Research article

The predictive value of prognostic nutritional index in patients with COVID-19

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ABSTRACT

Introduction and Aim: It is crucial to identify and start treating the COVID-19 patients who are most at risk of becoming seriously ill as soon as possible. There is some evidence that prognostic nutritional index (PNI) could predict the outcome of some diseases. The study objective was to determine whether PNI is a useful prognostic tool for predicting the outcome of COVID-19-positive patients.

Patients and Methods: At Al-Shifaa Hospital in Baghdad Medical City, a total of 160 patients with COVID-19 participated in a study that was designed as a cross-sectional. At the time of admission, information was collected on the patient's history, including clinical, laboratory, and demographic details. The PNI score was determined by 10 × serum albumin (g/dL) + 0.005 × total lymphocyte count (/mm^3). Patients were followed up for survival.

Results: The mortality rate was 14.37%. Survived patients had a mean age of 55.85±16.03 years compared with 64.30 ±14.76 years for died patients with a significant difference. Diabetes was more common among died (39.13%) than survived patients (15.33%) with a significant difference. The median serum level of C-reactive protein (CRP), D-dimer and ferritin in deceased patients was 84 mg/L, 2208 ng/ml and 650 ng/ml, respectively compared with 48 mg/L, 858 ng/ml and 550 ng/ml in survived patients with highly significant differences. The mean PNI in survived and non-survived patients was 40.89±5.9 and 37.86±4.36, respectively with a significant difference. The area under the curve (AUC) for PNI was 0.888, 95%CI = 0.827 and 0.939, p = 0.002 At an ideal cutoff value of 39.08, the test's sensitivity and specificity are 80 % and 74 %, respectively.

Conclusion: The PNI score is an easy-to-use, speedy, and cost-effective tool that has the potential to be utilized on a routine basis to predict mortality in patients with COVID-19.

Keywords: PNI score; mortality; sensitivity; COVID-19.

INTRODUCTION

Coronavirus disease 2019 (Covid-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was stated as a pandemic on 11 March 2020 by the World Health Organization (1). During its peak treating Covid-19 patients with comorbidities was a serious challenge. Studies attempting to identifying key markers for the early prediction of Covid-19 showed a few factors such as C-reactive protein, interleukin-6 (IL-6), lactate dehydrogenase (LDH), neutrophil, D-dimer, creatinine, aspartate aminotransferase (AST) and cortisol to be of significance for prediction COVID-19 case progression (2). However, most of these markers are affected by the medications taken by the patient even before hospitalization. Hence, it is reasonable to find alternative markers such as patient's immunity response and nutritional status, which are deemed important in acute viral infections, including Covid-19 (3).

It is common knowledge that a person's nutritional status plays a significant role in the regulation of his/her immune responses. Immunodeficiency has been linked to protein-energy malnutrition in few studies (3). This immunodeficiency presents itself as a dysfunction in cell-mediated immunity, as well as in the function of phagocytes, the complement system, and the production of cytokines. Patients who have a severe form of the infection have been seen to exhibit these symptoms, in addition to having lower counts of lymphocytes and T cells and higher levels of inflammatory cytokines. According to the findings of some studies, a lack of protein and energy can lead to immunodeficiency (4). Critically ill patients frequently suffer from anorexia due to severe inflammation. Further, the patient's physical limitations, along with the difficulties of collecting anthropometric and dietary data, make it challenging to determine a patient's nutritional status using standard tools. Therefore, it is important to consider using a quick nutritional screening tool like the prognostic nutritional index (PNI) to determine the patients' nutritional status. PNI has been used as a marker in predicting the clinical outcome in patients suffering from cardiovascular diseases, cancer, and chronic kidney disease (5,6,7,8). In such patients, PNI investigation throughout the course of disease has been imperative to clinical practitioners not only in early detection but also in improving prognosis, and reducing mortality. In this study, we aimed to investigate the PNI values in Covid-19 patients and evaluate its correlation to the severity of COVID-19 disease, ability in early detection, and as a predictor for progression of the disease.

MATERIALS AND METHODS

The study population

This prospective cross-sectional study included 160 real time polymerase chain reaction (RT-PCR) confirmed Covid-19 positive patients and receiving treatment at Al-Shifaa Hospital, Baghdad Medical City, Iraq between August-December, 2021. Data were obtained from each participant after briefing them about the purpose of the study and obtaining a written consent. They were also ensured of confidentiality and information used for research purpose only.

Patient data

Patient information such as age, gender, weight, and smoking status and other comorbidities was obtained through direct interviews. Each patient was evaluated for his/her complete blood count indices and inflammatory markers. The PNI was calculated based on the serum albumin concentration and the peripheral blood lymphocyte count. PNI was calculated using the formula:

PNI= (10×serum albumin (g/dL) + (0.005×lymphocytes count (mm^3))

Each patient's PNI was monitored until discharge from the hospital or until death. As a result, patients were categorized as those that survived or deceased.

Statistical analysis

Continuous data obtained was subjected to statistical analysis. Based on data distribution either the Student's t-test or the non-parametric Mann Whitney U test was used in comparing data. The Chi square test was used in analyzing binomial data, and the results given as frequency and percentage. The PNI best cutoff value in predicting mortality was evaluated using the receiver operating characteristic (ROC) curve. All data were analyzed using SPSS for Windows v.25.0 software.

RESULTS

Characteristics of the patients' demographics

The demographic characteristics of patients included in the study are presented in Table1. The patients' average age ranged between 20-87 years with a mean of 57.06±16.09 years. Men were more likely than women to be hospitalized (89 versus 71). The average serum albumin concentration was 34.184.59 g/L. Common comorbidities included diabetes mellitus, hypertension and heart disease, which affected 38.1%, 23.1% and 5.6% of patients respectively. Majority of the patients were non-smokers (86.9%), while the remaining were smokers who either quit or smoked occasionally (Table 1).

Table 1: Population characteristics of the study population (n=160)

Variables	Values
Age, years	
Mean ± SD	57.06±16.09
Range	20-87
Gender	
Males	89 (55.6%)
Females	71 (44.4%)
Weight, Kg	
Mean±SD	83.93±14.21
Range	55-120
Serum albumin level, g/L	
Mean±SD	34.18±4.59
Range	23.6-51.0
Smoking status	
Never	139 (86.9%)
Ex/current	21(13.1%)
Comorbidity	
Yes	71(44%)
Hypertension	61(38.1%)
Diabetes mellitus	37(23.1%)
Ischemic heart disease	9(5.6%)

Hematological parameters

The mean hemoglobin level was 12.97±9.67 g/dL as in Table 2. The total platelet count was 244.94±90.16 $\times 10^3$/mL. The total WBC, neutrophil and lymphocyte count was 9.83±4.08 $\times 10^3$/mL, 8.09±3.88 $\times 10^3$/mL and 1.23±0.79 $\times 10^3$/mL, respectively.

Table 2: Hematological data of the study population (n=160)

Variables	Values
Hb, g/dL	
Mean±SD	12.97±9.67
Range	4.51-16.8
Platelets count $\times 10^3$/mL	
Mean±SD	244.94±90.16
Range	74-603
Total WBC count $\times 10^3$/mL	
Mean±SD	9.83±4.08
Range	2.7-21.4
Neutrophil count $\times 10^3$/mL	
Mean±SD	8.09±3.88
Range	1.8-19.6
Lymphocyte count $\times 10^3$/mL	
Mean±SD	1.23±0.79
Range	0.22-4.1

Inflammatory markers

Table 3 shows the patients' inflammatory parameters. The median CRP level was 53.5 mg/L, D-dimer level 950.5 ng/mL, LDH 535 IU/L, and ferritin 565.5 ng/mL.

Table 3: Inflammatory markers of the study population (n=160)

Parameter	Median (range)
C-reactive protein level (mg/L) Median Range	 53.5 (2.0-317.0)
D-dimer level (ng/mL) Median Range	 950.5 (100-16000)
LDH level, IU/L Median Range	 535.0 (82.0-1255.0)
Ferritin level, ng/mL Median Range	 565.5 (66.0-1650.0)

Patient outcome and characteristics

One hundred and thirty-seven patients (85.63%) survived the COVID-19 sickness, while 23 (14.37%) succumbed to the disease. The characteristics for survived and deceased patients are presented in Table 4. As shown the mean age of deceased patients was higher than survived patients (64.30±14.76years versus 55.85±16.03years) with significant difference. Although serum albumin was higher in survived than deceased patients (34.46±4.73 g/L versus 32.51±3.19 g/L), the difference was not significant. Comorbidities were more common in deceased (65.22%) than in those patients that survived (40.88%). In particular, Type 2 diabetes mellitus was more frequent in deceased compared to patients (39.13% versus 15.33%) that survived with a significant difference (Table 4).

Table 4: Association of patients' characteristics with the outcome

Variables	Survived (n=137)	Deceased (n=23)	p-value
Age, years Mean±SD Range	 55.85±16.03 (50-87)	 64.30±14.76 (35-82)	 0.019
Gender Male Female	 107(60.45%) 70(39.55%)	 18(78.26%) 5(21.74%)	 0.097
Weight, kg Mean±SD Range	 82.61±13.77 (65-120)	 81.78±14.51 (70-118)	 0.726
Serum albumin, g/L Mean±SD Range	 34.46±4.73 (23.6-51.0)	 32.51±3.19 (27-39.4)	 0.058
Smoking history Yes No	 121 (88.32%) 16 (11.68%)	 18(.8.26%) 5 (21.74%)	 0.186
Comorbidity Yes Hypertension Diabetes mellitus Ischemic heart disease	 56 (40.88%) 49 (35.77%) 21 (15.33%) 8 (5.84%)	 15 (65.22%) 12 (52.17%) 9 (39.13%) 1(4.35%)	 0.030 0.134 0.049 0.774

Patient outcome and association to hematological parameters

Generally, none of the included hematological parameters was associated with the outcome. Although lymphocyte count was remarkably higher in survived than deceased ($1.27±0.79×10^3$/mL versus $0.98±0.70×10^3$/mL) patients, the disparity was insignificant (Table 5).

Table 5: Association of hematological parameters with the outcome

Variables	Survived (n=137)	Deceased (n=23)	p-value
Hb, g/dL Mean±SD Range	 12.20±1.75 (7.6-16.9)	 12.35±2.19 (9.5-17)	 0.703
Platelets count $×10^3$/mL Mean±SD Range	 249.76±92.33 (74-603)	 216.26±71.11 (100-386)	 0.108
Total WBC count $×10^3$/mL Mean±SD	 9.65±3.93	 10.95±4.82	 0.177

Range	(2.7-21.4)	(3.2-18.4)	
Neutrophil count $\times10^3$/mL Mean±SD Range	7.90±3.75 (1.8-19.6)	9.19±4.53 (1.9-16.3)	0.229
Lymphocyte count $\times10^3$/mL Mean±SD Range	1.27±0.79 (0.22-4.1)	0.98±0.70 (0.22-3.1)	0.079

Patient outcome and association to inflammatory markers

The median serum level of CRP, D-dimer and ferritin levels were higher in deceased patients (84 mg/L, 2208 ng/ml and 650 ng/mL, than among patients that survived (48 mg/L, 858 ng/ml and 550 ng/ml), the results of which were highly significant (Table 6).

Table 6: Association of inflammatory markers with the outcome

Variables	Survived (n=137)	Deceased (n=23)	p-value
C-reactive protein (mg/L) Median Range	48.0 2-317	84.0 11-145	**0.003**
D-dimer (ng/ml) Median Range	858.0 100-9009	2208.0 335-16000	**0.001**
LDH, IU/L Median Range	532.0 82-1255	646.0 157-1200	0.154
Ferritin, ng/mL Median Range	550.0 66-1650	650.0 198-1650	**0.006**

Prognostic nutritional index

The mean PNI in survived patients was 40.89±5.9 which was higher than that observed for deceased patients (37.86±4.36) showing a statistical significant difference (p=0.019; Fig. 1).

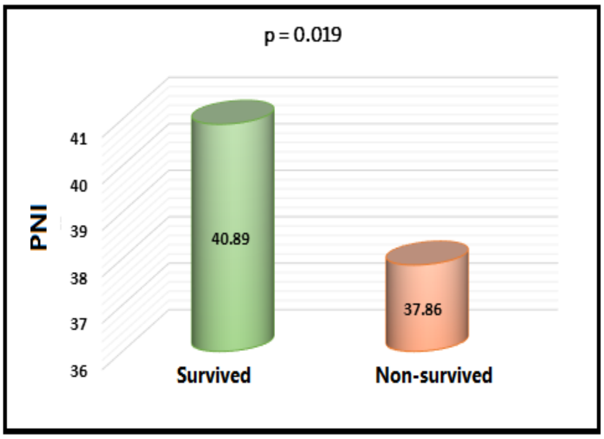

Fig. 1: The PNI of the study population

Inflammatory markers and PNI for prognosis

The predictive value of inflammatory markers and PNI in predicting mortality in hospitalized patients diagnosed with COVID-19 was evaluated using the ROC curve. The CRP level's area under the curve (AUC) was 0.692, with a 95% confidence interval of 0.589–0.795 and a p value=0.003. At a cut-off value of CRP level = 63.15 mg/L, the test's sensitivity and specificity were 70 % and 61 %, respectively. While, the AUC for D-dimer was 0.711, with a 95% CI of 0.596 to 0.826 and a p value of 0.001. The test's sensitivity and specificity were 78 and 65 % respectively, at the cutoff value of D-dimer = 1133.5 ng/ml. The ferritin AUC was observed to be 0.681, with a 95% confidence interval of 0.571–0.792 and a p value of 0.006. At a threshold ferritin level = 619.5 ng/ml, the test's sensitivity and specificity were 61 % and 64 %, respectively (Fig. 2). On another hand, The AUC for PNI was 0.883, with a 95% CI of 0.827 to 0.939 and a p value of 0.002. At a cutoff value of PNI = 38.09, the test's sensitivity and specificity were 80% and 74%, respectively. (Fig. 3).

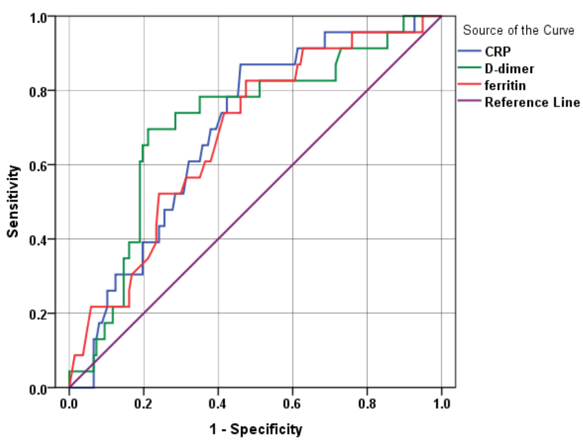

Fig. 2: ROC for inflammatory markers in predicting survival in COVID-19 patients

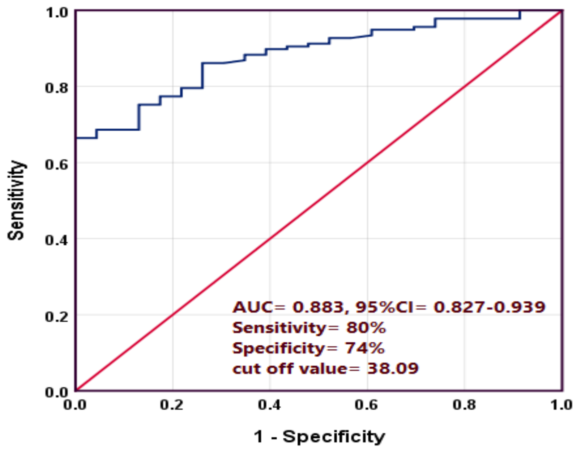

Fig. 3: ROC curves for PNI in predicting survival in COVID-19 patients

DISCUSSION

Patients diagnosed with COVID-19 who required hospitalization had a mortality rate of 14.37%. While this fatality rate was almost similar to that reported earlier for COVID-19 patients in United Kingdom and in France (9,10), it was relatively higher than that reported for COVID-19 hospital in - patients in China (5.3%), United States (6.05%), Spain (11.76%) and Italy (13.98%; 9,11,12). In most of these studies, the differences for mortality rates have been traced back to differences in the patients' demographics and medical conditions at the time of infection.

In this investigation, we observed aged patients to succumb to the disease as compared to younger patients. Research studies worldwide have shown age to be a key demographic factor and a consistent reliable indicator of an individual's likelihood of passing away due to the disease. In a large cohort study involving 2226 Spanish patients, it was reported the death rate among patients under 40 years old, between 40-49 years and 50-59 years to be 0.5%, 1.5%, and 3.8% respectively (13). This probably is due to a weakened immune system in the elderly and aged people or more likely due to a cytokine storm on exposure to COVID-19 (14). Immunosenescence is the process by which people's immune systems gradually weaken as they get older. Studies also show that immunosenescence in elderly people makes them more likely to be susceptible to infections of the respiratory tract as a consequence of compromised immune system leading to decreased mucociliary clearance, lowered mucosal barrier, or the presence of respiratory inflammation brought on by pathogenic microorganisms (13).

This study found a relationship between type 2 diabetes and death. This is consistent with previous investigations. Guan and colleagues evaluated 575 Chinese hospitals. Study endpoints were intensive care unit (ICU) hospitalization, invasive ventilation, or death. COVID-19 cases with comorbidities exhibited lower clinical outcomes. Malignancy, diabetes, and hypertension were risk factors. Patients with one comorbid ailment had a 1.79 hazard ratio, but those with two or more had a 2.59 hazard ratio (15). Further, cross-observational studies have pointed to the fact that patients associated with risk factors such as cardiovascular disease, hypertension, diabetes, chronic kidney disease, and cancer were all prone to higher risk of mortality when infected with COVID-19 (12,16).

In the present study, mortality rate was significantly associated with an elevation of CRP, D-dimer and ferritin at admission. Chen *et al.*, (11) reported a steady rise in CRP levels throughout the progression of pneumonia severity from mild to moderate to severe. Thus, evaluating the CRP levels may probably demonstrate the development of the infection in mildly afflicted persons and predict whether severely ill patients will recover or not. Similarly, Ferritin levels have been correlated with the severity of COVID-19 illness (17). It is well established that elevated serum ferritin levels is indicative of an iron overload state serving as a marker for inflammatory, autoimmune, infectious and malignant conditions (18).

Study with D-dimer levels in patients with infections has also shown that there is an increase in their levels as the disease progresses from a mild to severe form (19). A study by Gungor *et al.*, (20) reported that COVID-19 patients with an elevated D-dimer level on admission had an increased risk of severity and mortality compared to patients whose D-dimer levels were normal. Bansal *et al.*, (21) in their study revealed that COVID-19 hospitalized patients with high D-dimers levels to be associated with mortality, intensive care unit admission or suffer from acute respiratory distress syndrome.

Investigation into the prognostic value of PNI in this study showed interesting results and was found as a better marker than CRP, D-dimer, and ferritin in predicting severity and death in these patients (AUC=0.883; 39-cut off value). Studies on PNI as a predictive marker for mortality in COVID-19 patients are limited. However, the results obtained for PNI in this study was found closed to a similar study conducted by Cinar *et al.*, (22) wherein they compared the prognostic value of PNI with CURB-65 and 4C mortality risk score as predictor of in-hospitalized mortality among 294 patients. The authors reported a PNI sensitivity and specificity of 81.8% and 72% respectively, AUC value of 0.79 and a cut-off value of 42 in accurately predicting in-hospital survival. Wei *et al.*, (23) reported PNI with AUC score of 0.711 with a cutoff value of 33.405 to predict and signify mortality in patients diagnosed with COVID-19. Yet in another Chinese study, Hu *et al.*, (24) found a higher AUC of 0.817 (95% CI, 0.733-0.901; P <0 .001) and a cutoff value of 49 in COVID-19 patients. The differences observed for PNI predictive values in these values could be attributed to several other factors, the most important being demographic and ethical variation, and the targeted outcome. Recent observational studies have found that patients with a lower serum albumin concentration lead to developing COVID-19. This link was found in patients with a lower risk of developing COVID-19 (25). It is interesting to note that a state of inflammation stimulates albumin degradation, which results in a lower level of albumin in the liver (26). Results of previous studies as well as this study show that in patients diagnosed with COVID19, the nutritional, immune, and inflammatory status can all be characterized using the PNI score and used as a clinical predictor of mortality with severe COVID-19.

The current study suffers from a number of shortcomings. The study was initially carried out in a single place with a finite number of participants in each group. As a consequence, the finding cannot be extrapolated to any other centers. Second, there was no information available about the patients' dietary habits before they were admitted to the hospital.

CONCLUSION

The results seen in this study suggests that PNI may be useful as a predictor of mortality in hospitalized COVID-19 patients. Evaluating PNI scores is straightforward, uncomplicated, and economical and therefore PNI should be used as a routine test for all hospitalized patients diagnosed with COVID-19. This test should be used as an additional predictor of disease outcome in addition to clinical and laboratory markers.

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CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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