Research Article

Annals of Clinical and Medical Case Reports

Prognostic Nutritional Index (PNI) In Patients With Severe Encephalitis As A UsefulPrognostic Indicator:A Multivariate Analysis

Bo Hui*, Di Zhao*, Fang Du, Xiao Zhang, Fang Yang and Xiaodan Shi

Department of neurology, Xijing Hospital, Air Force Medical University, No. 127 West Changle Road, Xi'an, 710032, China

*Corresponding author:
Bo Hui,
Department of neurology, Xijing Hospital, Air Force Medical University, No. 127 West Changle Road, Xi'an, 710032, China,

Author Contribution:
Bo Hui drafted the manuscript, Di Zhao collected,organized, analyzedand interpretedthe data. Xiao Zhang helped with data collections and performed the literaturesearch, Xiaodan Shi designed the studyand took responsibility for data integrity and theaccuracy of data analysis; Fang Du and Fang Yang guided and helped revise themanuscript.Xiaodan Shi is corresponding author.Bo Hui and Di Zhao are co-first

Authors:
The order of the authorship was based on their contributions to this study.

Received Date: 18 April 2024
Accepted Date: 29 May 2024
Published Date: 03 June 2024

Citation:
Bo Hui. Prognostic Nutritional Index (PNI) In Patients With Severe Encephalitis As A UsefulPrognostic Indicator:A Multivariate Analysis. Annals of Clinical and Medical Case Reports 2024.

1. Abstract

1.1. Background:
The prognostic impact of poor nutritional status in severe encephalitis is not clearly understood. We aim to investigate the relationship betweenthe prognostic nutritional index (PNI) and poor outcomes of severe encephalitis.

1.2. Method:
We conducted a retrospective study involving patients with severe encephalitis to determinewhether the nutritional and inflammatory biomarker is linearly related to the prognosis of encephalitis. The PNI was calculated as follows: 10×serum albumin (g/L) + 5×total lymphocyte count (109/L). The PNI scores were analyzed as continuous variables and categorical variables divided by quartiles from top to bottom. Restricted cubic splines and logistic regression were applied.

1.3. Result:
In this study, 307 patients were enrolled. We found that the advanced age(<0.001), respiratory failure(<0.001), status epilepticus(<0.001) and GCS<8(<0.001) were significantly higher in the poor-prognosis group. The relationship between PNI score and poor prognosis of severe encephalitis was linear. According to a logistic regression model, a lower PNI score had a poorer prognosis for encephalitis. [per 1-point decrement; adjusted OR=1.10; 95% CI, 1.05-1.14; compared with Quartile 1 (PNI ≥ 50.36), Quartile 4 (PNI <40.15), unadjusted OR =3.60, 95% CI:1.67-7.74; and adjusted OR=3.33, 95% CI:1.46-7.62].

1.4. Conclusion:
According to our study, lower PNI score was correlated with poorer outcome in severe encephalitis patients. Itsuggested that PNI is a useful prognostic indicator in patients with severe encephalitis.

2. Keywords:
Prognostic Nutritional Index (PNI); Severe encephalitis; Prognostic factor; Outcomes

3. Introduction

Encephalitis is a severs central nervous system infection disease. Despite its low incidence, the disease is still associated with significant morbidity (50%) and mortality (15%) in most cases [1]. Although the accurate diagnoses and therapeutic is significant for good outcome, but the mortality rate of severe encephalitis can still reach up to 25%, and 55% survivors lived with moderate-to-severe neurodevelopmentin ICU [1]. People with severe encephalitis need to be more closely monitored in case they progress to death. Researchers have found that malnutrition plays an important role in the prognosis of many diseases, including infectious diseases, inflammation, and cancers. A lack of nutrition increased the susceptibility to infection, as well as reducing the quality and durability of vaccine responses [2]. An Indian study about nutritional status and pulmonary tuberculosis shown 85% patients with undernutrition had increased risk of death [3]. A child viral encephalitis study confirmed a highlight association between undernutrition and adverse outcome [4]. However, there are no study about a screening tool to predict the outcome of encephalitis patients and the status of nutrition. Based on serum albumin concentrations and lymphocyte counts, the prognostic nutritional

index (PNI) can be used to screen patients with poor prognosis [5]. It's an objective measurement of nutritional status. A number of diseases have been associated with the PNI and poor postoperative outcomes[6]. And previous studies have proved the correlation between PNI and unfavorable prognosis of various cancers [7], myocardial infarction[8](MI) and acute ischemic stroke [9](AIS). However, no study investigated the prognostic value for PNI and severe encephalitis. Therefore this study aims to explore whether severe encephalitis prognosis is associated with PNI.

4. Material and Methods

4.1. Study Design and Participants

This retrospective study analyzed data from consecutive patients with the discharge diagnosis of encephalitis who were admitted to the neurological intensive care unit (NICU) of First Affiliated Hospital of the Fourth Military Medical University from June 2015 to June 2020.A standardized and anonymous process was used to collect data on patients with encephalitis diagnosed through the hospital's electronic medical record system (EMR). A patient's electronic medical record provided information on demographics, comorbidities, clinical manifestations, laboratory findings, neuroimaging, and clinical outcomes in the hospital. The inclusion criteria were the following:1). The definition of encephalitis in this study was adapted fromthe recommendations of the International Encephalitis Consortium [10]: a. Major Criterion: the altered mental status lasting ≥24 h (decreased or altered level of consciousness or personality change); b. minor Criteria: fever>38° C lasting for 72 hours; seizures were confirmed by clinical symptoms or EEG; new onset of focal neurological deficits; Increased CSF cells, and EEG or neuroimaging changes; 2) All patients were over 18 years of age; and 3)The length of NICU stay was longer than 48 hours(to eliminate those who only had transient critical care needs). Exclusion criteria were as follows: 1) Incomplete or non-existent lumbar puncture CSF examination; 2) Traumatic or surgical-induced intracranial infection; 3) Be identified as cerebral abscess; 4) Encephalopathy triggered by infectious and non-infectious factors, including sepsis, septicemia and toxic or metabolic diseases; 5) The patients with human immunodeficiency virus (HIV) infection, those with malignancy, organ transplantation, people with autoimmune disease, those on long-term hormones therapy, and those with primary immunodeficiency, or those usedimmunosuppressive drugs; and 6)patient lost during follow-up. This study was supported by the Ethics Committee of First Affiliated Hospital of the Fourth Military Medical University. As we used only anonymousretrospective data collected routinely, informed consent was not required.

4.2. Data Collection

A variety of data were collected and analyzed, including age, gender, risk factors, clinical manifestations, laboratory parameters, and imaging tests. ALB (albumin concentration) and ALC (absolute lymphocyte count) were assessed 24 hours after admission.

4.3. Endpoint and Definition

The primary endpoint was patients' neurological outcomes at hospital discharge. The outcome was assessed by Glasgow Outcome Score (GOS) which is designed to assess disability after head injury in an inpatient setting.In this study, GOS scores were dichotomized into favorable (GOS scores 4-5 [good recovery or moderate disability]) or unfavorable (GOS scores 1-3 [severe disability, vegetative state, or death]). Hospitalized patients were assessed for their nutritional status using the PNI score. A formula based on 10 × serum albumin (g/L) and 5 × total lymphocyte count (109/L) was calculated.

4.4. Statistical Analysis

As a descriptive statistic, mean (SD) and median (interquartile range [IQR]) are used for continuous variables with normal distribution and abnormal distribution, respectively. A categorical variable is reported as a number (percentage). Continuous variables with normal distribution were compared using independent samplesStudent's t-test. Differences between categorical variables were compared by the chi-square test. As a result of a logistic regression model, odds ratios (ORs) and their 95% confidence intervals (CIs) were calculated for the independent associations between the PNI and outcomes. Age, male gender, smoking history, hypertension, diabetes mellitus, hyperlipidemia, Glasgow Coma Score (GCS) on admission, status epilepticus (SE), and pulmonary infection were covariates in the model. In this study, SR software, version 3.6.3 (R Foundation for Statistical Computing), was used for statistical analyses. Statistical significance was determined by P values <0.05.

5. Results

5.1 Clinical characteristics of patients with encephalitis.

Based on the inclusion and exclusion criteria (Figure 1), all 307 patients were included. The mean age of the study population was 42.59, with 56.3% of man and 43.7% of female distribution. Patients were grouped according to their clinical outcome.

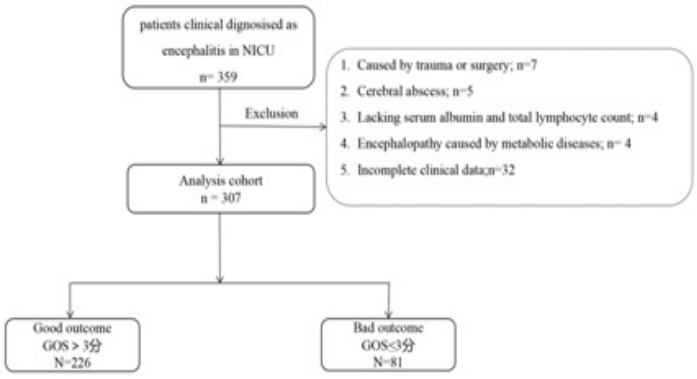


Figure 1: Flowchart of patient recruitment in the study.

5.2 The biomarker of bad outcome of the encephalitis.

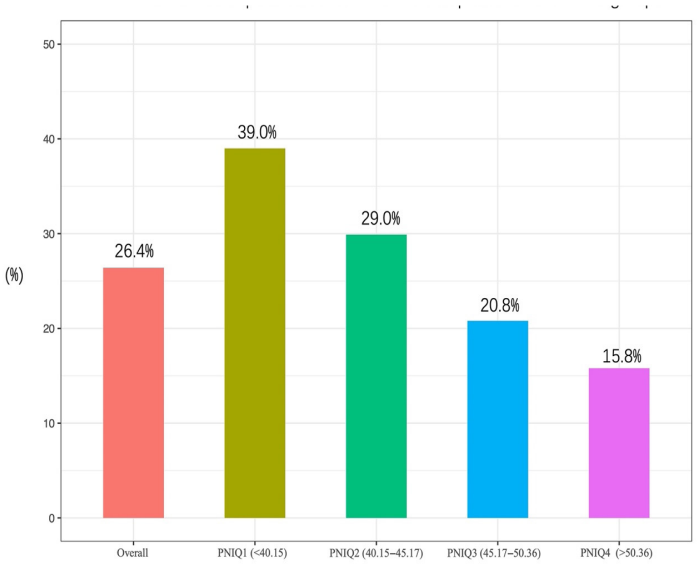
In the cohort, 81(26.4%) patients had bad outcome. Table 1 shows the

baseline characteristics of the two groups. We found that the advanced age(<0.001), respiratory failure(<0.001), status epilepticus(<0.001) and GCS<8 (<0.001) were significantly higher in the poor-prognosis group. Compared with patients in poor-prognosis group, the levels of CSF protein(0.012) and blood neutrophil count(0.024), were lower in good-prognosis group, while lymphocyte count <(0.001), Neutrophil/ lymphocyte (NLR) (<0.001), albumin (0.005) and PNI <(0.001) were higher.We divided the PNI level into quartiles, the incidence of poor-prognosis in the four PNI groups from high to low was 15.8%, 20.8%, 29.9%, and 39.0%, respectively (Figure 2).

Table 1: Baseline characteristics

Demographics and Clinical Characteristics	severe encephalitis		
	Good outcome	Bad outcome	P value
	GOS <3;	GOS≤3;	
	N=226	N=81	
Demographic information			
Age	40 (27-54.25)	46 (27-58)	<0.001
sex <male(%)	135 (59.7)	39 (48.1)	0.071
Smoking History (%)	35 (15.5)	16 (19.8)	0.376
Clinical features			
Fever(%)	166(73.5)	56(69.1)	0.456
Headache(%)	146(64.6)	47(58.0)	0.293
Major focal deficit(%)	31(13.7)	18(22.2)	0.073
Seizures(%)	70(31.0)	22(27.2)	0.52
Psychiatric symptoms(%)	66(29.2)	27(33.3)	0.488
Lung infection(%)	146(64.6)	58.0(58.0)	0.293
Respiratory failure(%)	5(2.2)	12(14.8)	<0.001
Status epilepticus (%)	25(11.1)	18(22.2)	0.013
GCS score (<8)	40(17.7)	42(51.9)	<0.001
Comorbidity			
Hypertension (%)	34(15.0)	14 (17.3)	0.634
Diabetes (%)	15(6.6)	5(6.2)	0.884
Hyperlipidemia (%)	7(3.1)	1(1.2)	0.686
Brain CT/MRI			
Inflammation(%)	57(25.2)	25 (30.9)	0.325
Hydrocephalus(%)	8(3.5)	5 (6.2)	0.339
Edema(%)	4 (1.8)	5 (6.2)	0.058
CSF Laboratory findings			
CSF White cell (cells/mm3)	44 (7-158.25)	52 (11.5-170)	0.482
CSF protein (g/L)	0.60 (0.315\1.10)	0.83 (0.405-1.495)	0.012
CSF glucose (mmol/L)	3.085 (2.4703.600)	3.000 (2.390 3.645)	0.846
Blood Laboratory findings			
leukocyte count(×109/L)	9.15 (6.86-9.15)	9.96 (7.77-14.9)	0.155
Neutrophils count (×109/L)	7.16 (4.81-11.31)	8.20 (6.12-12.08)	0.024
Lymphocyte count (109 /L)	1.19 (0.78-1.79)	0.90 (0.55-1.42)	<0.001
Hemoglobin(g/L)	135 (122-147.25)	129 (117-144)	0.075
Albumin (g/L)	39.6 (35.375-43.1)	37.6 (32.65-41.15)	0.005
Sodium (mmol/L)	137.8 (133.1-141.8)	136.4 (132.95-141.0)	0.228
Platelets(×109/L)	203.5 (156.5-258.75)	194.0 (144.5-262)	0.385
PNI	46.215 (41.368-50.96)	40.75 (38.055-46.545)	<0.001
NLR	7.08 (3.59-12.76)	9.07 (5.44-15.2)	<0.010

Figure 2: The incidence of poor outcome of sever encephlitis and four PNI groups



5.3 The relationship of the PNI score and severe encephalitis.

Using restricted cubic splines models, we fitted univariate and multivariate logistic models to investigate the association between PNI score and poor prognosis in severe encephalitis (Figures 3(a) and 3(b)). There is a linear relationship between PNI score and poor prognosis in severe encephalitis (P for nonlinearity was 0.57and 0.15). Decreased PNI score is associated with poor prognosis in severe encephalitis patients.In patients with severe encephalitis after adjustment for clinical variables, low PNI values was associated with poor prognosis (Figure 4). A lower PNI value in multivariable regression was associated with a poorer prognosis (per

1-point decrement; adjusted OR=1.10; 95% CI, 1.05-1.14). Multivariable model analysis also included PNI score as a categorical variable, divided into four quartiles by high to low. In all participants, the lowest quartile of PNI score as associated with 60% and 33% higher risk of poor-prognosis compared to the highest quartile [compared with Quartile 1 (PNI ≥ 50.36), Quartile 4 (PNI <40.15), unadjusted OR =3.60, 95% CI:1.67-7.74; and adjusted OR=3.33, 95% CI:1.46-7.62].

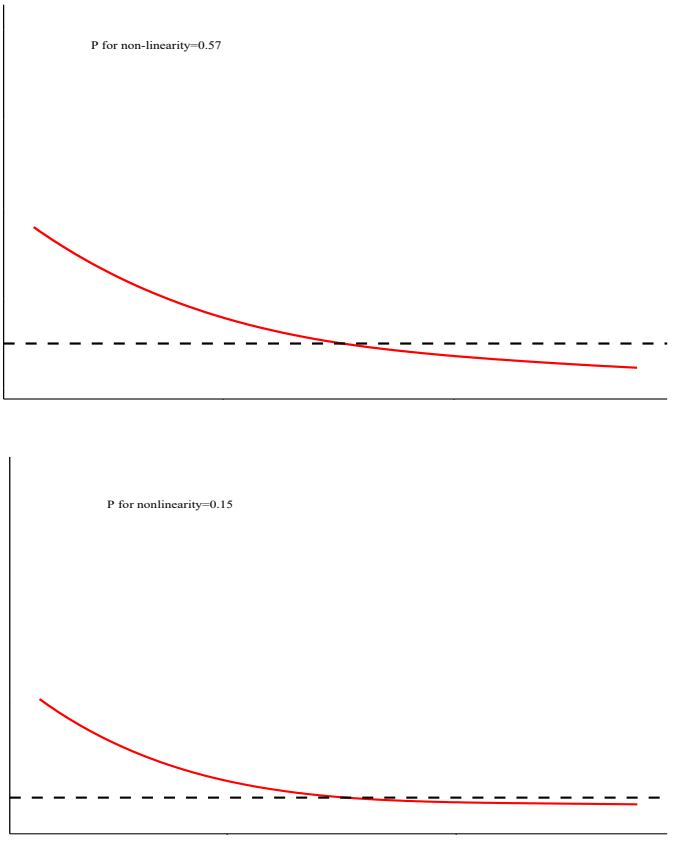


Figure 3: Restricted spline curve of the PNI score odds ratio for poor-prognostic encephalitis (a) The restrict spline curve of the univariate cox model. (b) The restrict spline curve of the multivariate logistic model. *Adjusted for age, male, smoking history, hypertension, diabetes mellitus, hyperlipidemia, Glasgow Coma Score (GCS) on admission, status epilepticus (SE), pulmonary infection, blood hemoglobin and blood neutrophil.

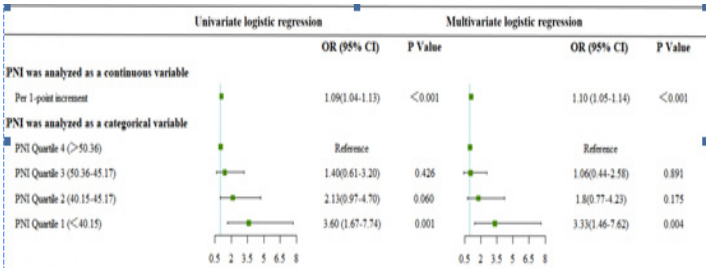


Figure 4: Restricted spline curve of the PNI score odds ratio for poor-prognostic encephalitis. *Adjusted for Adjusted for age, male, smoking history, hypertension, diabetes mellitus, hyperlipidemia, Glasgow Coma Score (GCS) on admission, status epilepticus (SE), pulmonary infection, blood hemoglobin and blood neutrophil.

6. Discussion

Inthisretrospectiveanalysis, weexamined the clinical characteristics of severe encephalitis and identified baseline risks ofage, respiratory failure, status epilepticus, and GCS<8. These factors were significantly associated with poor-prognostic. The age, GCS and status epilepticus were same as previous studies [1]. The respiratory failure has not been reported. There were 17 respiratory failures which included with 8/17(47.05%) autoimmune encephalitis, 7/17(41.17%) Japanese encephalitis, 1 viral encephalitis and 1 purulent encephalitis. It has suggested that more attention should be paid to respiratory system, for patients with autoimmune encephalitis in NICU. In this cohort, the prognostic nutritional index (PNI) was initially representing patients' immune and nutritional status about severe encephalitis. We were first investigating how immune-nutritional status influencedprognosis in encephalitis. Previous studies on PNI have identified PNI as a malnutrition predictor of poor survival in patients with various malignant and perioperative period diseases.In some neurologic disease, such as acute ischemic stroke (AIS), cognitive function impairment (CFI), the PNI score was associated with a higher risk of adverse effects. Interestingly, whether the PNI score was the marker of prognostic of infectious disease had not been widely studied.

From the pathophysiology, PNI is composed by albumin and lymphocyte. Serum albumin is not only a marker of nutrition but also an inflammatory indicator [11]. The Serum albumin has a long half-life, which is insensitive to acute changes in nutritional status. Consequently, the Society of Critical Care Medicine (SCCM) as well as the American Society for Parenteral and Enteral Nutrition (ASPEN) do not recommend albumin as an indicator of nutritional status in critically ill patients [12]. According to some studies, the low serum albumin not only indicated acute malnutrition, but also correlated with antioxidant, anti-inflammatory effects, and maintenance of homeostasis. Thus, cytokine storm, oxidative stress, blood clotting, and even organ failure may be caused by low serum albumin. In our study, the lower albumin was also related with a poor-prognostic(P<0.005). Comparing with PNI score, it was not significant in poor-prognostic. Lymphocytes are a crucial part of immune cells in body and participate in cellular immunity. Decreased lymphocytes count indicatesphysiological stress and poor health and many studies have shown it might be associated with poor prognosis in numerous disease such as cancer, infections, immune dysfunctions. The lymphocyte count is considered as a blood marker for malnutrition [13]. We also calculated the NLR, as an immune marker. As a result, the NLR and PNI were with the same trend, but NLR were less significant than PNI (P<0.010). In recent studies, the PNI was superior to the NLR as a prognostic marker in many cancer patients. Above all, Albumin and Lymphocytes are also an immune-nutrition indicator in infectious disease.

In this cohort, we first retrospectively revealed the line relationship between the PNI Score and prognosis of patients with severe encephalitis in NICU. Severe encephalitis patients were manifested as an inflammatory cascade and associated with a massive release of inflammatory cytokines that triggers systemic inflammatory reaction. As a result of inflammation, an infection can result in prolonged vasodilatation and increased capillary permeability. Blood vessel components, such as albumin, leaked into thetissue spaces, causing a decrease in plasma albumin concentration. This reflected the process of PNI to some extent. Consequently, PNI may reflect the immune and nutritional status of patients with severe encephalitis at the same time, which may explain the poor prognosis with low level of PNI. In NICUs, we focused on high-risk patients who required clinical attention. Early sufficient nutritional support for the severe encephalitis patients may improve patients' outcome and reduce mortality. PNI are easy to calculate and composed by albumin and lymphocytes which is facile for application. This study, however, had some limitations. Firstly, this study is a single-center retrospective study with relatively small number of patients. We were the largest NICU in western China, so our sample was representative and convincing. Secondly, because the etiology of encephalitis was complex and difficult to identify, we did not perform an additional subgroup analysis. Differences in outcomes may be seen for patients with different kinds of encephalitis, such as infectious encephalitis and autoimmune encephalitis. Thirdly, in this study, only PNI scores obtained during the first 24 hours following a patient's admission to the NICU were included, which reflected the baseline level. It was unknown whether a dynamic change in the PNI score during NICU treatment affected the prognosis of patients. Finally, the study was observational and retrospective. It is therefore necessary to conduct a well-designed, prospective, multi-center, randomized controlled study to verify the conclusion.

7. Conclusion

As a result of our study, lower PNI score was associated with poorer functional outcomes in patients with severe encephalitis.PNI is a useful prognostic indicator in patients with severe encephalitis.

8. Acknowledgments

The authors are grateful to all the doctors and nurses from NICU of Xijing Hospitalduring the course of study.

Reference

1. Meyfroidt G, Kurtz P & Sonneville R. Critical care management of infectious meningitis and encephalitis. Intensive Care Med. 2020; 46: 192-201.
2. VanValkenburg A, Kaipilyawar V, Sarkar S, Lakshminarayanan S, Cintron C, Babu SP, Knudsen S, et al. Malnutrition leads to increased inflammation and expression of tuberculosis risk signatures in recently exposed household contacts of pulmonary tuberculosis. Front Immunol.2022; 13: 1011166.
3. Feleke BE, Feleke TE & Biadglegne F. Nutritional status of tuberculosis patients, a comparative cross-sectional study. BMC Pulm Med. 2019; 19: 182.
4. de Blauw, D,Bruning AHL, Busch CBE, Kolodziej LM, Jansen NJG, van Woensel JBM, et al. Epidemiology and Etiology of Severe Childhood Encephalitis in The Netherlands. Pediatr Infect Dis J. 2020;39(4):267-272.
5. Wei W, Wu X, Jin C, Mu T, Gu G,Min M,et al. Predictive Significance of the Prognostic Nutritional Index (PNI) in Patients with Severe COVID-19. J Immunol Res, 2021; 2021: 9917302.
6. Lu Y, Ren C & JiangJ. The Relationship Between Prognostic Nutritional Index and All-Cause Mortality in Critically Ill Patients: A Retrospective Study. Int J Gen Med. 2021; 14: 3619-3626.
7. Qu Z, Lu Y, Feng J,Chen Y, Shi L, Chen J, et al. Preoperative Prognostic Nutritional Index and Neutrophil-to-Lymphocyte Ratio Predict Survival Outcomes of Patients with Hepatocellular Carcinoma After Curative Resection. Front. Oncol. 2022; 11: 823054.
8. Kim HR, Kang MG, Kim K, Koh J, Park JR, Hwang S, et al. Comparative analysis of three nutrition scores in predicting mortality after acute myocardial infarction. Nutrition. 2021; 90: 111243.
9. Bao Y,Zhang Y, Du C, Ji Y, Dai Y, Jiang W. Malnutrition and the Risk of Early Neurological Deterioration in Elderly Patients with Acute Ischemic Stroke. Neuropsychiatr Dis Treat. 2022; 18, 1779-1787.
10. Feng G, Tian X, Wang L, Zhao L & Wang X. Low TT4 as a predictor of poor outcomes in severe encephalitis: a multivariate analysis of 94 patients. Expert Rev Neurother. 2018; 18: 443-451.
11. De Simone G, di Masi A & Ascenzi P. Serum Albumin: A Multifaced Enzyme. Int J Mol Sci. 2021; 22: 10086.
12. McClave SA,Taylor BE, Martindale RG, Warren MM, Johnson DR, Braunschweig C, et al. Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). JPEN J Parenter Enteral Nutr. 2016; 40: 159-211.
13. Laulund AS, Lauritzen JB, Duus BR, Mosfeldt M & Jørgensen HL. Routine blood tests as predictors of mortality in hip fracture patients. Injury. 2012; 43: 1014-1020.