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Original Article

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Clinical value of prognostic nutritional index in predicting the presence and severity of neonatal sepsis

Abstract

Aim: The Prognostic Nutritional Index (PNI) is a novel inflammation biomarker that reflects the nutritional and inflammatory status of patients. While there are studies on its use in cancer, cardiovascular, and renal diseases, there are no studies on preterm neonatal late sepsis. This study aims to emphasize the value of PNI in neonatal sepsis.
Materials and Methods: Newborns with a birth weight of less than 1500 grams and a gestational age of less than 32 weeks, along with healthy controls, were included in the study. The ability of PNI to predict sepsis, septic shock, and mortality was evaluated.
Results: PNI was an independent and inversely related parameter to the presence and severity of neonatal sepsis. The cut-off value of PNI to predict the presence of sepsis was ≤49.5, with a sensitivity of 98.3% (95% CI: 91.1-100.0) and a specificity of 96% (95% CI: 86.3-99.5). The area under the curve (AUC) was 0.995 (95% CI: 0.957-1.000) ($p<0.001$). The optimum cut-off value of PNI to predict the presence of septic shock was ≤37.1, with a sensitivity of 92.3% (95% CI: 64.0-99.8) and a specificity of 77.3% (95% CI: 67.7-85.2). The AUC was 0.894 (95% CI: 0.821-0.945) ($p<0.001$). The optimum cut-off value of PNI to predict mortality was ≤37, with a sensitivity of 92.3% (95% CI: 64.0-99.8) and a specificity of 78.4% (95% CI: 68.8-86.1). The AUC was 0.899 (95% CI: 0.827-0.948) ($p<0.001$).
Conclusion: PNI can be used as an independent dynamic biomarker to predict the presence and prognosis of neonatal sepsis.

Keywords: Sepsis, mortality, neonatal, premature, prognostic nutritional index

INTRODUCTION

Despite recent advances in neonatology, neonatal sepsis continues to have a high morbidity and mortality rate. Early-onset sepsis (EOS) appears within the first 72 hours after birth as a result of transplacental and, more commonly, infections originating in the maternal genital tract (1). Late-onset neonatal sepsis (LOS) can occur anywhere from 4 to 30 days after birth, with the 10th to 22nd days being the most common (1). LOS is more common in newborns with low or very low birth weight that require invasive mechanical ventilation and long-term total parenteral nutrition (2). According to reports, the incidence of late neonatal sepsis in hospitalized newborns ranges between 0.61% and 14.2% (3). In our country, the incidence has been reported as 41-64/1000 live births with a mortality rate of 0-75%, and the mortality rate has decreased from 30-40% to 5-10% in recent years (4).

In cases of neonatal sepsis, it is critical to make an early diagnosis and to begin appropriate antibiotic and supportive treatment as soon as possible. However, diagnosis becomes difficult in preterm patients. False-negative results can be obtained in blood culture, which is still considered the gold standard diagnostic

method today. As a result, biomarkers to support culture results are still required in the diagnosis of sepsis.

The Prognostic Nutritional Index (PNI) is calculated using serum albumin levels and peripheral lymphocyte counts, reflecting a patient's nutritional and immune status. It also predicts overall survival in various cancers and diseases (5). It has become a reliable prognostic marker that is frequently used in the evaluation of acute heart failure, esophageal cancer, and lymphoma to determine the relationship between the patient's immune-nutritional status and prognosis (6-8). PNI predicts the prognosis of adult sepsis patients with acute kidney injury and is a predictor of mortality in patients on chronic dialysis (9,10). Additionally, PNI has been linked to survival in patients hospitalized with acute and chronic heart failure (11,12). A lower PNI value was found to be associated with greater tumor depth and lymphatic permeation in gastric carcinoma (13). PNI has been shown to have high sensitivity in predicting prognosis in cancer, regardless of the primary site (14). PNI has also been linked to mortality in severe COVID-19 patients (15-17).

PNI's role in the prognosis of patients with sepsis is unknown. PNI has been shown to be an independent risk factor in adult sepsis patients (18). Tiewei Li et al. discovered that PNI was lower in newborns with sepsis and decreased significantly with the severity of sepsis, there are only a few studies in the literature on the relationship between neonatal sepsis and PNI (5).

Our aim is to evaluate the PNI of preterm newborns diagnosed with LOS and reveal its role in predicting mortality and morbidity.

MATERIALS AND METHODS

The study was conducted between January 2018 and January 2022 in the neonatal intensive care unit. A retrospective database review was conducted for all babies born less than 32 gestational weeks and weighing less than 1500 grams, diagnosed with LOS via positive blood culture, and on postnatal days 7-30. PNI score was evaluated on the first day of sepsis. If an infant had more than one late episode of sepsis, only the first episode was included. The control group was hospitalized in our unit at the same time as the patient group, with gestational ages and birth weights gestational ages and birth weights ranging from 7 to 30 weeks, and showed no clinical or laboratory signs of sepsis.

Patients with hematological system diseases, malignancy or major congenital malformations, congenital hereditary metabolic disease, TORCH infection, cyanotic congenital heart disease, chromosomal disorder with genetically determined dysmorphism, perinatal asphyxia, neural tube defect, congenital hereditary kidney disease, perinatal asphyxia, neural tube defect, congenital hereditary kidney disease, congenital gastrointestinal anomalies requiring surgery were not included to the study. For septic shock, it was accepted that at least one inotropic support had been started, and for mortality, it was accepted that only death due to sepsis had occurred.

Demographic data, birth characteristics (delivery mode, 1st-5th minute APGAR scores, chorioamnionitis, premature rupture of membranes, resuscitation status, antenatal steroid use), maternal characteristics, comorbidities, day of sepsis, clinical features, invasive/non-invasive mechanics need for ventilation, presence of a catheter, number of sepsis attacks, enteral/total parenteral nutrition (TPN) duration, leukocyte count, lymphocyte count, neutrophil count, platelet count, hemoglobin and hematocrit value, albumin value, C reactive protein (C-RP) value, PNI, length of hospital stay (days), inotrope need, septic shock, and mortality status were evaluated. Prognostic Nutritional Index was calculated using the formula serum albumin level (g/L) + 5 x total lymphocyte count (103/mL) (5).

Clinical and laboratory parameters of cases diagnosed with sepsis were evaluated according to the European Medicines Agency (EMA) sepsis scoring (19). In patients with at least two clinical and laboratory findings, sepsis was suspected, blood and urine cultures were taken, and empirical antibiotics were started. According to the literature, septic shock is defined using the following criteria: Hypotension or cardiovascular dysfunction requiring vasoactive medications or intravenous fluid administration (normal saline, albumin, or fresh frozen plasma) (20).

The study protocol was prepared in accordance with the Declaration of Helsinki. Approval was received from the Local Ethics Committee on 01.06.2022 with the protocol code 2011-KAEK-25 2022/O6-10. All procedures performed in this study were performed as part of routine clinical practice, and data that could identify patients were removed.

Statistical Analysis

Statistical analyses were performed using IBM SPSS V 25.0 (IBM SPSS, Turkey). The Shapiro-Wilk test was used to evaluate whether a data set is normally distributed. The Mann-Whitney U test and the independent samples t-test was used to compare differences between two independent groups. Categorical variables are expressed as n (%). The Pearson chi-square test, Fisher's exact test, and Fisher-Freeman-Halton test were used to compare the distribution of categorical variables between groups. A receiver operating characteristic curve (ROC) analysis was performed for each of the continuous variables conducted to determine the diagnostic value of the PNI, with optimum cut-off values identified using the Youden J index. Calculations were made for the sensitivity, specificity, and 95% confidence intervals and the optimum cut-off value. A significance level of $p<0.05$ was considered statistically significant

RESULTS

110 newborns, (60 cases in the sepsis group and 50 cases in the control group), were included in the study. These 2 groups were evaluated according to their demographic, natal, and maternal characteristics (Table 1). The mean postnatal age of the sepsis group was 12.1±4.3 days, and that of the control group was 11.2±5.5 days. Of the 60 patients diagnosed with sepsis, 36 (60%) were boys and 24 (40%) were girls.

Table 1. Demographic and laboratory characteristics of sepsis and control groups

	Sepsis (n=60)	Controls (n=50)	p
Gestational age (weeks)	27.0 (3.0)	29.0 (3.0)	**0.001***
Birth weight (gr)	912.5 (351.0)	1152.5 (343.0)	**<0.001***
Type of birth, n (%)			0.288**
NSVD	6 (10.0)	2 (4.0)	
C/S	54 (90.0)	48 (96.0)	
Gender, n (%)			0.143+
Male	36 (60.0)	23 (46.0)	
Female	24 (40.0)	27 (54.0)	
APGAR 1. minute	5.0 (4.0)	6.0 (3.0)	**0.001***
APGAR 5. minute	7.0 (2.0)	8.0 (2.0)	**0.001***
Antenatal Steroid, n (%)			0.245+
None	29 (48.3)	20 (40.0)	
Single dose	14 (23.3)	19 (38.0)	
Full dose	17 (28.3)	11 (22.0)	
Compatibility of birth weight with gestational age, n (%)			0.103++
SGA	20 (33.3)	8 (16.0)	
AGA	37 (61.7)	39 (78.0)	
LGA	3 (5.0)	3 (6.0)	
IUGR, n (%)	15 (25.0)	11 (22.0)	0.712+
Hospitalization length (days)	62.5 (49.0)	36.0 (25.0)	**<0.001***
Mortality, n (%)	13 (21.7)	0 (0.0)	**<0.001+**
Maternal features			
Mother age (years)	27.9±6.9	27.3±5.7	0.639***
Multiparity, n (%)	35 (58.3)	28 (56.0)	0.805+
Multiple pregnancy, n (%)	8 (13.3)	7 (14.0)	0.919+
Preeclampsia/Eklampsia, n (%)	13 (21.7)	8 (16.0)	0.451+
Placenta previa, n (%)	6 (10.0)	1 (2.0)	0.124**
Gestational hypertension, n (%)	7 (11.7)	8 (16.0)	0.510+
Gestational diabetes, n (%)	4 (6.7)	3 (6.0)	1.000**
Smoking, n (%)	4 (6.7)	5 (10.0)	0.729**
Risk factors for neonatal sepsis			
EMR (>18 hours), n (%)	11 (18.3)	3 (6.0)	0.053+
Umbilical catheter, n (%)	41 (68.3)	20 (40.0)	**0.003+**
Polyhydramnios, n (%)	2 (3.3)	1 (2.0)	-
Oligohydramnios, n (%)	7 (11.7)	3 (6.0)	0.342**
Chorioamnionitis, n (%)	4 (6.7)	0 (0.0)	0.124**
Preeclampsia, n (%)	13 (21.7)	8 (16.0)	0.451+
Urinary tract infection, n (%)	7 (11.7)	2 (4.0)	0.178**
Maternal bleeding, n (%)	12 (20.0)	5 (10.0)	0.149+
Resuscitation, n (%)	27 (45.0)	17 (34.0)	0.241+
Invasive ventilation duration (days)	16.0 (31.0)	1.0 (7.0)	**<0.001***
Non-invasive ventilation duration (mean, days)	14.0 (28.0)	10.0 (24.0)	0.370*
TPN duration (days)	15.0 (19.0)	7.0 (3.0)	**<0.001***
Positive blood culture, n (%)	60 (100.0)	0 (0.0)	**<0.001+**
Comorbidity			
BPD, n (%)			**0.049****

*Mann-Whitney U test, **Fisher exact test, +Pearson chi squared test, ++Fisher Freeman Halton, ***Independent sample t test, WBC: white blood cell, HbG: hemoglobin, HCT: hematocrit, PLT: platelet, ALT: alanine amino transferase, AST: aspartate amino transferase, LDH: lactate dehydrogenase, CRP: C reactive protein, PNI: prognostic nutritional index

Table 1. Demographic and laboratory characteristics of sepsis and control groups

	Sepsis (n=60)	Controls (n=50)	p
Mild	13 (21.7)[a]	5 (10.2)[a]	
Moderate	17 (28.3)[a]	10 (20.4)[a]	
Severe	5 (8.3)[a]	1 (2.0)[a]	
RDS, n (%)	49 (81.7)	29 (58.0)	**0.007+**
PHT, n (%)	8 (13.3)	2 (4.0)	0.108+
PDA, n (%)	36 (60.0)	15 (30.6)	**0.002+**
IVH, n (%)			-
Stage 1	23 (38.3)	17 (34.0)	
Stage 2	6 (10.0)	2 (4.0)	
Stage 3	9 (15.0)	1 (2.0)	
Stage 3 and parenchyma	0 (0.0)	1 (2.0)	
NEC, n (%)			-
Stage 1	8 (13.3)	3 (6.0)	
Stage 2	3 (5.0)	0 (0.0)	
Stage 3	3 (5.0)	0 (0.0)	
ROP, n (%)			-
Stage 1	11 (19.6)	12 (26.1)	
Stage 2	7 (12.5)	1 (2.2)	
Stage 3	6 (10.7)	2 (4.3)	
Stage 4	1 (1.8)	0 (0.0)	
Cholestasis, n (%)	2 (3.3)	0 (0.0)	-
Laboratory parameters			
WBC (10^3/mm^3)	13.8 (11.2)	10.59 (4.9)	**0.010***
HbG (g/dL)	12.2 (4.0)	13.35 (5.4)	0.064*
HCT (%)	36.0±8.9	40.1±11.9	**0.048*****
PLT (10^3/mm^3)	156.0 (226.0)	348.5 (233.0)	**<0.001***
Neutrophil (10^3/mL)	9.7 (10.2)	3.7 (3.6)	**<0.001***
Lymphocyte (10^3/mL)	1.9 (1.3)	5.0 (2.2)	**<0.001***
AST (U/L)	31.5 (21.0)	25.0 (9.0)	**<0.001***
ALT (U/L)	10.0 (9.0)	8.0 (5.0)	**<0.001***
LDH (U/L)	425.5 (268.0)	365.5 (223)	0.226
Albumin (g/L)	27.1±4.3	34.5±3.3	**<0.001*****
CRP (mg /L)	66.2 (58.2)	3.0 (0.0)	**<0.001***
PNI	36.8 (6.3)	59.7 (10.7)	**<0.001***
(min-max)	(21.7-50.6)	(42.5-91.5)	

*Mann-Whitney U test, **Fisher exact test, +Pearson chi squared test, ++Fisher Freeman Halton, ***Independent sample t test, WBC: white blood cell, HbG: hemoglobin, HCT: hematocrit, PLT: platelet, ALT: alanine amino transferase, AST: aspartate amino transferase, LDH: lactate dehydrogenase, CRP: C reactive protein, PNI: prognostic nutritional index

While the mean gestational age, birth weight, and 1st and 5th minute APGAR values were lower in the sepsis group than in the control group, the mean hospitalization, invasive ventilation, TPN duration, and the rate of umbilical catheter were higher ($p<0.001$). Among the comorbidities, bronchopulmonary dysplasia (BPD), respiratory distress syndrome (RDS), and patent ductus arteriosus (PDA) were found to be higher in the sepsis group ($p<0.05$) (Table 1).

Among the symptoms encountered in the sepsis group, apnea (63.3%), change in skin color (45%), gastrointestinal problems (35%), impaired peripheral circulation (23.3%), jaundice (21.7%), tachycardia (20%), restlessness (18.3%), respiratory distress (16.7) and hypotonicity/decrease in activity (16.7%), fever (11.7%), and bradycardia (5%) were the main findings.

While WBC, neutrophil, alanine aminotransferase (AST), aspartate aminotransferase (ALT), and CRP parameters were found to be higher in the sepsis group; platelet count, lymphocyte, and albumin parameters were found to be lower ($p<0.001$).

Positive blood culture was detected in all patients included in the sepsis group (n=60). While gram-positive agents were isolated

in 46 patients (76%), gram-negative agents were detected in 14 patients (23%), and fungal agents were detected in 4 patients (6%).

Median PNI was 36.8 (6.3) in the sepsis group and 59.7 (10.7) in the control group, and was found to be statistically significantly lower in the sepsis group. The relationship between PNI values and laboratory parameters in the late neonatal sepsis and control groups is examined in Table 2. While there was a low-level direct correlation between PNI and PLT and albumin in the sepsis group, a moderate direct correlation was detected between PNI and lymphocytes. A moderate, inverse relationship was detected between PNI and CRP (Table 2).

Table 2. The relationship between PNI values and laboratory parameters

		WBC	HbG	PLT	Neutrophil	Lymphocyte	AST	ALT	LDH	ALB	CRP
Sepsis	**r**	-0.126*	-0.029**	0.301*	-0.252*	0.517*	-0.158*	-0.103*	-0.063*	0.063**	-0.631*
	p	0.338	0.826	**0.019**	0.052	**<0.001**	0.227	0.436	0.635	**<0.001**	**<0.001**
Control	**r**	0.387*	0.040*	0.221*	-0.144*	0.911*	-0.194*	0.007*	0.082*	0.279*	0.003*
	p	**0.006**	0.784	0.124	0.317	**<0.001**	0.177	0.960	0.570	0.050	0.984

* Spearman rank correlation coefficient, **Pearson correlation coefficient, WBC: White blood cell, HbG: Hemoglobin, HCT: Hematocrit, PLT: Platelet, ALT: Alanine amino transferase, AST: Aspartate amino transferase, LDH: Lactate dehydrogenase, ALB: Albumin, CRP: C reactive protein

In all cases, there was a direct and low correlation between PNI values and gestational age and birth weight. There appears to be a strong inverse relationship between the number of sepsis attacks and PNI. There is also a low and inverse relationship between PNI and length of stay, reaching full enteral blood pressure and TPN duration. There was also a statistically significant difference between PNI and gender (p=0.046). The median PNI values of boys were 42.2 (21.0) and 50.0 (21.7) lower than girls (Table 3).

Table 3. Correlation of PNI with parameters

	Gestational age	Birth weight	Number of sepsis attacks	Hospitalization length	Time to reach full enteral	TPN duration
r	0.321*	0.345*	-0.704*	-0.233*	-0.265*	-0.386*
p	**0.001**	**0.001**	**<0.001**	**0.014**	**0.006**	**<0.001**

* Spearman rank correlation coefficient, TPN: Total parenteral nutrition

A logistic model was established with the variables of gestational age, birth weight, and PNI. Increasing the PNI score by one unit reduces the presence of sepsis by 0.572 times. The median day to reach full enteral therapy was longer in the sepsis group than in the control group (p=0.004). In all cases, a direct and moderately statistically significant relationship was found between the time to reach full enteral and the duration of hospitalization (r=0.573; p<0.001). In all cases, a direct and moderately statistically significant relationship was found between TPN duration and the number of sepsis attacks (r=0.492; p<0.001). A moderate inverse relationship was detected between the number of sepsis attacks-gestational age and the number of sepsis attacks-birth weight (r=-0.435, p<0.001; r=-0.481, p<0.001, respectively). The duration of receiving TPN in the sepsis group was found to be longer than in the control group (p<0.001) (Table 4).

Table 4. Determination of factors predicting the presence of sepsis

	β	S.E.	Wald statistic	p	OR	OR for 95% CI	
						Low	High
Constant	32.145	10.159	10.011	0.002			
Gestational age	-0.207	0.271	0.580	0.446	0.813	0.478	1.384
Birth weight	0.001	0.003	0.041	0.839	1.001	0.994	1.007
PNI	-0.559	0.157	12.672	**<0.001**	0.572	0.420	0.778

*Variables included in the model: gestational age, birth weight, PNI. Method: Enter; CI: Confidence interval. p<0.001is statistically significant

In the ROC analysis performed to calculate the diagnostic value of PNI in sepsis; The optimum cut-off value of PNI was ≤49.5, sensitivity 98.3% (95% confidence interval: 91.1-100.0), specificity 96% (95% confidence interval: 86.3-99.5), AUC: 0.995 (95% confidence interval 0.957-0.100) (p<0.001) (Figure 1).

A statistically significant difference was found between the progression to septic shock and mortality and PNI values of the patients in the sepsis group (p=0.002; p=0.001, respectively). The median PNI value of patients with septic shock was 33.8 (10.4) lower than that of patients without septic shock, by 37.2 (6.8). Similarly, it was observed that the mean PNI of the deceased patients was 32.2 (5.2) lower than that of the surviving patients, 38.3 (5.3).

ROC curve analysis was performed to calculate the diagnostic value of PNI in septic shock (Figure 1). The optimum cut-off value of PNI to predict the presence of septic shock was ≤37.1, sensitivity 92.3% (95% confidence interval: 64.0-99.8), specificity 77.3% (95% confidence interval: 67.7-85.2), AUC: 0.894 (95% confidence interval: 0.821-0.945) (p<0.001) (Figure 2). In the ROC curve analysis performed to calculate the diagnostic value of PNI in the presence of mortality, the optimum cut-off value of PNI is ≤37, sensitivity 92.3% (95% confidence interval: 64.0-99.8), specificity 78.4% (95% confidence interval: 68.8-86.1), AUC: 0.899; (95% confidence interval: 0.827-0.948) (p<0.001) (Figure 3).

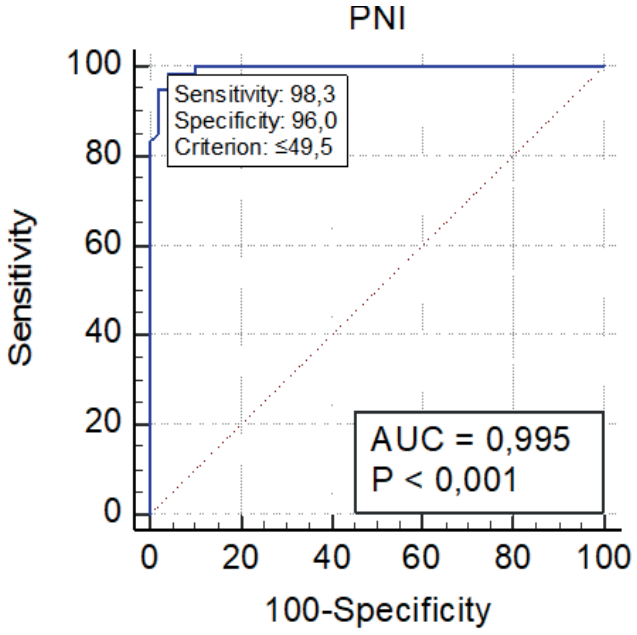

Figure 1. ROC curve for PNI in predicting the presence of sepsis

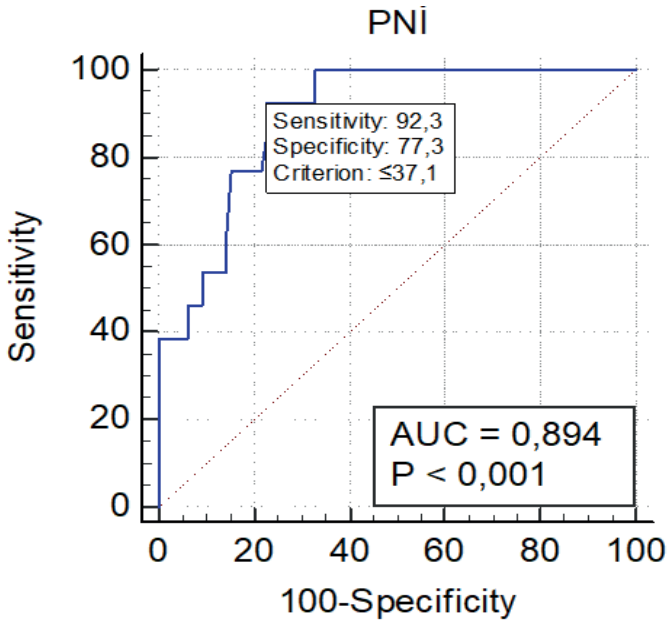

Figure 2. ROC curve for PNI in predicting the presence of septic shock

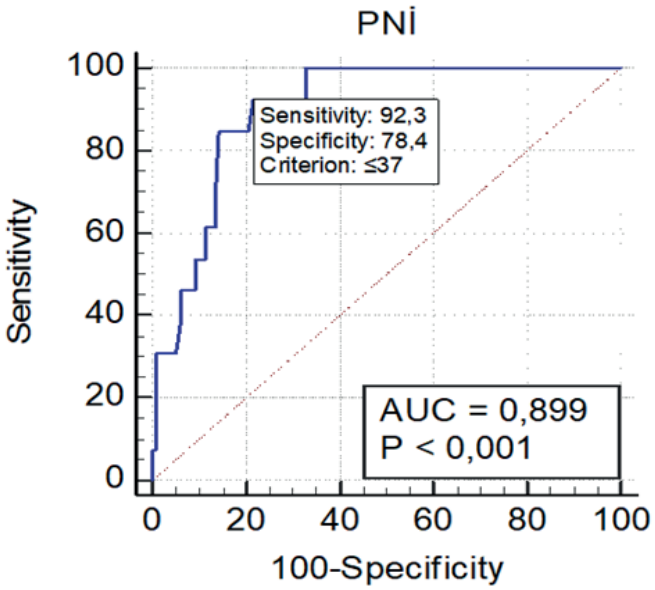

Figure 3. ROC curve for PNI in predicting the presence of mortality

DISCUSSION

Tests used to diagnose sepsis have low sensitivity and specificity, new diagnostic and prognostic methods are required in sepsis to make the correct diagnosis as quickly as possible. We aimed to investigate its role in the diagnosis and prognosis of sepsis by calculating PNI in premature with LOS.

It has been reported that the infection rate in premature newborns with LOS decreased as birth weight and gestational age increased (21,22). In our study, the mean gestational week and birth weight were lower in the sepsis group and a moderate inverse relationship was found between the number of sepsis attacks and gestational age and birth weight consistent with the literature. While there was a positive and low relationship between PNI values and gestational age and birth weight in all cases, there was a negative and strong relationship with the number of sepsis attacks.

Fuse et al. and Giannoni et al. found that male gender was more common in preterm and low birth weight babies with positive blood cultures, as well as a higher mortality rate and more postnatal complications (23,24). Male gender was found to be more dominant in our study. Furthermore, a statistically significant difference was discovered between PNI and gender. Boys had significantly lower median PNI values compared to girls. Additionally, 69% of the cases resulting in death were male. The 'male disadvantage hypothesis' has been cited in the literature to explain the predominance of morbidity and mortality among males.

RDS was found to be the most common comorbidity in our cases, followed by BPD and IVH. BPD, mechanical ventilation, invasive interventions such as catheter insertion, insufficient breast milk intake, long-term parenteral nutrition, suppressed

stomach acid, and surgical interventions are also listed as major risk factors for late neonatal sepsis (2,25). In our study, 55% of the patients had a history of invasive intervention with an umbilical catheter, more in the sepsis group. Our sepsis group patients were subjected to invasive ventilation and fed parenteral for a much longer period of time.

In all of our cases, there was a significant positive correlation between the duration of TPN and the number of sepsis attacks. According to Barreto et al., when the time to achieve full enteral nutrition exceeds 10 days, the length of stay increases, and late-onset sepsis attacks become more common (26). In our study, the average day to reach full enteral was longer in the sepsis group than in the control group. A significant positive correlation was discovered between the time to full enteral flow and the length of hospitalization, which was found to be consistent with the literature.

The presence of neutrophilia /neutropenia, lymphopenia, anemia, and thrombocytopenia are the main important criteria in neonatal sepsis (27). Consistent with the literature the number of neutrophils increased significantly and the number of lymphocytes decreased in cases diagnosed with sepsis. A moderate, direct correlation was detected between lymphocyte count and PNI ($r=0.517^*$, $p=<0.001$). CRP is an acute phase reactant with high sensitivity and specificity that is used to diagnose and monitor neonatal sepsis. In our study, we discovered a moderately inverse relationship between PNI and CRP in sepsis patients.

In newborns, Tiewei Li et al. and Bulur et al. discovered a significant negative correlation between PNI and infection and inflammation markers (5,28). Inflammatory cytokines secreted during sepsis affect the erythropoietin response and the proliferation of erythroid progenitors in the bone marrow, resulting in anemia by shortening the erythrocyte lifespan (29). In our study, the sepsis group's HbG levels were found to be lower than the controls but no statistically significant results were obtained. This was thought to be due to the study's inclusion of only cases with LNS. Thrombocytopenia in neonatal sepsis is explained by the elimination of platelets by the reticuloendothelial system, the development of platelet autoantibody formations, spleen secretion, and megakaryocyte suppression in the bone marrow (29). A direct and low correlation was found between PNI values and platelet levels of patients in the sepsis group in our study.

Sepsis has a direct impact on the nutritional status of the body because it causes gastrointestinal and liver dysfunction. The serum albumin level is the most basic parameter for determining the body's nutritional status. Serum albumin levels that are low have been linked to more severe inflammation. According to Yang et al., hypoalbuminemia is common in newborns with sepsis, and lower albumin levels may be associated with a worse prognosis (30). In our study, albumin levels were found to be significantly lower in patients with sepsis compared to controls, and it had a direct correlation with PNI values. PNI is calculated using serum albumin levels and the total number of peripheral blood lymphocytes, and it is widely used as a marker of nutritional status as well as inflammation. PNI has been reported to be a clinically relevant biomarker in adults for coronavirus disease (COVID-19), cardiovascular diseases, and sepsis (11,16,18). Wu et al. discovered that PNI<29.3 was defined as an independent predictive prognostic factor for 30-day all-cause mortality in adult patients diagnosed with sepsis (18).

Tiewei Li et al. discovered that newborns with sepsis had a significantly lower PNI score (5). PNI has been shown to be an independent and inversely related marker of neonatal sepsis presence and severity. PNI was found to be negatively correlated with levels of the inflammatory markers procalcitonin (PCT) and CRP, as well as the length of hospital stay. For the first time, the clinical significance of PNI in predicting the presence and severity of sepsis in preterm newborns was investigated in our study. According to the findings, PNI was lower in newborns with sepsis, and a gradual decrease was observed with the severity of sepsis. We show that a low PNI value is an independent risk factor for the presence and severity of neonatal sepsis in preterm infants.

Our study has some limitations. First of all, our study had a small sample size and was a single-center retrospective study. PNI was calculated using routine data collected during the time period when the diagnosis of sepsis was considered.

CONCLUSION

Although the incidence of neonatal sepsis has decreased in recent years, it remains a serious cause of mortality and morbidity in all neonatal units. There is still a need for new ideal markers and additional research for the early diagnosis of sepsis in this critical population. Our findings show that the PNI can provide clinicians with useful prognostic information about the presence and severity of late-onset sepsis in preterm newborns with high sensitivity, specificity, and important biomarkers for clinical use.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
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Ethical Approval
The study protocol was prepared in accordance with the Declaration of Helsinki. Approval was received from the Local Ethics Committee on 01.06.2022 with the protocol code 2011-KAEK-25 2022/O6-10.

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