Middle Black Sea Journal of Health Science / Mid Blac Sea J Health Sci **November 2022; 8(4):481-489**

RESEARCH ARTICLE **DOI:** 10.19127/mbsjohs.1114583

What is the predictive value of the prognostic nutritional index for the severity of COVID 19 hospitalized patients?

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Received: 13 May 2022, Accepted: 11 September2022, Published online: 30 November 2022

Abstract

Objective: Malnutrition is a risk factor for severe coronavirus disease 2019 (COVID-19) and early nutritional risk assessment should be performed consistently and promptly to determine the proper nutritional therapy and lead to a good prognosis. We aimed to investigate the predictive value of the prognostic nutritional index (PNI) in determining the severity of hospitalized COVID-19 patients.

Methods: In this retrospective single-center research, a total of 686 hospitalized adult patients with COVID-19 between April 2020-June 2020 were analyzed. Demographic, clinical, radiological and laboratory data were registered from patient files. Nutritional status was evaluated using the BMI and PNI. Patients were divided into three groups according to PNI values: severe (PNI ≤ 35), moderate (35<PNI<38) and normal (PNI≥38).

Results: The study group's average PNI score was 35.56 ± 4.58.PNI values were found to be normal in 37.3 percent (N: 256) of the patients, moderate in 28.3 percent (N: 194), and severe in 34.4 percent (N: 236). Male patients, those over the age of 65, referred patients, intubated patients, and those who died were at a higher risk of severe PNI. Patients with normal computed tomography scans were found to have a higher incidence in the normal PNI. The length of hospitalization increased in proportion to the severity of PNI. As the severity of the PNI category increased, so did albumin, C reactive protein, D-dimer, ferritin, lactate dehydrogenase, and neutrophil levels. The total protein value decreased, as the severity of the PNI category increased.

Conclusion: PNI can be determined easily and quickly using routine blood tests and it can be useful for early detection of potentially fatal illnesses, giving medical care and improving prognosis.

Key words: COVID 19, malnutrition, Prognostic Nutritional Index, prognosis

Suggested Citation: Yenibertiz D, Güven D, Koc F, Gökler E, Bolu F, Bulus H. What is the predictive value of the prognostic nutritional index for the severity of COVID 19 hospitalized patients? Mid Blac Sea J Health Sci, 2022; 8(4):481-489

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INTRODUCTION

Coronavirus disease 2019 (COVID-19) is still the most serious public health problem all over the World, by the end of the 2021, the number of COVID-19 patients reported worldwide was over 273 million, while the number of deaths exceeded 5 million according to the World Health Organization (WHO) (1).

COVID-19's clinic spectrum varies from asymptomatic infection and moderate upper respiratory tract infection to severe pneumonia with life-threatening complications such as acute respiratory failure which can lead to multi-organ dysfunction and death (2-6).

High levels of inflammation are linked to severe malnutrition. COVID-19 patients with severe or life-threatening disease exhibit extreme systemic inflammation as well as poor nutritional status (7). The majority of COVID 19 fatalities occur in older, multi-morbid patients with severe malnutrition (6). Malnutrition can both enhance the risk and severity of infections by compromising the patient's immune system and treatment effectiveness, as well as develop as a result of infections (8). It is regarded as a risk factor for increased morbidity and mortality (9). Poor nutritional status and immunological dysfunction have been identified as potential risk factors for severe COVID-19 (10).

Malnutrition is a modifiable risk factor and early nutritional risk assessment in COVID-19 patients, as in other infectious diseases, should be done consistently and immediately in order to determine the appropriate nutritional therapy that may promote a stronger immune response and lead to a favorable prognosis (11,12). As a result, a simple and effective index for assessing COVID-19 patients' nutritional status should be developed. There is, however, no known standard tool for nutritional risk screening and nutritional status assessment.

The Prognostic nutritional index (PNI), which was originally developed to predict the risk of postoperative complications following gastrointestinal surgery, is calculated using the serum albumin levels and total lymphocyte counts in peripheral blood (13,14). It is a measurable indicator of immune, inflammatory, and nutritional condition. It has been demonstrated to have prognostic significance in a number of clinical situations such as cancers, infectious diseases, cardiovascular diseases. In COVID-19 patients, PNI also more accurately reflects nutritional and inflammatory status, and a lower score indicates poor nutritional status (15-16).

There are few studies that have investigated the function of PNI in reflecting the inflammatory status and predicting the disease severity in COVID 19 patients (17-20).

The purpose of this study was to investigate the relationship between PNI and COVID-19 severity in hospitalized patients as well as the

predictive usefulness of PNI for the severe form of COVID-19.

METHODS

We performed a single-center, retrospective research on 686 adult patients with COVID-19 hospitalized in a Pandemic Hospital between April 2020-June and 2020 to evaluate the prognostic role of PNI. All patients were diagnosed with COVID-19 based on the criteria of World Health Organization. Patients with missing data and other diagnoses during hospitalization were excluded from the study. Age, gender, symptoms, severity of the disease according to radiological appearance, length of hospital stay, discharge status, body mass index (BMI), polymerase chain reaction (PCR) test results and laboratory parameters of the patients checked at the time of diagnosis (lactate dehydrogenase (LDH), procalcitonin, D-dimer, Ferritin, C reactive protein (CRP), albumin, total protein, neutrophil, lymphocyte, and platelet) were recorded from patient files. Nutritional status was evaluated using the BMI and PNI. BMI was calculated as body weight (kg) divided by the square of the height (m2) (21). PNI scores were calculated as 10 x serum albumin level (g/dL) + 0,005 x absolute lymphocyte count (/mm3). Patients were stratified into the following three groups according to PNI values: severe PNI (PNI ≤ 35), moderate PNI (35<PNI<38), and normal PNI (PNI≥38) (15).

Informed consent was obtained from participants in the study and the ethics committee approval were obtained from the hospital ethics committee (Approval date and number: 24.06.2020/ 2012-KAEK-15/2130).

IBM SPSS v20.0 (IBM Corp., Armonk, NY, USA) was used for the data analysis. The demographic characteristics of the study group were reported using descriptive statistics (frequencies, proportions, means, medians) and dispersion measures (standard deviation, min-max, 25-75% quartile range). Initially, the normality of the total scores was tested using the Kolmogorov-Smirnov normality test and graphs. Therefore, the median scores were compared using Kruskal Wallis (and Bonferroni's ad hoc test), and groups were compared using a Chi-Square test. A significance level of $\alpha = 0.05$ (two-tailed) was applied for all p values.

RESULTS

A total of 686 hospitalized adult patients with COVID-19 were included in the study. The mean age of the research group was 58.27±14.67 (between 18-93) years, and 46.1 percent of the participants were female (N: 316). The study group's average PNI score was 35.56±4.58 points (ranging from 12.01 to 48.01). PNI values were found to be normal in 37.3 percent (N: 256) of the patients, moderate in 28.3 percent (N: 194), and severe in 34.4 percent (N: 236). Male patients, those over the age of 65, referred patients, intubated patients, and those who died were at a higher risk of

severe PNI. Furthermore, patients with normal computed tomography (CT) scans were found to have a higher incidence in the normal PNI category. The distribution of demographic data of the study group according to PNI degrees is presented in Table 1.

The research group's mean BMI was 28.46±3.95 (range 16.72-40.43). It was determined that the average length of stay in the hospital for COVID-19 patients was 8.49±6.80 (range 1-79) days. Patients with normal PNI were found to be overweight and to have a higher BMI than those with severe PNI. The length of hospital stays increased with rising PNI grade. The distribution of the study group's height, weight, BMI, and length of hospitalization according to PNI grades was demonstrated in Table 2.

In our investigation, as the severity of the PNI category increased, so did the levels of albumin, C reactive protein (CRP), D-dimer, ferritin, lactate dehydrogenase (LDH), and neutrophil rose. The total protein value decreased, as the severity of the PNI category increased. The distribution of various laboratory results based on the research group's PNI degrees is presented in Table 3.

Table 1. The distribution of the research group's demographic characteristics based on PNI degrees

		PNI normal		PNI moderate		PNI severe		p
		n	%	n	%	n	%	
Gender	Male	119	50.4	95	49.0	156	60.9	**0.017**
	Female	117	49.6	99	51.0	100	39.1	
Age	<65 years	193	81.8	140	72.2	118	46.1	**<0.001**
	>65 years	43	18.2	54	27.8	138	53.9	
Status of death	No	236	100.0	194	100.0	241	94.1	**<0.001**
	Yes	0	0.0	0	0.0	15	5.9	
Status of intubation	No	234	99.2	192	99.0	236	92.2	**<0.001**
	Yes	2	0.8	2	1.0	20	7.8	
Status of dispatch	No	234	99.2	193	99.5	242	94.5	**0.001**
	Yes	2	0.8	1	0.5	14	5.5	
CT involvement	No	55	23.3	22	11.3	25	9.8	**<0.001**
	Mild	83	35.2	60	30.9	74	28.9	
	Moderate	79	33.5	81	41.8	111	43.4	
	Severe	19	8.1	31	16.0	46	18.0	

DISCUSSION

The prognostic nutritional index has been identified as a tool for risk stratification in a variety of disorders (7-10). In this study, the role of the PNI in predicting the severity of COVID-19 was researched. Some COVID-19 individuals have minor symptoms in the early stages of the disease that worsen over time. Such COVID-19 cases have a dismal prognosis and a high fatality severity and enable therapy in the have been described in the literature in order to

Table2. The distribution of the study group's height, weight, BMI, and number of hospitalized days according to PNI degrees

	PNI normal			PNI moderate			PNI severe			P[1-2] P[1-3] P[2-3]
	Median	Q_1	Q_3	Median	Q_1	Q_3	Median	Q_1	Q_3	
Height	165.0	160.0	173.0	165.0	160.0	173.0	168.0	160.0	173.0	0.285 0.285 0.285
Weight	80.0	70.0	90.0	80.0	70.0	86.0	80.0	70.0	85.0	1.000 **0.033** 0.433
Body Mass Index	29.0	25.9	31.9	28.7	25.8	31.2	27.7	25.6	30.7	0.131 **0.006** 1.000
Number of hospitalized days	5.0	5.0	7.0	6.0	5.0	10.0	8.0	5.0	12.0	**<0.001** **<0.001** **0.014**

Q_1:25th percentile, Q_3:75th percentile

Table3. The distribution of various laboratory results based on the research group's PNI levels

	PNI normal[1]			PNI moderate[2]			PNI severe[3]			P[1-2] P[1-3] P[2-3]
	Median	Q_1	Q_3	Median	Q_1	Q_3	Median	Q_1	Q_3	
Albumin,(g/dL)	4.0	3.8	4.1	3.6	3.5	3.7	3.2	3.0	3.3	**<0.001** **<0.001** **<0.001**
CRP(mg/L)*	8.3	3.4	19.0	17.5	7.9	39.2	37.9	13.3	91.5	**<0.001** **<0.001** **<0.001**
D-dimer(mg/L)	370.0	270.0	595.0	480.0	310.0	740.0	720,0	430.0.	1260.0	**<0.001** **<0.001** **0.013**
Ferritin(ng/mL)	186.9	79.4	355.8	293.6	168.4	588.9	401.0	208.0	725.6	**0.025** **<0.001** **<0.001**
LDH*(IU/L)	233.0	207.5	279.0	260.0	224.0	312.0	282.5	231.0	366.0	**0.028** **<0.001** **0.001**
Lymphocytes, x10^3/µL	1.7	1.4	2.2	1.6	1.1	2.1	1.2	0.8	1.6	**0.026** **<0.001** **<0.001**
Neutrophils, x10^3/µL	3.3	2.6	4.6	4.1	2.8	5.6	5.2	3.4	7.5	**0.002** **<0.001** **<0.001**
Platelet, x10^3/µL	243.0	196.0	318.0	300.0	230,0	397.0	274.5	215.0	383.0	0.462 **<0.001** **0.002**
Procalsitonin, (ng/mL)	0	0	0	1	0	0.2	0.1	0.1	0.2	0.086 0.086 0.086
TotalProtein (g/dL)	7.1	6.9	7.5	6.9	6.6	7.1	6.4	6.0	6.7	**<0.001** **<0.001** **<0.001**

Q_1:25th percentile, Q_3:75th percentile
*LDH: Lactat dehydrogenase; CRP: C-Reactive Protein

estimate hospital mortality and illness severity in COVID-19 hospitalized patients (17-21).

In our study, the status of death, intubation early stages of disease. A few studies on PNI,

dispatch, length of hospital stays, and severe CT involvement all increased with increasing PNI grade. Patients with severe COVID-19 have severe systemic inflammation and poor nutritional status (23, 24). Nutritional disorders can cause nosocomial infections that directly increase mortality and morbidity (25). Our findings indicate that a severe PNI predisposes to severe COVID illness.

Patients with severe PNI were found to be male and older age in our study. In previous studies, age and severe COVID-19 were found to be substantially associated and older age was an important prognostic factor of death for COVID-19 patients. Older age may be associated with more comorbidities, resulting in a higher mortality rate (26-29). Data from countries around the world show that women and men have similar numbers of cases, but men have a higher case fatality rate. New data on disease progression and severity suggest that males are 50 percent more likely than women to be hospitalized (30-32).

In our investigation, as the severity of the PNI category increased, the levels of albumin, CRP, D-dimer, ferritin, LDH, PLT and neutrophil rose. The total protein, lymphocyte value decreased, as the severity of the PNI category increased. Previous research found that patients with severe COVID-19 had higher levels of neutrophils, CRP, fibrinogen, D-dimer, ferritin and lower levels of lymphocyte, PLT, albumin (33-38). Serum albumin levels and lymphocyte counts are the primary determinants of PNI. Albumin is a measure of the liver's function, the body's nutritional status, and the body's overall health. Hypoalbuminemia is associated with severe inflammation (39). The hyperinflammatory state associated with the "cytokine storm" has highlighted the possible predictive relevance of hypoalbuminemia and a low albumin level may result in the exudation of intravascular fluid. Both reasons may exacerbate the severity of pulmonary edema in COVID-19. The albumin level in patients with COVID-19 was found to be inversely related to patients who developed acute respiratory distress (ARDS) (40). In most of these patients, there was a correlation between lymphopenia and the severity of the disease. Considering the lymphocyte rates of COVID-19 patients who died, it was found that they were significantly lower than those who survived (33, 41, 42). These findings corroborated our findings, which revealed that PNI was important parameter for prognosis of COVID-19 patients.

CONCLUSION

As a result, PNI represents an immune-nutritional condition as well as chronic inflammation and immunological dysfunction is a major cause of severe COVID-19. PNI can be easily and quickly determined using routine blood tests and it can be useful for early detection of potentially fatal illnesses,

providing medical care and improving prognosis.

Ethics Committee Approval: Ethics committee approval was obtained from the hospital ethics committee (Approval date and number: 24.06.2020/ 2012-KAEK-15/2130
Peer-review: Externally peer-reviewed.
Author Contributions:
Concept: DY, EG; Design: DY, FK; Supervision: DY, HB, FK; Data Collection and/or Processing: DY, EG, FB; Analysis and/or Interpretation: DY, DG, FB; Writing: DY, DG, EG; Critical: DY, DG, EG;Review: D.G, E.G
Conflict of Interest: No conflict of interest was declared by the authors.
Financial Disclosure: The authors declared that this study hasn't received no financial support.

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