Open Peer Review on Qeios

Medical Nutrition Therapy in Hospitalized Pulmonary Tuberculosis Patients: A Retrospective Analysis of Its Effect on Monocyte-to-Lymphocyte Ratio (MLR), Neutrophil-to-Lymphocyte Ratio (NLR), and Prognostic Nutritional Index (PNI)

Aminuddin Aminuddin[1], Urfa Patunru, Suryani As'ad[2], Andi Yasmin Syauki[2], Agussalim Bukhari[2], Nurpudji Astuti Taslim[2]

1 Universitas Hasanuddin

2 Hasanuddin University

Funding: No specific funding was received for this work.

Potential competing interests: No potential competing interests to declare.

Abstract

Introduction: The management of malnutrition plays a pivotal role in the treatment of pulmonary tuberculosis. Laboratory indices routinely examined such as monocyte-to lymphocyte ratio, neutrophil-to-lymphocyte ratio, and prognostic nutritional index may be of importance to evaluate nutrition intervention and/or overall therapy of in-patient pulmonary tuberculosis.

Objective: This study aims to examine the effects of medical nutrition therapy on monocyte-to-lymphocyte ratio, neutrophil-to-lymphocyte ratio and prognostic nutritional index in hospitalized pulmonary tuberculosis patients

Methods: A retrospective study was conducted on pulmonary TB patients who underwent medical nutrition therapy at Wahidin Sudirohusodo Hospital between 2018 and 2020. Data were collected and extracted for analysis from eligible subjects' medical records

Results: Out of 418 pulmonary TB patients who were institutionalized in the period, data from 133 subjects who underwent medical nutrition therapy who met inclusion criteria were extracted. All subjects were malnourished either moderately or severely based on Subjective Global Assessment. All subjects showed significant improvement in all three indices namely monocyte-to-lymphocyte ratio, neutrophil-to-lymphocyte ratio, and prognostic nutritional index at the end medical nutrition therapy. Improvement magnitude of monocyte-to-lymphocyte ratio and neutrophil-to-lymphocyte ratio is higher if levels of average energy and protein intake are >1500 kcal and >75 gram, respectively

Conclusion: Medical nutrition therapy plays a crucial role in hospitalized pulmonary tuberculosis patients' clinical improvement as shown by monocyte-to-lymphocyte ratio, neutrophil-to-lymphocyte ratio, and prognostic nutritional index.

Aminuddin Aminuddin[1,4,*], **Urfa Patunru**[2], **Suryani As'ad**[1,3], **Andi Yasmin Syauki**[1,5], **Agussalim Bukhari**[1,5], and

Nurpudji Astuti Taslim[1,5]

[1]*Department of Nutrition, Faculty of Medicine Hasanuddin University, Makassar, Indonesia*

[2]*Clinical Nutrition Specialist Program, Faculty of Medicine Hasanuddin University, Makassar, Indonesia*

[3]*Faculty of Medicine Muhammadiyah University, Makassar, Indonesia*

[4]*Hasanuddin University Hospital, Makassar, Indonesia*

[5]*Wahidin Sudirohusodo Hospital, Makassar, Indonesia*

*Corresponding author. Email: aminuddin@med.ac.id

Keywords: Pulmonary TB, Medical Nutrition Therapy, MLR, NLR, PNI.

Introduction

Malnutrition is known to be associated with pulmonary TB (PTB).[1] Malnutrition may impair immune system and increase vulnerability to infections; on the other hand, PTB leads to anorexia, malabsorption of nutrients, and hypermetabolism leading to malnutrition. Hospitalized PTB patients have been found to have an increased risk of malnutrition and all-cause mortality in the follow-up.[2] Therefore, managing malnutrition is crucial during pulmonary TB treatment to achieve better clinical outcomes.

The expression of inflammatory factors and the heightened activity of certain leucocyte cells, some of them can be measured using the monocyte to lymphocyte ratio (MLR) and Neutrophil to Lymphocyte Ratio (NLR) to evaluate PTB response to therapy including medical nutrition therapy.[3] These ratios may show low-cost and effective markers for PTB therapy including medical nutrition therapy especially for those PTB patients with and/or at risk of malnutrition.

Objective

The objective of this study is to assess the effect of medical nutrition therapy on MLR, NLR as well as PNI in hospitalized patients with PTB.

Research Methods

This is a retrospective study focused on patients with PTB who underwent medical nutrition therapy at Wahidin Sudirohusodo Hospital in Makassar between 2018 and 2020. The ethical clearance of the study was approved by Ethical Clearance Committee Faculty of Medicine Hasanuddin University Decree No 8/UN4.6.4.5.31/PP36/2023. All data were extracted from medical records.

Inclusion criteria were as follows: [1] patients aged over 18 years, diagnosed with pulmonary TB by pulmonologists; [2] patients underwent medical nutrition therapy by clinical nutrition physicians;[3] patients were hospitalized for more than 5 days; [4] availability of laboratory test results (routine blood, albumin), nutritional status assessment using Subjective Global Assessment (SGA). Subjects were excluded if they had Glasgow Coma Scale (GCS) score less than 5, died during treatment, and were HIV co-infected. All patients received standard pulmonary TB therapy by pulmonologists and when they were referred to clinical nutrition physicians further received nutritional supports through oral nutrition, enteral, parenteral or combination. In addition to nutritional support, some patients received supplements of vitamin B complex, Zinc, vitamin A, vitamin C, and vitamin D within recommended dietary allowance dosages.

Nutritional status was defined according to SGA assessment: A (well nourished), B (moderate malnutrition), or SGA C (severe malnutrition). Monocyte to Lymphocyte Ratio was derived from absolute count of monocytes divided by absolute count of lymphocyte, whereas Neutrophil to Lymphocyte Ratio was derived by dividing absolute count of neutrophils by absolute count lymphocytes. Prognostic Nutritional Index (PNI) was calculated using equation: (10 x serum albumin (gram/dl) + (0.005 x total lymphocyte count). Magnitude of change of MLR (Δ MLR) and NLR (Δ NLR) were calculated by subtracting MLR and NLR ratios at admission to their ratios at the end of MNT.

All statistical analysis were performed with SPSS. Statistical significance was set at $P < 0.05$.

Results

Of the 418 pulmonary TB patients institutionalized during the period, 133 subjects underwent medical nutrition therapy and met the inclusion criteria, subsequently included in data processing and analysis. All subjects were either moderately or severely malnourished based on SGA assessment in the admission time. Majority of them were hospitalized for less than 14 days. Of note, average intake of energy and macronutrients between PTB patients with SGA score B and C was comparable during medical nutrition therapy. On average, subjects received MNT in half of their length of stay in hospital (see Table 1).

We then compared intake of energy and macronutrients, as well as indices such as MLR, NLR and PNI between subjects before referral for and at the end of medical nutrition therapy when optimal nutritional support is usually achieved. Intake of energy and macronutrients as well as all three indices have improved significantly (see Table 2).

Table 1. Subject characteristics

Subject Characteristics		ALL	SGA		P
			B	C	
			N (%)	N (%)	
Age (Mean ± SD) year		48.35 ± 15.71	52.98 ± 13.69	45.38 ± 16.28	
Gender	Man (%)	92 (69.2)	36 (69.2)	56 (69.1)	
	Woman (%)	41 (30.8)	16 (30.7)	25 (30.8)	
Marital status	Not Married (%)	20 (15)	3 (5.7)	17 (20.9)	
	Married (%)	111 (83.5)	48 (92.3)	63 (77.7)	
	Widow (%)	2 (1.5)	1 (1.9)	1 (1.2)	
LOS	≤14 days (%)	76 (57.1)	30 (57.7)	46 (56.8)	
	> 14 days (%)	57 (42.9)	22 (42.3)	35 (43.2)	
Average LOS ± SD (days)		15.17 ± 8.93			
Average on MNT± SD (days)		8.54 ± 4.90			
Actual Body Weight (Mean ± SD) Kg		42.65 ±10.38	49.36 ± 11.47	37.11 ± 6.28	
Body Height (Mean ± SD) cm		160.14 ± 8.39	163.56 ± 7.38	158.29 ± 15.15	
MUAC (Mean ± SD) cm		20.15 ± 3.43	22.85 ± 2.74	18.40 ± 2.60	
BMI (Mean ± SD)		23.79 ± 9.13	27.36 ± 11.03	20.37 ± 5.07	
Average Intake during MNT	Energy (Mean ± SD) kcal	1413.54 ± 1066.39	1667.36± 1590.81	1233.14 ± 446.06	0.089
	Proteins (Mean ± SD) gram	57.98 ± 24.36	63.53 ± 24.04	53.70 ± 24.62	0.052
	Carbohydrate (Mean ± SD) gram	198.54 ± 55.63	211.65 ± 39.58	190.01 ± 59.76	0.085
	Fat (Mean ± SD) gram	40.74 ± 17.65	44.77 ± 20.41	38.12 ± 15.16	0.120

MUAC: Mid Upper Arm Circumference, BMI: Body Mass Index; SGA: Subjective Global Assessment; LOS: Length of Stay SD: Standard Deviation; MNT: Medical Nutrition Therapy. Anthropometric data were from within admission, LOS was calculated from day 1 admission until discharge. Statistical analysis to compare average intake during MNT were performed using Mann-Whitney U test.

Table 2. Comparison of energy and macronutrient Intake, MLR, NLR, and PNI before and at the end of medical nutrition therapy

Variable	Before MNT Mean ± SD	End of MNT Mean ± SD	p value
Energy Intake	639.96 ± 373.98	1616.27 ± 530.86	0.011*
Protein Intake	31.23 ± 18.81	73.91 ± 28.85	0.007*
Carbohydrate Intake	108.77 ± 64.26	270.04 ± 252.85	0.000*
Fat Intake	13.56 ± 13.05	45.35 ± 20.05	0.000*
MLR	0.84 ± 0.65	0.27 ± 0.31	0.006*
NLR	10.15 ± 12.38	6.93 ± 5.50	0.001*
PNI	34.80 ± 97.52	44.52 ± 12.16	0.001*

*MLR: Monocyte to Lymphocyte Ratio; NLR: Neutrophil to Lymphocyte Ratio; PNI: Prognostic Nutritional Index. MNT: Medical Nutrition Therapy; SD: Standard Deviation. Statistical analysis was performed using Wilcoxon test. * p < 0.01*

Table 3 shows that decreasing magnitude of MLR and NLR are higher if mean energy and protein intake >1500 kcal and >75 grams, respectively. We arbitrarily set these cut-off points because they correspond to 35.7 kcal and 1.78 gram intake of energy and protein per average subject body weight (~42 kg), respectively, which we consider adequate levels.

Table 3. Magnitude of change of MLR and NLR based on arbitrary average energy and protein intake cut-off points

Variable	Energy		P value
	< 1500 (n: 54)	≥1500 (n:79)	
	Mean ± SD	Mean ± SD	
Δ MLR	2.73 ± 8.71	-0.53 ± 2.11	0.027
Δ NLR	-0.31 ± 10.72	-2.32 ± 4.44	0.031
Variable	**Proteins**		**P value**
	<75 gr (n: 57)	≥ 75 gr (n: 76)	
	Mean ± SD	Mean ± SD	
ΔMLR	- 0.16 ± 0.36	-0.51 ± 0.59	0.012
ΔNLR	-0.63 ± 5.41	-3.32 ± 11.33	0.004

Statistical analysis performed using Mann-Whitney U test, significance was set at p < 0.05

Discussion

Energy intake of PTB patients is commonly low before hospitalization leading to an increased risk of malnutrition.[4] As shown in our subjects, all of them were moderately or severely malnourished based on SGA assessment. Prolonged inadequate energy intake can cause macro- and micronutrient deficiency. A study in Brazil shows that median intake of

less than 1400 kcal is associated with high prevalence of protein, vitamins and minerals in older adults.[5] Furthermore, it has been shown by studies that PTB patients show multiple low levels of micronutrients when they are on active TB treatment as out-patients.[6][7]Our data shows that energy intake of hospitalized PTB before referral was low. In our data, majority of these PTB patients were referred for MNT after 4 days of admission (data not shown). On average our subjects received MNT half of their length of stay in hospital. It is highly likely that our subjects also had prolonged inadequate energy intake before hospitalization as all of them were malnourished when admitted for hospitalization.

At the end of MNT, average intake of PTB patients reached +1600 kcal, little above arbitrary 1500 kcal cut-off point at which MLR and NLR indices showed stronger improvement. Indeed, at the end of MNT all indices that are correlated to therapy effectiveness i.e. MLR, NLR, and PNI show significant improvement. However, this favorable effect can not solely attributable to medical nutrition therapy the subjects had, as this study did not control for the other therapies including standard therapy of PTB with tuberculostatic medicines. This a drawback of this study that may be addressed in future study by comparing hospitalized PTB patients who receive MNT and those with no MNT by clinical nutrition physicians. In Indonesia, clinical nutrition physicians are board-certified medical doctors specialized in prescribing and managing nutritional support for patients in hospital setting.

As malnutrition in PTB patients in hospital setting are associated with increased mortality and decreased rate of successful therapy, provision and evaluation of MNT are becoming more important. Effective MNT is, in part- depending on provision of adequate energy, macro- and micronutrients during therapy in hospital. Evaluating adequacy of nutritional provision may use low cost, routinely available, but informative indices such as MLR, NLR, and PNI as this study shows. Moreover, these indices as well as others have been shown to have versatile function such as markers of immune status, inflammatory status, prognostic prediction, bacterial negative-pulmonary tuberculosis.

Conclusion

Medical nutrition therapy plays a crucial role in hospitalized pulmonary tuberculosis patients' clinical improvement as shown by monocyte-to-lymphocyte ratio, neutrophil-to-lymphocyte ratio, and prognostic nutritional index. Ensuring adequate energy and protein intake during medical nutrition therapy as well as micronutrient supplementary -if deemed necessary- is an important step of effective MNT. [8][9][10]

References

1. [a, b]*Li A, Yuan SY, Li QG, Li JX, Yin XY, Liu NN. Prevalence and risk factors of malnutrition in patients with pulmonary tuberculosis: a systematic review and meta-analysis. Front Med (Lausanne). 2023 Aug 10;10:1173619.*
2. [a, b]*Ma JJ, Guo YJ, Li Z, Chen Y, He H, Li WM. Prevalence and prognostic significance of malnutrition risk in patients with pulmonary tuberculosis: A hospital-based cohort study. Front Public Health. 2022 Dec 13;10:1039661.*
3. [a, b]*Omair M, Baig MS, Farooqui WA, Kousar S, Noori MY, Zeehan N, et al. Relationship of neutrophil lymphocyte ratio, monocyte lymphocyte ratio and neutrophil monocyte ratio with treatment response in pulmonary tuberculosis patients*

during intensive phase treatment. BMC Infect Dis [Internet]. 2024 Dec 1 [cited 2024 Jun 27];24(1):1–7. Available from: https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-024-09454-2

4. [a, b]*Hung NT, Nga NTH, Hung LX, Thao NP, Cuong NK, Nhung LTT. Nutritional status and dietary intake before hospital admission of pulmonary tuberculosis patients. AIMS Public Health [Internet]. 2023 [cited 2024 Jun 28];10(2):443. Available from: /pmc/articles/PMC10251045/*
5. [^]*Magalhães NV, Waitzberg DL, Lopes NC, Vicedomini ACC, Prudêncio APA, Jacob-Filho W, et al. High Prevalence of Energy and Nutrients Inadequacy among Brazilian Older Adults. Nutrients [Internet]. 2023 Jul 1 [cited 2024 Jun 28];15(14). Available from: /pmc/articles/PMC10384757/*
6. [^]*Feleke BE, Feleke TE, Mekonnen D, Beyene MB. Micronutrient levels of tuberculosis patients during the intensive phase, a prospective cohort study. Clin Nutr ESPEN [Internet]. 2019 Jun 1 [cited 2024 Jun 28];31:56–60. Available from: http://clinicalnutritionespen.com/article/S2405457719300944/fulltext*
7. [^]*Karyadi E, Schultink W, Nelwan RHH, Gross R, Amin Z, Dolmans WMV, et al. Poor Micronutrient Status of Active Pulmonary Tuberculosis Patients in Indonesia. J Nutr. 2000 Dec 1;130(12):2953–8.*
8. [^]*Liu QX, Tang DY, Xiang X, He JQ. Associations between nutritional and immune status and clinicopathologic factors in patients with tuberculosis: A comprehensive analysis. Front Cell Infect Microbiol. 2022 Nov 24;12:1013751.*
9. [^]*Chai B, Wu D, Fu N, Huang P, Shen Y, Li Y, et al. Evaluation of prognostic inflammatory and systemic inflammatory response indices in auxiliary diagnosis of bacteria-negative pulmonary tuberculosis: A diagnostic accuracy study. Medicine [Internet]. 2023 Mar 24 [cited 2024 Jun 28];102(12):E33372. Available from: https://pubmed.ncbi.nlm.nih.gov/36961144/*
10. [^]*Ma JJ, Guo YJ, Li Z, Chen Y, He H, Li WM. Prevalence and prognostic significance of malnutrition risk in patients with pulmonary tuberculosis: A hospital-based cohort study. Front Public Health [Internet]. 2022 Dec 13 [cited 2024 Jun 28];10. Available from: https://pubmed.ncbi.nlm.nih.gov/36582380/*