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ORIGINAL ARTICLE

Relationship between protein intake and nutritional status with response therapy of intensive phase in pulmonary tuberculosis patients in Dili and Oecusse

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Abstract

Tuberculosis (TB) infection triggers a decrease in appetite and disrupts protein metabolism. Protein provides the main source of amino acids for immune system formation and tissue repair, both of which are impaired in tuberculosis patients. Intensive phase anti-tuberculosis therapy aims to boost immunity, reduce bacterial load, and improve nutritional status. Pulmonary TB is the leading cause of death in Timor Leste (94% mortality rate by 2021), yet few studies have explored the relationship between nutrition and treatment response. This study investigated the relationship between protein intake, nutritional status, and treatment response in pulmonary TB patients undergoing intensive therapy in Dili and Oecusse. Using a cross-sectional research design, 104 participants were recruited using consecutive sampling. Data collection included primary and secondary data. Analyses were conducted using independent sample t-test, Mann-Whitney, Fisher's Exact Test and nutrisurvey 2007 to analyse protein intake. There are 66.3% at risk of malnutrition based on upper arm circumference, a mean body mass index of 17.86 kg/m². The median daily protein intake was 1.07 g/kgBW/day, with lower intake of animal protein compared to plant protein (0.44 g/kgBW/day vs. 0.59 g/kgBW/day). The study found no significant relationship between protein intake and nutritional status in response to the intensive phase therapy ($p>0.05$).

There is no significant relationship between protein intake and nutritional status with response therapy of intensive phase in pulmonary TB patients. Further research with a case-control study design is needed to confirm findings and evaluate factors affecting unbalanced therapy response.

Keywords: tuberculosis, protein intake, nutritional status and respons therapy

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Introduction

According to the Global Report Tuberculosis (TB) (2021), there were 10.6 million TB incidents with a mortality rate of 1.6 million. Timor Leste is one of the developing countries with the second highest TB incidence and mortality in the South East Asian Region (SEARO) in 2021 with an incidence of 486/100,000 and a mortality rate of 94/100,000 population. The national strategic plan to end TB by 2030 in Timor Leste is in line with the End TB strategy which has become a global commitment.[1,2] The years 2022-2026 are a crucial period with various intervention programs and comprehensive activities as well as targets to reduce TB cases by achieving a TB treatment success rate of 94% by 2022. This research was conducted in Dili, the capital city with the largest population of 324,269 people and the highest TB incidence of 1862 cases, as well as Oecusse with a total population of 80,725 with a TB incidence of 469 cases.[2]

Tuberculosis infection leads to an increase in pro-inflammatory cytokines, characterized by a hypermetabolic state that raises energy requirements, which are met by using the body's protein reserves in the form of amino acids.[3,4] The reduction in protein reserves hinders the process of protein synthesis (anabolic block phenomenon), resulting in malnutrition. Side effects of anti-tuberculosis drugs are also a factor causing gastrointestinal problems, leading to reduced nutrient intake, including protein. Limited understanding and low income, which restrict access to a balanced and nutritious diet, are other factors influencing malnutrition in TB patients.[5,6] Research on malnutrition in adults due to infectious diseases is still very limited.[7,8] Previous studies have suggested that inadequate nutritional status in TB patients is correlated with insufficient nutrient intake, particularly protein, which serves as a crucial source of nutrition for recovery, growth, and the body's defense mechanisms. Once consumed, protein is degraded into amino acids that play essential roles in the body's metabolic processes.[9]

To determine eating patterns and levels of nutritional intake, especially protein intake, with the response to intensive phase therapy, the Semi Quantitative-Food Frequency Questionnaire (SQ-FFQ) technique was used.[10] This technique uses a questionnaire regarding the types of plant and animal protein foods consumed by TB patients in the last month during the intensive phase of treatment. Assessment of nutritional status using body mass index (BMI) measurements based on World Health Organization (WHO) Asia Pacific and Mid-upper arm circumference (MUAC) as an ideal alternative to assess fat-free mass in conditions of muscle atrophy due to malnutrition.[11,12] Tonder et al., concluded that MUAC is a better method to identify malnutrition with a sensitivity of 89.3% and specificity of 82.3%.[13]

Based on the high incidence of TB and malnutrition and research in Timor Leste regarding the relationship between nutrition and response to therapy in the intensive phase of TB, this research aims to determine the relationship between protein intake and nutritional status and response to intensive therapy. phase therapy in pulmonary TB patients in Dili and Oecusse.

Methods

This study used an observational analytical method with a cross-sectional study design to determine the relationship between protein intake and nutritional status and response to intensive phase therapy in pulmonary TB patients in Dili and Oecusse - Timor Leste. The sample is a population diagnosed with TB and in the intensive phase of pulmonary TB for the period February – May 2024 in Dili and Oecusse.

Ethical Approval

The study has been approved by the Unit of Ethical Research and Development of Timor-Leste with letter approval number of 05/INSP-TL/UEPD/II/2024. All participants in this study were treated based on Declaration of Helsinki and gave spoken, written informed consent before participating this study.

Participants

Participants were 104 people aged over 18 years, and bacteriologically confirmed case of pulmonary TB in the intensive phase for 2 months/56 days taken in outpatient/inpatient settings in Dili (Comunity Health Center (CHC) Comoro, CHC Becora and Bairopite clinic) and Oecusse (4 CHCs and 1 Referral Hospital). Subjects were excluded if they were pregnant, in critical condition, had defects or abnormalities in the upper extremities that affected the MUAC and BMI examination process and results, as well as patients with incomplete data.

Data Collection

Data collection for this study was conducted from February to May 2024. Primary data was obtained through interviews using a socio-demographic characteristics questionnaire and the SQ-FFQ to assess protein intake, along with anthropometric measurements of the research subjects. Secondary data, including laboratory examination results such as Acid-Fast Bacilli (AFB) sputum smear tests, Rapid Molecular Testing with GeneXpert, Human Immunodeficiency Virus (HIV) testing, and chest radiography results, were gathered from the medical records of research subjects at each health facility that served as a research site.

Socio-Demographic Characteristics

Socio-demographic variables consist of age, gender, education, income level, comorbidity, HIV status, AFB sputum smear examination results, adverse effects, and medication adherence. The characteristics of subject were collected from medical records.

Total protein intake

Total protein intake data was collected through interviews using a SQ-FFQ which contains a list of types of plant and animal protein food sources along with portions and frequency of food consumption. This questionnaire was previously pretested to assess validity by knowing the types of food sources of protein consumed daily according to the research location. Training and calibration were conducted between the researcher and the enumerators on using a food photo book with portion sizes based on household measurements. Protein intake assessment data were analyzed with Nutrisurvey 2007.

Nutritional Status

The nutritional status of TB patients was assessed using two key anthropometric measurements: MUAC and BMI. Based on these measurements, the patients were classified into two categories: at risk of malnutrition or not at risk. MUAC was measured using a WHO-standard MUAC tape for adults and BMI was calculated as weight in kilograms divided by the height in metres squared (kg/m^2). The BMI is categorized according to the asian-pasific cut-off points: severe underweight (< 16.0 kg/m^2), underweight (< 18,5-16.0 kg/m^2), normal weight (18,5-22,9 kg/m^2), overweight (23-24.9 kg/m^2), obese (≥ 25 kg/m^2). Weighing body weight (BW) and measuring height using a SECA branded measuring instrument. Training and calibration were conducted between the researcher and the enumerators on anthropometric measurements. To determine the consistency of the anthropometric measurements of the enumerators, the Kappa test was used and the results of the kappa coefficient were 1.00 or > 0.6. Thus it was considered that the perception between the researcher and the enumerators was the same or consistent.

Response Therapy of Intensive Phase

We evaluate the response to TB therapy during the intensive phase is based on the results of bacteriological examination for AFB at the health facility. If the follow-up bacteriological examination shows no conversion of Mycobacterium Tuberculosis (AFB positive), the therapeutic response is considered unsuccessful. Otherwise, if no TB bacteria are detected (AFB negative), the therapeutic response is considered successful. Bacteriologic results for AFB are taken from medical records.

Statistical analysis

Furthermore, all data were analyzed with the Statistical Package for Social Sciences (SPSS) version 29. Statistically significant differences if p > 0.05 between groups were analyzed using Chi-Square and independent T-test to compare means of subjects' numerical data.

Results

The target population includes all patients diagnosed with pulmonary TB, the facilities involved 6 CHC, 1 Sponsored Clinic (Bairopite Clinic) and 1 general hospital. Total subjects in this study is by a physician in various healthcare facilities in Dili and Oecusse, specifically 104 subjects. The findings of this study, as summarized in Table 1, highlight key demographic and clinical characteristics of the subjects. The majority were in the productive age group, with an average age of 31 years, and males comprised 53.8% of the total population. Most subjects (61.5%) had a high level of education, predominantly completing high school or its equivalent. Economically, 89.4% of the participants earned below the minimum wage in Timor Leste. After the intensive phase of TB therapy, 92.3% of subjects tested negative for AFB on sputum examination. Despite 84.6% reporting side effects from anti-TB drugs, adherence to therapy was commendably high, with 91.3% of participants demonstrating good adherence. Comorbid conditions were identified in only 20.2% of the subjects, and 2.9% tested positive for HIV/AIDS. Overall, 92.3% of the participants successfully completed the intensive phase of treatment based on AFB test results.

The nutritional status of the subjects based on upper arm circumference measurements, 66.3% were found to be at risk of malnutrition. The mean body weight among the subjects was 44.6 kg with a BMI of 17.9 kg/m², indicating the prevalence of underweight individuals in the group. Categorization results based on WHO Asia Pacific, 33.7% had normal/excess nutritional status, 47.1% were underweight and 19.2 % were severe underweight.The analysis of this study revealed that a significant majority of the study subjects (63.5%) had inadequate protein intake. The median value of total protein intake among the subjects was 1.07 grams/kgBW/day. This amount represents the combined intake of animal and plant protein sources which were 0.44 gr/kgBW/day and 0.59 gr/kgBW/day respectively.

Total Protein Intake with Nutritional Status

The relationship between protein intake with nutritional status during the intensiven phase of TB treatment was explored by Chi-square with Fisher's Exact Test and there was no significant result (**Table 2**).

Relationship between protein intake and nutritional status with response therapy

The relationship between protein intake and nutritional status with response therapy during the intensiven phase of TB treatment was explored by Chi-square test with Fisher's Exact Test. The findings from this analysis revealed no significant relationship between the levels of protein and nutritional status with response therapy during the intensive phase (**Table 3**)

Discussion

Protein is critical in supporting the immune response and overall recovery during the intensive phase of TB therapy. It is a fundamental macronutrient that supports tissue repair, immune function, and the synthesis of enzymes and hormones vital for maintaining body processes, especially under stress or disease conditions like TB.[14,15] It helps the body combat the infection and recover during and after treatment. Protein malnutrition can compromise the immune response, delay recovery, and worsen the overall prognosis. Inadequate protein intake leads to malnutrition which potentially leading to poorer health outcomes and nutritional status. Studies consistently show that malnourished TB patients, particularly those with low protein intake, have poorer treatment outcomes. Malnutrition can lead

Table 1. Characteristics of the subjects

Variables	N	%	Mean ± SD / Median (min-max
Age (years)			31 (18-75)
Gender			
Female	48	46.2	
Male	56	53.8	
Education level			
High	64	61.5	
Low	40	38.5	
Socio Economic level			
High	11	10.6	
Low	93	89.4	
Adverse effect			
No	14	15.4	
Yes	88	84.6	
Medical Adherence			
High	95	91.3	
Low	9	8.7	
Comorbidity			
No	83	79.8	
Yes	21	20.2	
HIV-AIDS status			
Negative	101	97.1	
Positive	3	2.9	
Response therapy			
Succeed (AFB test negative)	96	92.3	
Failed (AFB test positive)	8	7.7	

Related to **table 1**. Characteristics of the subjects

Variables	N	%	Mean ± SD / Median (min-max)
Protein intake			
gr/kgBW/day			1.07 (0.29-3.69)
Adequate	38	36.5	
Inadequate	66	63.5	
Animal-based protein (gr/kgBW/day)			0.44 (0.01-3.12)
Plant-based protein (gr/kgBW/day)			0.59 (0.09-2.26)
Weight (kg)			44.6 ± 6.65
Height (cm)			157.6 ± 0.07
Malnutrition (MUAC)			
Not at risk	35	33.7	
At Risk	69	66.3	
BMI (kg/m^2) before therapy			17.3±1.94
Normal/overweight	30	28.8	
Underweight	46	44.2	
Severe underweight	28	26.9	
BMI (kg/m^2) After therapy			17.9±1.93
Normal/overweight	35	33.7	
Underweight	49	47.1	
Severe underweight	20	19.2	

Table 2. Relationship Between Total Protein Intake With Nutritional Status

Variable	Total Protein intake		*p value*
	Inadequate	Adequate	
	n (%)	n (%)	
Nutrition Status: BMI (kg/m²)			0.399[a]
Well-Nourished	19 (54.3)	16 (45.7)	
Malnourished	44 (63.8)	25 (36.2)	

[a] Fisher's Exact.

Table 3. Relationship between protein intake and nutritional status with response therapy

Variable		Response therapy				*p*
		Succeed (Negatif)		Failed (Positif)		
		n (%)	Mean ± SD/ Median (Max-Min)	n (%)	Mean ± SD/ Median (Max-Min)	
Total Protein intake	Adequate	38 (92.7)		3 (7.3)		1.00[c]
	Inadequate	58 (92.1)		5 (7.9)		
	gr/kgBW/ day		1.09 (0.29-3.69)		0.88 (0.45-2.22)	0.86[a]
Animal-based protein	gr/kg BW/day		0.44 (0.01-3.12)		0.32 (0.06-1.19)	0.55[a]
Plant-based protein	gr/kgBW/ day		0.59 (0.09-2.26)		0.64 (0.23-1.03)	0.53[a]
Malnutrition	Not at risk	32 (91.4)		3 (8.6)		1.00[c]
	At risk	64 (92.8)		5 (7.2)		
BMI	Kg/m2		17.85 ± 1.93		18.05 ± 2.12	0.78[b]
	Normal/ overweight	32 (91.4)		3(8.6)		
	Underweight	46(93.9)		3(6.1)		
	Severe underweight	18(90.0)		2(10.0)		

[a]Mann Whitney, [b] T-test, [c] Fisher's Exact

to delayed sputum conversion, increased side effects from medication, and a higher likelihood of treatment failure.[16-19] A study from Ethiopia highlighted a significant relationship between nutritional status and treatment outcomes after the intensive phase of TB therapy ($p<0.05$), underlining the importance of proper nutrition during TB treatment.[9]

Based on the WHO 2013 guidelines, the recommended protein requirement is around 15-30% of energy or 1.2 - 1.5 g/kgBW/day, which translates to approximately 75-100 gr/day.[20,21,22] According to Mahan et al.[23] to prevent muscle tissue damage and accelerate recovery in patients with chronic infections, the required protein intake is 15% of energy needs. In severe infection conditions, this requirement can increase to 2.0 g/kgBW/day to support the immune system against infections. The Indonesian Ministry of Health's recommended dietary allowance (RDA) for 2019 was used in this study.[24]

The analysis of this study revealed that a significant majority of the study subjects (63.5%) had inadequate protein intake. This aligns with the findings of Ren et al., who reported a median protein intake of 43.15 grams per day.[5] However, the results different from those of Yunda et al., who found an average protein intake of 55.35±19.38 gr/day.[25] Additionally, Alaina et al.[26] reported a much lower average protein intake of 24.61±9.91 gr/day. The median intake of plant-based protein among the subjects was 0.59 gr/kgBW/day . Common sources of plant-based protein included rice or porridge (from rice), soy beans, and red beans. The median intake of animal-based protein was 0.44 gr/kgBW/day . Major sources of animal protein were processed milk products and imported chicken, which is affordable and readily accessible.

The statistical analysis indicates that the majority of patients consumed more plant-based protein compared to animal-based protein. This trend can be attributed to several factors:

1. *Economic Factors:*
The relationship between TB and poverty is complex and mutually reinforcing. Poverty increases the risk of malnutrition and TB severity, while TB exacerbates poverty by draining families of economic resources. This study found that 89.4% of subjects (TB patients) had incomes less than the minimum wage in Timor Leste. It is inline with Multidimensional Poverty Index (MPI) for Timor-Leste in 2023 estimates that 48.3% of the population is classified as multidimensionally poor.[27] Low income of familiy with the high living costs limit their access to food, especially animal protein sources which are more expensive in Timor Leste.[9] As a solution, the government of Timor Leste, through the TB Programme, has provided food subsidies and material assistance to some TB patients with low economic status. However, a large proportion of TB patients still struggle to meet their balanced nutritional needs due to low income compared to the high cost of living. According to various studies, these economic constraints force many households to rely on more affordable sources of plant-based protein.[28,29]

2. *Food Insecurity and Dietary Diversity*:
The 2019 survey on food security in Timor-Leste highlighted that while almost all households (94%-100%) could meet their energy needs, only a small proportion (15%-37%) could afford a nutritious diet.[8,30] Consequently, diets are heavily reliant on carbohydrate-rich staple foods like rice, corn and tubers such as sweet potato, cassava, taro, and sago. Vegetables are consumed in minimal quantities, and the intake of animal protein and other nutritious foods is very limited. The affordability and accessibility of plant-based proteins make them the primary choice in daily diets, especially in economically constrained setting. Also, Inadequate and poorly diversified diets are directly linked to malnutrition, which impairs the body's ability to function effectively, particularly in vulnerable groups such as children and patients with chronic conditions like tuberculosis.[30] The consequences of inadequate and poorly diversified diets in this study, based on the analysis of the relationship between total protein intake and nutritional status, showed that most subjects had inadequate protein intake, both among malnourished subjects (63.8%) and well-nourished subjects (54.3%) (Table 2).

The results indicated that there was no significant relationship between nutritional status and the response to therapy during the intensive phase. A similar study by Amalia et al, used Chi-square analysis and found no significant relationship (p=0.960) between nutritional status and the response to tuberculosis therapy during the intensive phase.[31] A different outcome was observed in a study conducted in Kupang City, which focused on the changes in patients' nutritional status after the intensive phase of tuberculosis therapy. The study found significant changes in nutritional status after the intensive phase. The percentage of subjects with normal nutritional status increased to 40.5% after the intensive phase and the percentage of subjects with poor nutritional status decreased from 72.6% before treatment to 59.5% after the intensive phase.[14] This suggests a significant improvement in overall nutritional status following the intensive phase of treatment, in contrast to the previous studies that did not find a significant relationship between nutritional status and treatment response.[26] Several previous cross-sectional studies have described how nutritional status significantly affects the response to therapy, treatment outcomes, and recovery rates during the intensive phase for TB patients.[32] The proportion of patients affected ranged from 45.8% to 55.86%, which has been associated with increased disease severity and unfavorable treatment outcomes, while some studies did not find a direct significant relationship between nutritional status and response to treatment during the intensive phase of tuberculosis. There is evidence suggesting that the treatment itself can lead to improved nutritional status.[32,33,34] This indicates that health improvements from tuberculosis therapy may help enhance patients nutritional status. In this study, a high rate of medication adherence (91.3%) was observed, as evaluated using the Chinese version of the Morisky Treatment Adherence Scale.[35] Observations and interviews identified several key factors contributing to this exceptional adherence, including government subsidies, the proactive involvement of healthcare workers, and strong family support in monitoring patients throughout the treatment period. This high adherence level significantly improved the subjects' nutritional status and respons therapy of intensive phase in pulmonary TB patient. This was evident from the results of the subject's nutritional status analysis, which showed a mild improvement of 4.9% after the intensive phase of therapy (**Table 1**).

This is the first study to investigate the relationship between protein intake and nutritional status with the response to intensive phase therapy in pulmonary tuberculosis patients in Timor-Leste. Additionally, it introduces the use of SQ-FFQ to measure protein intake in future study in Timor-Leste. Additional studies with consistent methodologies and larger sample sizes are needed to better understand the relationship between nutritional status and response therapy to tuberculosis pulmonary . Regardless of the differing results, it is crucial to consider good nutritional management during tuberculosis therapy to support the overall recovery of patients.

Conclusion

There is no significant relationship between protein intake and nutritional status with the response therapy of intensive phase in pulmonary TB patients in Dili and Oecusse. However, understanding this relationship is crucial for designing better treatment protocols and nutritional support systems to improve patient outcomes during the intensive phase of TB therapy.

Open Access

Conflict of Interest

The author(s) declare(s) that there is no conflict of interest regarding the publication of this article.

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