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Correlation between Protein Intake, Fat Free Mass, and Total Lymphocyte Count with Quality of Life in Pulmonary Tuberculosis Patients Undergoing Intensive Phase Treatment in Pekanbaru, Riau Province

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Background: Malnutrition and tuberculosis (TB) have a bidirectional relationship, which interacts between each other. In chronic infection, there is an imbalance between protein degradation and protein synthesis which marked with the loss of fat-free mass (FFM). Malnutrition can cause the atrophy of the thymus gland resulted in the reduction of lymphocyte production. Malnutrition in TB patients will reduce the quality of life. On the other hand, a good quality of life will increase the treatment success rate and decrease the risk of morbidity and mortality.

Materials and Methods: A cross-sectional study was conducted in 12 primary health centers (PHC) chosen randomly from 23 PHC in Pekanbaru, Riau Province. The random selection was performed by using simple random sampling (random number generator). Data were collected from May until July 2019. Samples were selected using a consecutive sampling method and 72 subjects fulfilled all research criteria. The interview was used to collect basic characteristic data, dietary intake data, and quality of life score. Anthropometric measurement (body weight, body height, and FFM) and laboratory examination (total lymphocyte count) were done.

Results: Research showed median age subjects was 33 years old (18-59 years old). Most of the subjects were male (56.9%), had a middle level of education, low income, were active smokers with underweight nutritional status. More than 50% of subjects had low protein intake, low fat-free mass, normal lymphocyte count and had a good quality of life.

Conclusion: There was a statistically significant correlation between fat-free mass with PCS ($r=0.239$, $p=0.044$), but not for protein intake and total lymphocyte count.

Keywords: fat-free mass, protein, quality of life, total lymphocyte count, tuberculosis

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Introduction

Tuberculosis (TB) remains a global health issue because it is part of the most common cause of mortality, above the Human Immunodeficiency Virus (HIV)/Acquired Immune Deficiency Syndrome (AIDS).¹ Indonesia ranked the second after India with the highest number of TB patients across the globe followed by China, Philippines, and Pakistan.² Based on Basic Health Research (Riset Kesehatan Dasar/Riskesdas) 2018, the prevalence of population diagnosed with pulmonary TB was 0.4%. The provinces with the highest prevalence of pulmonary TB were Banten and Papua which was 0.8% from the population. However, in Riau Province, the prevalence doubled from 0.1% to 0.2% in 2018.^{3,4} Riau suffers from annual severe air pollution due to forest fire that implicated in the reduced cellular immunity within the airway and in the lung. This will eventually increase the risk of TB reactivation.⁵

Malnutrition and TB are highly prevalent and both interact between each other or called a bidirectional relationship. Malnutrition in an individual can increase the risk of infected by *Mycobacterium tuberculosis* (Mtb) and the infection itself can cause malnutrition.⁶ TB infection increases the energy required to maintain the normal function of the body. The increased energy requirement could reach 10–30% from energy requirement in a healthy individual.⁷ In addition, there is an imbalance between protein degradation with protein synthesis which is caused by the increasing body basal metabolism to fight Mtb bacteria. This condition causes the usage of protein storage in the body resulting in the loss of free-fat mass. Energy requirement for TB patient is 35–40 kcal/kg BW and for protein 1.2–1.5 g/kg BW/day.^{8,9}

Total lymphocyte count (TLC) is one of the laboratory examinations that can be used to predict the nutrition status of TB patients. Malnutrition can affect intestinal villi which resulted in decreasing the secretion of IgA and the number of lymphocytes in intestinal Peyer's Patches.¹⁰⁻¹² A previous study involving adult inpatient with chronic degenerative diseases found an association between TLC <1,200 cells/mm³ with malnutrition status.¹³

Quality of life as a measurement of outcome in TB patients was sometimes being forgotten. TB treatment with a long period time needs physical, mental, and social supports from family and others. TB treatment consists of two phases, the first two months (intensive phase) and the minimal 4 months of continuation phase.^{14,15} The most

frequent instrument used to measure the quality of life is Short Form-36 (SF-36). This questionnaire is available in Indonesian language and has been validated and checked for its validity. It also has been used for many studies to measure the quality of life in lung TB patients.¹⁶ Previous experimental studies done in pulmonary TB patients who received high calories and protein supplementations found they had better physical, emotional, and social quality of life compared to those who did not receive supplementations. Good quality of life will improve the success rate of TB treatment by decreasing the risk of drug resistance, morbidity, and mortality rate.¹⁵ However, factors that affected the quality of life among TB patients receiving the intensive phase of anti-TB drugs remains to be elucidated. The purpose of this study is to determine the correlation between protein intake, fat-free mass and TLC with quality of life in TB patients under intensive phase of treatment.

Materials and methods

Subjects and Study Design

This was a cross-sectional study conducted in 12 randomly selected primary health centers located in Pekanbaru city, Riau province from May to July 2019. Inclusion criteria were pulmonary TB patients aged 18–60 years old which were currently in the intensive phase of TB treatment, and agreed to sign informed consent. This study has received ethical approval from the Health Research Ethics Committee of Faculty of Medicine Universitas Indonesia No. 446/UN2.F1/Etik/PPM.00.02/2019. Exclusion criteria were pulmonary TB patients with comorbidities like HIV, heart diseases, kidney failure, immunodeficiency, and liver diseases. The number of samples was calculated by the formula of a correlation study.¹⁷ The coefficient correlation was referred by the previous study ($r=0.33$).¹⁸ A minimal number of samples that were required with an extra 10% of possible non-response rate was 70 subjects. From 75 subjects in the population who fulfilled the study criteria, 3 subjects did not come for blood sample collection. Therefore 72 subjects enrolled in this study. The BMI was classified by using the World Health Organization classification as underweight, normal, overweight, and obese.¹⁹

Data Collection

Subjects were interviewed to collect basic characteristics data including age, gender, level of education, income, smoking status, and history of diabetes mellitus (DM).

Anthropometric measurements were done to collect data on body height, body weight, and body composition to measure fat-free mass. Body height was measured using a stadiometer Shorrboard 2m. Bodyweight and fat-free mass measured using bioelectrical impedance analysis (BIA) Tanita RD-545. Body mass index (BMI) was calculated as weight per height squared (kg/m^2). Energy and protein intake were measured using a 2x24 hour food recall and analyzed using a computer program Nutrisurvey 2007. The interview was also done to determine the quality of life using the SF-36 questionnaire. This questionnaire measured physical component score (PCS) and mental component score (MCS) with a normal score for quality of life was ≥ 47 and low if < 47 . PCS consists of physical functioning, role physical, pain, and general health domain, meanwhile MCS consists of vitality, social-functioning, role-emotion, and mental health domain. The higher the score means better quality of life.²⁰ Total lymphocytes count was examined using the flowcytometry method in Prodia Clinical Laboratory, Pekanbaru.

Statistics Analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS) version 20 (IBM Corporation, New York, USA). Normality of data distribution was tested using Kolmogorov-Smirnov. The normally distributed data ($p > 0.05$) were described using mean and standard deviation (SD), while median with minimum-maximum was used to describe non normally distributed data ($p < 0.05$). Categorical data presented in frequency (n) and percentage (%).

Bivariate analysis was done to determine the correlation between protein intake, fat-free mass, total lymphocytes count, and subject characteristics (age and BMI) with quality of life using Pearson correlation test if the data were normally distributed and using Rank Spearman if the data were not normally distributed. For categorical data (gender, level of education, income, smoking status, history of DM, and nutrition status) with not normally distributed data were analyzed using the Mann-Whitney test to compare means from two independent groups and using Kruskal Wallis test for > 2 independent groups.

Results

Basic characteristics data of subjects can be seen in Table 1 including age, gender, level of education, income, smoking status, history of diabetes mellitus, BMI, and nutrition

Table 1. Basic characteristics of the subjects.

Basic Characteristics (n=72)	Results
Age (years), median (min-max)	33 (18–59)
Gender	
Male, n (%)	41 (56.9)
Female, n (%)	31 (43.1)
Level of education	
Low, n (%)	19 (26.4)
Middle, n (%)	47 (65.3)
High, n (%)	6 (8.3)
Income	
Low, n (%)	42 (58.3)
Adequate, n (%)	30 (41.7)
Smoking status	
Active smoker, n (%)	29 (40.3)
Passive smoker, n (%)	25 (34.7)
Ex-smoker, n (%)	4 (5.6)
Non-smoker, n (%)	14 (19.4)
History of DM	
Yes, n (%)	2 (2.8)
No, n (%)	70 (97.2)
BMI (kg/m^2), mean \pm SD	18.73 \pm 2.94
Nutrition status based on BMI	
Underweight, n (%)	34 (47.2)
Normal, n (%)	32 (44.4)
Overweight, n (%)	4 (5.6)
Obese, n (%)	2 (2.8)

status. The median age of subjects was 33 (18–59) years old. Most of the subjects were males (56.9%), had a middle level of education (65.3%), and had low income compared to city minimum wage (58.3%). From all subjects, 40.3% were active smokers and 2.8% had a history of DM. The mean BMI was $18.73 \pm 2.94 \text{ kg}/\text{m}^2$ with 47.2% of the subjects categorized as underweight.

Table 2 shows the energy and protein intake of subjects. The mean of total energy intake was $1552.75 \pm 414.60 \text{ kcal}/\text{day}$ and most of the subjects (63.9%) had low total energy intake. Median protein intake was $55.35 \pm 19.38 \text{ g}/\text{day}$ and 59.7% subjects had low protein intake.

Table 3 shows the FFM and fat-free mass index (FFMI) of the subjects. The mean FFM of subjects was $38.19 \pm 7.20 \text{ kg}$ and FFMI was $14.72 \pm 1.85 \text{ kg}/\text{m}^2$. Most of the subjects had low FFM (86.1%) and FFMI (81.9%).

Table 2. Energy and protein intake of the subjects.

Variable	Results
Total energy intake (kcal/day), mean±SD	1552.75±414.60
Adequate (≥ 35 kcal/kg BW/day), n (%)	26 (36.1)
Low (< 35 kcal/kg BW/day), n (%)	46 (63.9)
Total protein intake (kcal/day), mean±SD	55.35±19.38
Adequate (≥ 1.2 g/kg BW/day), n (%)	29 (40.3)
Low (< 1.2 g/kg BW/day), n (%)	43 (59.7)

Table 4 shows the TLC of the subjects. Median TLC was 1,930 (620-4,230) cell/mm³ and most of the subjects (88.9%) had normal TLC.

Table 5 shows the quality of life scores of the subjects. Median PCS quality of life was 51.25 (26.87-92.50) and 53.41 (30.50-94.50) for MCS quality of life. Most of the subjects had normal PCS (65.3%) and MCS scores (73.6%).

Table 6 shows correlation between protein intake, FFM, and TLC with PCS and MCS. There was a statistically significant weak positive correlation between fat-free mass with PCS ($r=0.239$, $p=0.044$), however there was no correlation with MCS. No other correlations found between protein intake with PCS ($r=0.131$, $p=0.271$) and MCS ($r=0.085$, $p=0.475$) and TLC with PCS ($r=0.091$, $p=0.046$) and MCS ($r=0.095$, $p=0.429$).

Discussion

The mean BMI of subjects was 18.73±2.94 kg/m². Even though the mean BMI was within the normal category, almost half of the subjects (47.2%) nearly reached the underweight category. This result was higher compared to the previous study that stated the prevalence of malnutrition

among TB patients was 39.7%.²¹ Nutrition has a significant role in health and body function including the immune system. Malnutrition will weaken the immune system which can decrease the ability to fight against and control infection like TB.²²

Based on dietary intake data, 50% of subjects had low energy and protein intakes. This result was lower than the previous study which stated 80% of TB patients had low energy and protein intakes compared to the recommendation for energy requirement for TB patients.²³ The difference might be caused by several reasons like economic status in an area and recall bias in dietary intake measurement.

Energy requirement for TB patient is 35–40 kcal/kg BW/day and for protein is 1.2–1.5g/kg BW/day.^{8,9} This energy requirement is higher compared to healthy individual's requirement.²⁴ This higher requirement is caused by infection which body needs extra energy to fight against Mtb.^{23,25} Basic principle nutritional therapy for TB patients based on WHO: Nutritional Care and Support for patients with Tuberculosis stated that nutrition status of every active TB patient needs to be assessed and given nutritional therapy based his condition.⁷

Table 3. Fat-free mass and fat-free mass index of the subjects.

Variable	Results
Fat-free mass (kg), mean±SD	38.19±7.20
Normal, n (%)	10 (13.9)
Low, n (%)	62 (86.1)
Fat-free mass index (kg/m ²), mean±SD	14.72±1.85
Normal, n (%)	13 (18.1)
Low, n (%)	59 (81.9)

Table 4. Total lymphocyte count of the subjects.

Variable	Results
Total lymphocytes count, median (min-max)	1,930 (620-4,230)
Normal ($\geq 1,200$ cells/mm ³), n (%)	64 (88.9)
Low ($< 1,200$ cells/mm ³), n (%)	8 (11.1)

Based on body composition data, more than 80% of subjects had low fat free mass and low fat free mass index indeks or had a risk for malnutrition based on 2015 European Society for Parenteral and Enteral Nutrition (ESPEN) malnutrition criteria for adult.²⁶ Malnutrition caused by chronic diseases like TB will decrease fat-free mass in a rapid term. This is caused by an imbalance of metabolism inside the body. The amino acid requirement from protein will increase to gain more energy to fight against infection with low protein intake in TB patients will make the body uses protein storage in muscles and visceral protein in circulation, which are the main storage of protein inside the body.^{12,27}

Median TLC of the subjects were 1,930 (620–4,230) and 11.1% of subjects had low TLC. This result was lower than previous study in Indonesia³ which 33% inpatients in Cipto Mangunkusumo General Hospital with chronic diseases had low TLC. This difference can be caused by most of the subjects already received TB therapy, therefore the number of Mtb decreased which results increasing TLC. Furthermore, subjects in our study were from an outpatient setting with minimal comorbidity.

Quality of life assessment in this study used SF-36 questionnaire. SF-36 can measure physical health (with PCS) and mental health (with MCS). The result of this study shows most of the subjects had normal PCS and

MCS. From PCS, subjects were able to their daily activities without being disturbed by their illness and their ongoing treatment. In addition, from MCS, subjects rarely felt depressed, worried, or hopeless when they knew that they suffered from TB disease and needed to undergo long term treatment.²⁸

This study result shows there was no correlation found between protein intake with PCS ($p=0.271$) and MCS ($p=0.475$) and between TLC with PCS quality of life ($p=0.446$) and MCS ($p=0.429$). There was a weak positive correlation between FFM with PCS quality of life ($r=0.239$, $p=0.044$), but no correlation with MCS ($p=0.131$). This result was similar to the previous study⁴, in which TB patients who received high calories and high protein food supplementations for 12 weeks were examined for their handgrip strength and their quality of life. This hand grip strength describes the increasing FFM in TB patients. The result of this study found TB patients who received food supplementations had better hand grip strength and quality of life compared to those who did not receive food supplementations.

The strength of this study is that we provided the prevalence and determine the association between nutrition status, protein intake, FFM, TLC, and quality of life TB patients in primary health centers in Pekanbaru city, Riau province. Assessment of dietary intake was done by trained

Table 5. Quality of life of subjects.

Variable	Results
Physical component score (PCS), median (min-max)	51.25 (26.87-92.50)
Normal (≥ 47), n (%)	47 (65.3)
Low (< 47), n (%)	25 (34.7)
Mental component score (MCS), median (min-max)	53.41 (30.50-94.50)
Normal (≥ 47), n (%)	53 (73.6)
Low (< 47), n (%)	19 (26.4)

Table 6. Correlation between protein intake, fat-free mass, and total lymphocytes count with physical component score and mental component score (n=72).

Variable	Physical Component Score (PCS)		Mental Component Score (MCS)	
	r	p	r	p
Protein intake	0.131	0.271 ^S	0.085	0.475 ^S
Fat-free mass	0.239	0.044^P	0.180	0.131 ^P
Total lymphocytes count	0.091	0.446 ^S	0.095	0.429 ^S

r: correlation coef; p: p-value<0.05; ^P: Pearson test; ^S: Spearman test.

dietitian to collect food recall data. TLC examination was done in Prodia Clinical Laboratory, which is accredited by KAN International Organization for Standardization (ISO) 15189. The weakness of this study was the study design. This design has a limitation that only can examine the association within one-time assessment and cannot examine the changes within different periods. Recall bias can be happened during dietary intake assessment due to the food recall is relied on subjects' memory.

Conclusion

In conclusion, protein intake and TLC were not significantly correlated with quality of life. However, fat-free mass has a weak significant correlation with the physical aspect of quality of life. A high prevalence of malnutrition in TB patients can affect the quality of life. Good quality of life will increase the success rate of treatment. More studies needed to examine other factors that affect TB patients' quality of life.

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