Total Lymphocyte Count as a Nutritional Parameter in Hospitalized Patients

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ABSTRACT

Background: *Nowadays, there are still many malnourished patients during hospitalization, which comprises around 45-50% patients. Malnutrition is related to increased mortality and morbidity rate; therefore, nutritional state should be assessed in hospitalized patients. Total lymphocyte count (TLC) is related to decreased body function in malnutrition and it is a means of nutritional assessment. Until now, there is no data showing association between malnutrition and TLC in hospitalized patients in Indonesia. The objective of this study was to identify the association between malnutrition and TLC < 1,200 cell/mm³ in hospitalized patients.*

Method: *This study was a cross-sectional study. Subjects were new patients hospitalized at internal medicine ward of Cipto Mangunkusumo Hospital. Patients were collected by consecutive sampling. We conducted the study between April and May 2008. Fifty four patients were assessed for malnutrition by the subjective global assessment (SGA) and they also had undergone complete blood count. TLC was numbered with routine complete blood count test. Patients were classified into malnutrition according to SGA. TLC was classified with cut-off point of 1,200 cell/mm³. Statistical analysis included Chi-square test, which was used to compare proportion.*

Results: *There were 52% malnourished patients, 33% patients with TLC < 1,200 cell/mm³, 57% patients with malnutrition and TLC < 1,200 cell/mm³. This study showed that there was an association between malnutrition and TLC < 1,200 cell/mm³ (p = 0.001). Moreover, there was also significant association between severe malnutrition (SGA C) with TLC < 900 cell/mm³ (p = 0.02).*

Conclusion*: There is an association between malnutrition and TLC < 1,200 cell/mm³.*

Keywords: *malnutrition, total lymphocyte count, body mass index, subjective global assessment*

ABSTRAK

Latar belakang: *Hingga saat ini sekitar 45-50% pasien mengalami malnutrisi saat masuk rumah sakit. Malnutrisi berhubungan dengan peningkatan angka mortalitas dan morbiditas, karena itu status nutrisi harus dinilai pada setiap pasien yang dirawat. Jumlah limfosit total berhubungan dengan malnutrisi dan dapat digunakan untuk menilai status nutrisi. Sampai saat ini belum ada data yang menunjukkan asosiasi antara malnutrisi dengan jumlah limfosit total pada pasien yang sedang dirawat di rumah sakit di Indonesia. Tujuan penelitian ini adalah untuk menunjukkan asosiasi antara malnutrisi dengan TLC < 1.200 sel/mm³ pada pasien yang dirawat di rumah sakit.*

Metode: *Penelitian ini merupakan penelitian potong lintang yang dilakukan di Rumah Sakit Cipto Mangunkusumo pada bulan April–Mei 2008. Subjek penelitian adalah pasien yang baru masuk ruang perawatan penyakit dalam. Subjek direkrut konsekutif, sebanyak 54 pasien. Penilaian status nutrisi dilakukan dengan menggunakan subjective global assessment (SGA), dan dilakukan pemeriksaan darah perifer lengkap. Status nutrisi pasien diklasifikasikan menggunakan SGA. Jumlah limfosit total diklasifikasikan dengan batas 1.200 sel/mm³. Asosiasi dilihat dengan beda proporsi dan diuji statistik kai kuadrat.*

Hasil: *Didapatkan 52% pasien malnutrisi dan 33% pasien dengan TLC < 1.200 sel/mm³, 57% pasien malnutrisi dengan jumlah limfosit total < 1.200 sel/mm³. Penelitian ini mendapatkan asosiasi antara malnutrisi dengan jumlah limfosit total < 1.200 sel/mm³ (p = 0,001) dan asosiasi antara malnutrisi berat (SGA C) dengan jumlah limfosit total < 900 sel/mm³ (p = 0,02).*

Kesimpulan: *Terdapat asosiasi antara malnutrisi dengan jumlah limfosit total < 1.200 sel/mm³.*

Kata kunci: *malnutrisi, jumlah limfosit total, indeks massa tubuh, subjective global assessment*

INTRODUCTION

Nutrition is one of basic human needs. It preserves energy, regenerates cells and also may play a role in healing process.[1-3] Under nutrition or malnutrition refers to deficiencies in calories and protein, accompanied with decreased body mass and organ dysfunction, including immunosupression and reduced lymphocyte count.[3-5] Malnutrition may cause complications and delayed healing process, especially in hospitalized patients. Nowadays, there are still many malnourished patients in hospitals, which comprises 40-50% patients.[6-10] Malnutrition is an illness associated with considerable length of hospitalization stay, higher morbidity and mortality rate.[10-15] Therefore, it is important to assess nutritional state of each hospitalized patient to detect malnutrition.

There are many modalities to assess nutritional state, including anthropometry, laboratory tests, nutritional assessment tools, subjective global assessment (SGA), nutritional risk screening (NRS) 2002, and mini nutritional assessment (MNA). These methods are based on measurement of body mass or organ dysfunction due to malnutrition.

Low total lymphocyte count as one component of routine complete blood count test is related to malnutrition. Total lymphocyte count (TLC) < 1,200 cell/mm³ is related to malnutrition, and TLC < 900 cell/mm³ is related to severe malnutrition.[3,5] In acute or chronic starvation, T lymphocyte will decrease. The number will increase with realimentation.[5,6] Lymphocyte count can be used as a nutritional parameter and as a predictor of prognosis.[11,12] There had been no data on association between malnourished hospitalized patients and TLC in Indonesian general hospital. The aim of this study was to demonstrate the association between malnutrition and TLC in malnourished hospitalized patients.

METHOD

The study was a cross-sectional study conducted between April to Mei 2008 at Internal Medicine Ward, Cipto Mangunkusumo Hospital. Subject of the study involved all new patients who were hospitalized in the ward with various diagnoses. Inclusion criteria were all adult patients between the age of 18 and 59 years, who were able to stand on body weight and height measurement. The exclusion criteria were patient who has any evidence of aplastic anemia, myelodysplatia syndrome, acquired immune deficiency syndrome (AIDS), dengue fever, systemic lupus erythematosus (SLE), and leukemia; patient who has prior history of chemotherapy, steroid, and amputation.

The nutritional assessment of all patients was performed by using body mass index (BMI) classification form (body weight in kilograms divided by the square of the height in meters) and SGA classification technique form as outline by Detsky, et al, 1987.[16] All of these forms were translated to Indonesian and recorded in subject's form. Malnutrition in the study was classified as SGA B or SGA C and when the BMI was below 18.5 kg/m². Severe malnutrition was classified as SGA C and BMI of less than 16 kg/m². TLC was calculated by multiplying cell type in the differential count with the total white blood count. TLC was classified as < 1,200 cell/mm³ and ≥ 1,200 cell/mm³, which was determined using cell counter of the flow cytometry method. These examinations were performed as the patients were admitted to the ward.

Data were analyzed using a computer program, SPSS for windows, version 15.0. Data were presented as mean percentage and proportion; while the association was confirmed by using Chi-square test. The study was approved by the ethical committee, Faculty of Medicine, University of Indonesia.

RESULTS

Of 54 patients in the study, 32 (59%) were female. The age range was between 18 and 59 years, with the mean age of 43 years (SD = 12.2). Patient characteristics were shown in Table 1.

Table 1. Baseline patient characteristics

	Result	%
Age (years)		
Range	18-59	
Mean (SD)	43 (12.2)	
Sex		
Male	22	41
Female	32	59
Diagnosis of disease		
Heart disease	10	18.5
Digestive problems	10	18.5
Pulmonary disease	7	13
Lung tuberculosis	6	11.1
Liver disease	3	5.6
Malignancy	3	5.6
Diabetes mellitus	3	5.6
Tropical infection disease	6	11.1
Kidney disease	6	11.1
Number of disease problems		
1	19	35
> 1	35	65
Body mass index (kg/m^2)		
< 18.5	19	35
≥ 18.5	35	65
Mean (SD)	21 (5)	
Total lymphocyte count (cell/mm^3)		
< 1,200	18	33
≥ 1,200	36	67
Mean (SD)	1,663 (839)	
Subjective global assesment		
A	26	48
B	20	37
C	8	15
Albumin (g/dL)		
Mean (SD)	2.9 (0.8)	
Range	1.2-5	

Of 54 patients, 35 (65%) patients were with multiple diagnosis or problems, and 28 (52%) patients had malnutrition, which was assessed by SGA. The patient's primary problems and distribution of illness and nutritional state are listed in Table 2.

Table 2. Distribution of malnutrition among patients with illness

Disease	Malnutrition (SGA B/C) n (%)	Normal nutrition (SGA A) n (%)	n
Heart disease	5 (50)	5 (50)	10
Digestive problems	6 (60)	4 (40)	10
Pulmonary	4 (57)	3 (43)	7
Lung tuberculosis	5 (83)	1 (17)	6
Liver disease	1 (33)	2 (67)	3
Malignancy	2 (67)	1 (33)	3
Diabetes mellitus	0 (0)	3 (100)	3
Tropical infection	2 (33)	4 (67)	6
Kidney disease	3 (50)	3 (50)	6
Total	28 (52)	26 (48)	54

SGA: subjective global assessment

Most patients were hospitalized with one or more diseases or problems. This study showed significant association between having more than 1 diseases and malnutrition (OR = 3.7; 95% CI = 1.1-12; p = 0.03). We found no association between infectious diseases and malnutrition (OR = 1.7; 95% CI = 0.5-5.2; p = 0.36). However, we found significant differences in mean TLC between patients with malnutrition and normal nutrition. These results are consistent with some reports about nutritional status based on BMI criteria (p = 0.001; 95% CI = 733.1-1443.3) *(*Figure 1).

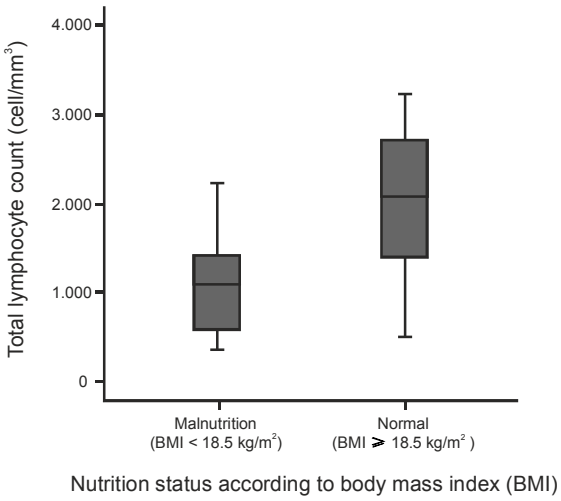

Figure 1. Median total lymphocyte count in patients with malnutrition and normal nutrition as measured by body mass index (BMI)

We found that there was a strong correlation between TLC and albumin concentration (r = 0.61; p = 0.001) (Figure 2). There was an association of malnutrition with TLC and nutritional status as assessed by SGA (p = 0.001; OR = 16; 95% CI = 3.1-81.3) (Table 3).

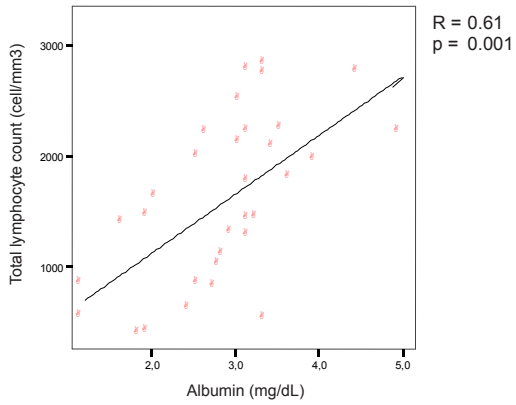

Figure 2. Correlation between albumin and total lymphocyte count

Table 3. The association between malnourished hospitalized patients and total lymphocyte count < 1,200 cell/mm³

Nutritional status (SGA)	Total lymphocyte count (cell/mm³)		n	p*
	< 1,200 n (%)	≥ 1,200 n (%)		
Malnutrition (SGA B/C)	16 (57)	12 (43)	28	
Normal (SGA A)	2 (4)	24 (96)	26	0.001
Total	18 (33)	36 (67)	54	

SGA: subjective global assessment; *chi-squre test

The study showed a significant correlation between malnutrition (as classified by BMI) and TLC (p = 0.01; OR = 8.3; 95% CI = 2.3-29.8) (Table 4). The study found 5 patients with severe malnutrition (SGA C or BMI < 16 kg/m²). Moreover, there was a correlation between severe malnutrition and TLC of < 900 cell/mm³. These correlations were consistent whether the nutrional status were assessed by BMI or SGA (p = 0.02; OR = 6.8; 95% CI = 3-34.1) (Table 5).

Table 4. The association between malnourished patients with total lymphocyte count < 1,200 cell/mm³

Nutritional status	Total lymphocyte count (cell/mm³)		n	p*
	< 1,200 n (%)	≥ 1,200 n (%)		
Malnutrition (BMI < 18.5)	12 (63)	7 (37)	19	
Normal nutrition (BMI ≥ 18.5)	6 (17)	29 (83)	35	0.01
Tota	18 (33)	36 (67)	54	

BMI: body mass index; *chi-square test

Table 5. The association between severe malnutrition and total lymphocyte count < 900 cell/mm³

Nutritional status	Total lymphocyte count (cell/mm³)		n	p*
	< 900 n (%)	≥ 900 n (%)		
SGA C	5 (63)	3 (37)	8	
SGA B + A	9 (20)	37 (80)	46	0.02
Total	14 (26)	40 (74)	54	

SGA: subjective global assessment; *chi-square test

DISCUSSION

This study was a cross-sectional study, which was conducted in hospitalized patients at the internal medicine ward. Most of the patients were hospitalized with 1 or more disease or problems. Malnutrition mostly is illness associated, and has multiple risk factors.[10,13-15,17-20] Illness-associated malnutrition is due to many factors such as less intake, metabolism changes, nutrient loss or decreased absorption. Inflammatory mediators such as interleukin, TNF-α were postulated to be related to malnutrition.[3,4,5,17,19,21]

The study has shown a significant correlation between having more than 1 disease and malnutrition. The study by Naber et al, indicated that there was increased risk of malnutrition when the patients had more than 1 diseases.[10] Hence, the hypothesis were increased number of disease increased would increase the risk of malnutrition and its complications.

Previous studies have shown correlation between diseases with malnutrition, such as malignancy and digestive disease.[22,23,24] In this study, we could not demonstrate such correlation since we had excluded many diseases including AIDS, aplastic anemia, myelodisplasia syndrome, leukemia, lymphoma, SLE, and dengue fever in order to control the confounding factors. The disease proportion in this study did not represent disease proportion in general population. This study has been designed with many restriction of disease to control the confounding factors. Therefore, we did not analyze the correlation between any diseases and malnutrition.

We did not find any significant correlation between infectious disease and malnutrition, which was consistent with the results of previous study.[25] The most important risk factors for malnutrition in hospitalized patients are increased nutrient loss, malabsorption, and severe infection sepsis.[3,18,19] However, we excluded sepsis patients because we could not measure these patients due to their conditions. Most sepsis patients have weak condition and therefore they are not able to stand on weight measurement.

In this study, nutritional status was measured using BMI classification and SGA technique, which categorized the patients into malnutrition and normal nutrition group. SGA is one of nutritional assessment tools recommended by American Society for Parenteral and Enteral Nutrition and other centers.[9,16,22-23,26-27] BMI is one of anthropometric measurements method. It is an objective method; however, it could not be used in patients who had experienced amputation and edema. Moreover, it could not be utilized for measuring weight loss in patients who still had their weight in normal range. SGA is more valid as it can describe the risk of malnutrition (SGA B). Furthermore, it is also useful for assessing nutritional status of hospitalized patients, but it cannot be used as a monitoring parameter.

The proportion of malnutrition in this study was 52% (based on SGA method), which is similar to previous study showing that approximately 50% of patients were malnourished.[8,9] There were differences

between malnourished patients who were classified by BMI and SGA. We found 3 patients with edema who were classified as patients with normal nutrition, but they were also classified as SGA B. Two patients were overweight and had lost weight due to illness, but they were still in normal based on the BMI classification. SGA, as a nutritional assessment to detect malnutrition seems to be better than BMI, in which risked malnutrition and moderately malnutrition are classified as SGA B.[3]

This study showed significant correlation between malnutrition and TLC < 1,200 cell/mm^3; as well as between severe malnutrition and TLC < 900/mm^3. Previous studies, which were conducted in population of patients with chronic kidney diseases and acute renal failure patients, have also demonstrated similar correlation.[24,28]

The correlation between malnutrition and lymphocyte was introduced by Chandra.[29,30] Malnutrition is considered to be related with decreased body mass, including thymus atrophy. Interleukin and zinc are also considered to be correlated with decreased lymphocytes in malnutrition.[31-36] The mechanisms of decreased lymphocyte in malnutrition has not been clearly described; however, it is most likely to be related to thymus atrophy and interleukin.

Total lymphocyte count < 900 cell/mm^3 is correlated with severe malnutrition. This result is consistent with similar study in patients with gynecologic malignancy conducted by Santoso et al.[37] The severity of malnutrition tends to be associated with degree of lymphocytopenia. This study showed that there was a correlation between TLC and nutritional parameters such as BMI, mid-arm circumference, and albumin. TLC can be used as one of nutritional parameters since it has significant association; however, it has shown a lack of sensivity and specifity.[23]

In clinical settings, underlying disease should be considered when interpreting TLC as a nutritional parameter. AIDS, hematopoietic disorder, hematopoietic malignancy, elderly age, and medications should be considered as confounding factors.[17,26,38-40] Therefore, TLC can be considered as an nutritional assessment.

We still don't know when lymphcocyte are decreased due to malnutriton. However, other study has shown that lymphocyte count may decrease in approximately 7 days in anorexic patients. Lymphocytes count may also decrease in acute starvation and increase after re-feeding. This study could not describe lymphocyte changes during hospitalization since we did not re-examine nutritional status and TLC.[41-43]

CONCLUSION

The study has shown a correlation between malnutrition and TLC < 1,200 cell/mm^3 in malnourished hospitalized patients. Such correlation is consistent with severe malnutrition and TLC < 900 cell/mm^3.

SUGGESTION

We suggest that TLC can be used as one of nutritional parameters in hospitalized patients. Other prospective cohort study is necessary to confirm TLC as a monitoring nutritional parameter in hospitalized patients.

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