosis patients in India in 2018. Protein deficit and undernutrition will reduce the ability of defense mechanisms and immunity in tuberculosis patients. In several investigations, albumin levels were also linked to the severity of symptoms and the results of AFB (acid fast bacilli) sputum. Hypoalbuminemia is also a predictor of mortality in hospitalized TB patients.[8,21]

One of the morbidities associated with tuberculosis is anemia. We found that 93.5% of all TB patients were anemic in our study, and 100% of TB-resistant patients had anemia. This number is higher than the global prevalence of anemia in tuberculosis, which ranges from 44–89.1%[22]. Anemia is a common complication of chronic illnesses like tuberculosis (TB). Iron deficiency in anemia is the most frequent anemia among tuberculosis patients. Functional iron deficiency in inflammatory conditions like TB is caused by elevated hepcidin levels, triggered by inflammatory cytokines such as Interleukin 1 (IL-1), IL-6 and Tumor Necrosis Factor (TNF- α). Hepcidin has a significant impact on iron control and iron transport in the body. Hepcidin inhibits iron transfer from macrophages and hepatocytes' iron reserves. Hepcidin also prevents iron from being absorbed by the digestive system (duodenum). This condition lowers the amount of iron available for binding to transferrin, causing hypoferremia and anemia.[19,22,23]

Iron is required for erythropoiesis, and iron deficiency anemia affects immune system mechanisms such as humoral, cellular, non-specific, and cytokine immunity. Iron is essential for the proliferation and activation of CD4+ helper T-lymphocytes, and intracellular iron deficiency can impair the function of the enzymes that drive the metabolic and redox reactions involved in these processes. Anemia also reduces oxidative activity and the ability of monocytes to engage in phagocytosis. The process of macrophage phagocytosis is critical for controlling tuberculosis infection by creating granulomas, which are immune system aggregation walls.[19,22] Anemia is also linked to undernutrition in tuberculosis patients. Micronutrients such as vitamin A, B12, folate, and riboflavin are innate immune system mediators by regulating the functions of both macrophages and dendritic cells and immunomodulating the process of antibacterial functions, autophagosomes formation, autophagy, and cytokine production. Multiple vitamins have been shown to have a role in immunity against *M. tuberculosis* infection or disease. A deficiency of certain micronutrients due to undernutrition impairs cellular immunity.[20,24]

Due to a lack of data and supporting investigations, it is impossible to determine whether this study's anemia is genuinely categorized as chronic infectious anemia. Supporting data, such as ferritin, transferrin, and serum hepcidin, are required to determine if the anemia is caused by chronic illness or iron deficiency. Anemia that develops before TB infection is linked to a higher risk of TB incidence, according to a meta-analysis. When compared to people without anemia, the risk of tuberculosis is said to be twice as high.[22] As this study was conducted using a descriptive approach, the researchers could not determine the correlation between anemia and tuberculosis (TB), that is, whether anemia was a risk factor for TB or TB caused anemia.

CONCLUSION

Our research at the Ulin Regional Hospital, South Kalimantan, from September to December 2021, found that male gender and age range of 20-60 years were the majority of this study's findings. Although there was no noticeable difference in the percentage of nutritional status between male and female patients, most patients aged 20 to 60 had undernutrition. We found evidence of a possible link between tuberculosis and undernutrition, with most patients in this study having anemia and hypoalbuminemia. Patients with

rifampicin resistance displayed similar characteristics. More than half of rifampicin-resistant patients had undernutrition. In addition, they were all anemic, and at least half of them had hypoalbuminemia. Screening, early diagnosis, and treatment for undernutrition, anemia, and hypoalbuminemia should be encouraged in patients with tuberculosis, whether they are susceptible or resistant to rifampicin, to lower the burden of the disease.

CONFLICT OF INTEREST

The authors declare that there are no competing interests related to the study.

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