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ORIGINAL RESEARCH

Inflammatory markers and delirium in the intensive care unit

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Abstract

Background: Delirium is an important complication in patients admitted to intensive care unit (ICU). However, delirium prediction in patients admitted to the ICU is difficult. Considering the role of neuroinflammation in delirium, peripheral blood-based biomarkers of inflammation pressure could predict delirium. The aim of study was to retrospectively analyze ratios of neutrophil/high density lipoprotein (HDL) (NHR), lymphocyte/HDL (LHR), platelet/HDL (PHR), monocyte/HDL (MHR), as well as systemic immune-inflammation index (SII) and systemic inflammatory response index (SIRI) in ICU patients diagnosed with delirium. **Methods**: The study included a total of 2141 patients with or without delirium. The risk factors for delirium development and the predictive power of individual laboratory parameters were evaluated with the Pearson chi-square test, Mann-Whitney U test, Spearman correlation test, logistic regression, and receiver operating characteristic analyses. **Results**: Length of ICU stay ($p < 0.001$), NHR ($p = 0.035$), LHR ($p < 0.001$), PHR ($p = 0.047$), MHR ($p < 0.001$), SIRI ($p < 0.001$), and SII ($p < 0.001$) were significantly higher in patients who developed delirium compared to those who did not. A significant negative correlation was found between the duration of delirium and SII ($r = -0.260$; $p = 0.004$). Older age, a history of psychiatric treatment, prolonged hospitalization, and high LHR, SIRI, and SII values were determined as risk factors for delirium ($p < 0.05$ for all). **Conclusions**: Elevated LHR, SIRI, and SII levels before ICU admission are associated with an increased risk of hyperactive delirium. If confirmed by prospective evidence, readily available biomarkers for inflammation could be used to evaluate the hyperactive delirium risk in ICUs.

Keywords

Intensive care; Delirium; Neutrophil/high-density lipoprotein; Lymphocyte/high-density lipoprotein; Platelet/high-density lipoprotein; Monocyte/high-density lipoprotein; Systemic immune-inflammation index; Systemic inflammatory response index

1. Introduction

Delirium is sudden onset of acute brain failure due to a medical condition [1]. Characterized by fluctuating disturbances in attention, awareness, and cognition that cannot be explained by preexisting neurocognitive disorders, delirium typically develops within hours to days and varies in severity throughout the day [2]. The incidence of delirium in intensive care unit is 31% and there are three subtypes: hyperactive type (4%) with restlessness, agitation, and psychotic symptoms; hypoactive type (11%) with motor slowdown, sedation, and apathy; and mixed type (7%) with both hyperactive and hypoactive symptoms [3, 4]. Mechanical ventilation, in particular, increases the risk of delirium by up to 80% in ICU settings [5]. The etiology of delirium has been explored through the investigation of genetic factors and metabolic disorders, with recent research focusing on the role of inflammation [6].

The neuroinflammation hypothesis suggests that neuroinflammation and immune responses triggered by acute injury or severe physical stress may lead to delirium [7]. Numerous inflammatory markers have been associated with cognitive dysfunction [8]. It is also known that inflammation activates pathways that play a role in delirium. However, studies monitoring inflammatory changes before, during, and after delirium in humans are limited, and the precise mechanisms by which these changes affect the brain remain under investigation [9, 10]. During delirium, endogenous or exogenous inflammatory activities are triggered, leading to the release of inflammatory cytokines, such as interleukin (IL)-1 and IL-6, some of which cross the blood-brain barrier. Furthermore, the production of these cytokines is stimulated in the endothelium and released directly into the brain parenchyma, potentially resulting in neuronal dysfunction, behavioral changes, and brain damage [11].

Length of hospitalization and poor quality of life are recognized as independent risk factors for delirium, alongside underlying medical conditions [12]. In recent years, researchers have investigated preventable delirium predictors to reduce associated morbidity and mortality [13]. In addition to the complexity of the pathophysiology of delirium, there is currently no definitive laboratory test or imaging method that can confirm its diagnosis. Therefore, the diagnosis of delirium continues to rely on clinical criteria, which are often overlooked or underappreciated. This has prompted researchers to investigate various methods for the early detection of delirium for ICU patients [14].

Lymphocytes, monocytes, and neutrophils are known to play key roles in inflammation [15]. Given the anti-inflammatory, antithrombotic, and antioxidant properties of high-density lipoprotein cholesterol (HDL-c), ratios such as neutrophil/high density lipoprotein (NHR), monocyte/high density lipoprotein (MHR), platelet-to-High-Density Lipoprotein Cholesterol Ratio (PHR), and lymphocyte/high density lipoprotein (LHR) have emerged as easily accessible, significant biomarkers of inflammation [16]. These parameters have been studied in various neuropsychiatric disorders where inflammation is implicated in disease etiology [17]. For example, Seo *et al.* [18] reported a close association between the neutrophil/lymphocyte ratio (NLR) and the onset of delirium. Recent studies have focused on new blood biomarkers calculated with platelet, neutrophil, lymphocyte, and monocyte counts that comprehensively reflect the state of inflammation such as systemic immune-inflammation index (SII) and systemic inflammatory response index (SIRI) [19, 20]. These novel parameters could provide information on the interactions between immune response, inflammatory response, and thrombosis [21]. Recently, preventable delirium predictors have been investigated to reduce morbidity and mortality [22]. A study has shown that cognitive dysfunction is associated with the dysregulation of various molecular signaling pathways in circulating exosomes and monocytes and an exaggerated proinflammatory response to acute bacterial infection [23]. Delirium in patients with hip fracture has been reported to be associated with activated immune-inflammatory pathways and decreased negative immune regulatory mechanisms [24]. A meta-analysis comparing blood values between patients with and without delirium suggested that NLR could help predict and prevent delirium [25]. Lu *et al.* [26] reported that high SIRI and NLR levels might be indicative of delirium in elderly patients following hip arthroplasty surgery.

To the best of our knowledge, no study has been conducted to analyze the differences in SII, SIRI, NHR, LHR, MHR, and PHR between ICU patients with and without delirium. Therefore, the current study aimed to explore these readily accessible, and cost-effective hemogram and biochemistry parameters, which could be suitable for routine evaluation, in predicting delirium risk in ICU patients.

2. Materials and methods

2.1 Sample

This retrospective, cross-sectional study was conducted on patients admitted to the ICU at Fethi Sekin Urban Hospital between January 2020 and January 2024. The study was approved by the Non-Interventional Ethics Committee of Fırat University (approval number: 2024/02-09). The study was conducted in accordance with the Helsinki Declaration, ensuring patient data confidentiality. As it is a retrospective review and analysis of the hospital's electronic medical records, the requirement for informed consent was waived by Fırat University Ethics Committee. Patient files available in the hospital database were reviewed. The data for our study were obtained from patients admitted to the internal medicine intensive care unit (ICU) of our hospital due to internal causes, including cardiac, respiratory, neurological, hematological, and hepatopancreatic conditions. Blood tests conducted at the time of ICU admission were retrospectively analyzed. In our study, we included patients with hyperactive delirium who were hospitalized in the ICU and exhibited delirium symptoms either upon initial admission or later during their hospitalization, with delirium considered as a preliminary diagnosis. The diagnosis of delirium was based on clinical suspicion and psychiatric consultation without the use of standard assessment tools (such as the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) or Intensive Care Delirium Screening Checklist (ICDSC)). As a result, a psychiatry consultation was requested. The hemogram and biochemistry values, routinely ordered within the first 24 hours of ICU admission, were retrospectively evaluated for these patients. Patients aged 65 years or older without a diagnosis of dementia in their medical history before admission to the ICU were included. Patients with a known history of neurological system diseases (cerebrovascular accident, *etc.*) were excluded. Additionally, patients with incomplete data were excluded. Following the exclusion of 139 patients with incomplete data, a total of 2141 ICU patients were included in the study.

2.2 Data collection tools

A sociodemographic and clinical data form was developed by the authors based on clinical experience and the existing literature, to record relevant data. This form included demographic details, such as age and marital status, as well as clinical variables, *e.g.*, length of ICU stay and delirium onset time. In addition, lymphocyte, monocyte, neutrophil, and platelet counts were recorded from routine blood examinations at admission. The following parameters were calculated: NLR (neutrophil count/lymphocyte count), PLR (platelet count/lymphocyte count), SIRI (neutrophil count $\times$ monocyte count/lymphocyte count) and SII (platelet count $\times$ monocyte count/lymphocyte count) [26].

2.3 Laboratory samples

In our hospital, routine venous blood samples are collected from every patient admitted to the ICU. Complete blood counts are analyzed using a DXH-800 device (Beckman Coulter, Inc., Miami, FL, USA), and biochemical parameters are analyzed using a Beckman AU-5800 device (Beckman Coulter Diagnos-

tics, Indianapolis, IN, USA). Neutrophil, lymphocyte, monocyte, and platelet counts, and HDL-c levels were determined. Using these parameters, NHR, PHR, and MHR were calculated manually (neutrophil count/HDL-c, platelet count/HDL-c, and monocyte count/HDL-c, respectively).

2.4 Data analysis

Statistical analyses were conducted with the Statistical Package for the Social Sciences (SPSS) version 22 (SPSS Inc., Chicago, IL, USA). Descriptive categorical findings were presented as numbers and percentages, while continuous data were presented as median and interquartile range (25th–75th percentile) values. Categorical variables were compared using Pearson's chi-square analysis. The normality of distribution of continuous variables was determined using the Kolmogorov-Smirnov test. The Mann-Whitney U test was employed to compare paired groups. Spearman's correlation test was conducted to analyze the correlations between continuous variables. Logistic regression analysis was used to calculate risk factors, starting with a univariable analysis, followed by a multivariable analysis for variables that were found significant in the first stage. Receiver operating characteristic (ROC) analysis was utilized to evaluate the diagnostic value of various parameters. The statistical significance level was accepted as $p < 0.05$.

3. Results

The study was conducted among 2141 ICU patients, of whom 118 (5.5%) presented with delirium. The incidence of delirium was 5.6% among male patients and 5.4% among female patients, indicating no significant difference according to sex ($p = 0.829$). The median age of the patients who developed delirium was significantly higher when compared to that of patients without delirium ($p = 0.022$). The incidence of delirium was also significantly higher among patients with a history of psychiatric treatment (20.4%) compared to that of patients without this history (3%) ($p < 0.001$). Length of ICU stay ($p < 0.001$) and NHR ($p = 0.035$), LHR ($p < 0.001$), PHR ($p = 0.047$), MHR ($p < 0.001$), SIRI ($p < 0.001$), and SII ($p < 0.001$) levels were significantly higher in patients with delirium than in those without delirium (Table 1). A significant negative correlation was observed between delirium onset time and SII ($r = -0.260$; $p = 0.004$) (Table 2).

Logistic regression analysis revealed that older age (odds ratio (OR) = 1.013, 95% confidence interval (CI) = 1.002–1.024), a history of psychiatric treatment (OR = 8.148, 95% CI = 5.542–11.980), a longer ICU stay (OR = 1.029, 95% CI = 1.017–1.042), and elevated LHR (OR = 1.801, 95% CI = 1.486–2.182), PHR (OR = 1.002, 95% CI = 1.001–1.003), SIRI (OR = 1.266, 95% CI = 1.144–1.401), and SII (OR = 1.013 , 95% CI = 1.001–1.003) levels were associated with an increased risk of delirium in univariable analysis. In multivariabe analysis, significant predictors were identified as older age (adjusted OR (aOR) = 1.018, 95% CI = 1.007–1.029), a history of psychiatric treatment (aOR = 11.307, 95% CI = 7.291–17.533), a longer ICU stay (aOR = 1.033, 95% CI = 1.018–1.049), and elevated LHR (aOR = 2.018, 95% CI = 1.618–2.518), SIRI (aOR = 1.293, 95% CI = 1.142–1.464), and SII (aOR = 1.002, 95% CI = 1.001–1.002) levels (Table 3).

ROC analysis was performed to assess the predictive power of the various parameters, determining their cut-off values for predicting the development of delirium among ICU patients. According to this analysis, NHR had a sensitivity of 86.4% and a specificity of 29.1% at a cut-off value of 0.13, LHR had 89% sensitivity and 36.9% specificity at a cut-off value of 1, MHR showed 72.9% sensitivity and 49% specificity at a cut-off value of 0.01, SIRI had a sensitivity of 61.9% and a specificity of 91.9% at a cut-off value of 1.91, and SII demonstrated 38.1% sensitivity and 86.9% specificity at a cut-off value of 763.73. Each of these five parameters was determined to be a direct predictor of delirium. Furthermore, PHR was identified as a poor predictor, showing 19.5% sensitivity and 96.9% specificity at a cut-off value of 460 (Table 4, Fig. 1).

4. Discussion

This study examined the correlations between SII, SIRI, NHR, LHR, MHR, and PHR levels and delirium in ICU patients. Our findings demonstrated that delirium developed in 5.5% of the ICU patients, and those with elevated NHR, LHR, PHR, MHR, SIRI, and SII levels were more susceptible to delirium. In addition, older age, a history of psychiatric treatment, a longer ICU stay, and high LHR, SIRI, and SII levels were identified as significant risk factors for delirium. These results suggest that NHR, LHR, MHR, SIRI, and SII could be used to predict delirium in ICU patients.

Various parameters have been reported to be risk factors for delirium [27]. The risk of developing delirium increases with age [28], likely due to the increased incidence of comorbidities in older patients. To maintain a consistent age range in our sample, we only included patients aged over 65. Psychiatric disorders are also recognized as independent risk factors for delirium [29]. For example, Ren *et al.* [30] reported that the prevalence of delirium in psychiatric patients with organic disease was around 33%. Furthermore, admission to the ICU is a risk factor for delirium, and prolonged ICU stay is an indicator of poor prognosis in those with delirium [31], probably due to the increased incidence of hospital-acquired complications, including infections, pressure injuries, and gastrointestinal bleeding in this patient population [32]. Although male sex has been suggested as another risk factor for delirium [33, 34], our study did not find a significant association between sex and delirium risk. The demographic characteristics of patients with delirium in our study were mostly consistent with those reported in previous research. We consider that more comprehensive studies are needed to investigate the risk factors associated with delirium in ICU settings and to elucidate long-term outcomes. A deeper understanding of delirium is essential for its early recognition and treatment, which warrants further investigating into its etiology [35].

Recent research has focused on identifying markers that could predict delirium, with the aim of reducing mortality and morbidity, as well as exploring key risk factors [36]. Neutrophils, monocytes, lymphocytes, and platelets are important components of the peripheral immune system [37], and their inflammatory response in the brain triggers delirium

TABLE 1. Inter-group comparison of study parameters.

	Patients with delirium		Patients without delirium		*p*
	n	%	n	%	
Sex					
Male	60	5.6	1008	94.4	0.829*
Female	58	5.4	1015	94.6	
Median age in years (IQR)	77.00 (65.00–83.00)		72.00 (57.00–82.00)		**0.022****
Concomitant organic disease					
Present	105	5.6	1784	94.4	0.794*
Absent	13	5.2	239	94.8	
Psychiatric treatment history					
Present	62	20.4	242	79.6	<**0.001***
Absent	56	3.0	1781	97.0	
Length of ICU stay in days	8.00 (4.00–14.00)		3.00 (1.00–7.00)		<**0.001****
Delirium onset time	2.00 (1.00–5.00)		-		-
NHR	0.26 (0.16–0.45)		0.25 (0.12–0.41)		**0.035****
LHR	2.10 (1.30–2.67)		1.30 (0.24–2.12)		<**0.001****
PHR	184.75 (24.73–287.12)		146.00 (24.36–225.00)		**0.047****
MHR	0.023 (0.014–0.036)		0.015 (0.009–0.026)		<**0.001****
SIRI	2.06 (0.78–2.14)		0.88 (0.74–1.05)		<**0.001****
SII	479.09 (221.81–901.21)		269.21 (192.34–488.61)		<**0.001****
Hemoglobin (mg/dL)	10.90 (3.50–19.70)		12.20 (0.00–19.70)		**0.003****
White Blood Cell ($\times 10^3/\mu$L)	10.50 (0.50–59.80)		10.65 (0.90–25.80)		0.326**
Platelet ($\times 10^3/\mu$L)	183.00 (10.00–2005.00)		226.50 (8.00–616.00)		<**0.001****
Neutrophil ($\times 10^3/\mu$L)	2.73 (0.10–14.00)		3.49 (0.90–14.00)		**0.001****
Lymphocyte ($\times 10^3/\mu$L)	1.80 (0.20–13.46)		2.10 (0.90–4.20)		**0.001****
Monocyte ($\times 10^3/\mu$L)	0.40 (0.00–1.70)		0.57 (0.01–1.60)		**0.013****

**Chi-square analysis, **Mann Whitney U test. IQR: inter-quartile range; ICU: intensive care unit; NHR: neutrophil/high-density lipoprotein; LHR: lymphocyte/high-density lipoprotein; PHR: platelet-to-High-Density Lipoprotein Cholesterol Ratio; MHR: monocyte/high-density lipoprotein; SIRI: systemic inflammatory response index; SII: systemic immune-inflammation index.*
Values in bold indicate statistically significant results ($p < 0.05$).

TABLE 2. Correlation between delirium onset time and study parameters.

Laboratory parameters	Delirium time	
	r	*p*
NHR	0.086	0.356
LHR	0.001	0.987
PHR	−0.142	0.126
MHR	0.063	0.498
SIRI	0.045	0.632
SII	**−0.260**	**0.004**

NHR: neutrophil/high-density lipoprotein; LHR: lymphocyte/high-density lipoprotein; PHR: platelet-to-High-Density Lipoprotein Cholesterol Ratio; MHR: monocyte/high-density lipoprotein; SIRI: systemic inflammatory response index; SII: systemic immune-inflammation index.
Values in bold indicate statistically significant results ($p < 0.05$).

TABLE 3. Logistic regression analysis of the presence of delirium.

	Univariable analysis				Multivariable analysis			
	B	*p*	Unadjusted OR	95% CI	B	*p*	Adjusted OR	95% CI
Age	0.013	**0.016**	1.013	1.002–1.024	0.018	**0.002**	1.018	1.007–1.029
Psychiatric treatment history (ref = absent)	2.098	<**0.001**	8.148	5.542–11.980	2.425	<**0.001**	11.307	7.291–17.533
Length of ICU stay	0.029	<**0.001**	1.029	1.017–1.042	0.033	<**0.001**	1.033	1.018–1.049
NHR	0.724	0.072	2.062	0.939–4.529				
LHR	0.588	<**0.001**	1.801	1.486–2.182	0.702	<**0.001**	2.018	1.618–2.518
PHR	0.002	**0.023**	1.002	1.001–1.003	0.001	0.087	1.001	0.998–1.003
MHR	0.707	0.597	2.029	0.147–7.938				
SIRI	0.236	<**0.001**	1.266	1.144–1.401	0.257	<**0.001**	1.293	1.142–1.464
SII	0.002	<**0.001**	1.002	1.001–1.003	0.002	<**0.001**	1.002	1.001–1.002

OR: odds ratio; CI: confidence interval; ICU: intensive care unit; NHR: neutrophil/high-density lipoprotein; LHR: lymphocyte/high-density lipoprotein; PHR: platelet-to-High-Density Lipoprotein Cholesterol Ratio; MHR: monocyte/high-density lipoprotein; SIRI: systemic inflammatory response index; SII: systemic immune-inflammation index.
Values in bold indicate statistically significant results ($p < 0.05$).

TABLE 4. Predictive performance of study parameters for delirium among ICU patients.

Cut-off value	AUC	*p*	95% confidence interval		Sensitivity	Specificity	PPV	NPV
			Lower limit	Higher limit				
NHR >0.13	0.557	**0.021**	0.536	0.578	86.4	29.2	6.6	97.4
LHR >1	0.669	<**0.001**	0.648	0.689	89.0	36.9	7.6	98.3
PHR >460	0.554	0.065	0.533	0.576	19.5	96.9	27.1	95.4
MHR >0.01	0.624	<**0.001**	0.603	0.644	72.9	49.0	7.7	96.9
SIRI >1.91	0.680	<**0.001**	0.660	0.700	61.9	91.9	30.9	97.6
SII >763.73	0.648	<**0.001**	0.627	0.668	38.1	86.9	14.5	96.0

ICU: intensive care unit; AUC: area under the curve; PPV: positive predictive value; NPV: negative predictive value; NHR: neutrophil/high-density lipoprotein; LHR: lymphocyte/high-density lipoprotein; PHR: platelet-to-High-Density Lipoprotein Cholesterol Ratio; MHR: monocyte/high-density lipoprotein; SIRI: systemic inflammatory response index; SII: systemic immune-inflammation index.
Values in bold indicate statistically significant results ($p < 0.05$).

via microglia activation [38]. Zhao *et al.* [39] reported that elderly internal medicine patients with an NLR of >3.626 had a significantly higher incidence of delirium compared to those with an NLR of ≤3.626 [39]. It has also been demonstrated that the biochemical HDL parameter is an antioxidant that can prevent endothelial damage [40]. SII, SIRI, NHR, LHR, MHR, and PHR have been investigated in various psychiatric conditions [26, 41]. A meta-analysis *involving* 11,579 critically ill patients, of whom 2439 were diagnosed with delirium, identified NLR as a biomarker capable of predicting delirium [42]. In another study, SIRI and NLR levels were found to be elevated in 29% of 116 elderly patients who developed delirium after hip arthroplasty, suggesting that preoperative SIRI levels could serve as a biomarker for delirium risk in this patient population [26]. In our study, patients who developed delirium in the ICU had high levels of SII, SIRI, NHR, LHR, MHR, and PHR. Elevated LHR, SIRI, and SII in the initial tests on the first day of ICU admission were associated with an increased risk of delirium. Our results suggest that high SII, SIRI, NHR, LHR, and MHR levels may have diagnostic value in predicting delirium in the ICU. These findings contribute to the growing body of evidence indicating an association between alteration in peripheral immune cells and delirium in ICU patients. Monitoring changes in these hemogram and biochemical parameters is a cost-effective, accessible, and practical approach to identifying patients at risk for delirium. Early detection and treatment of delirium may be facilitated by these examinations performed upon ICU admission. Although our findings indicate that SIRI could serve as a delirium biomarker, supporting the findings reported by Lu *et al.* [26], there is a need for further studies to determine delirium risk in ICU settings.

This study has some limitations worth acknowledging. The study was conducted at a single center with a heterogeneous patient population, and due to its retrospective design, we were unable to obtain some potentially relevant data, such as patients' past medical history, history of neurocognitive impairment, or ventilator requirement in the ICU. The exclusion of patients with neurological disorders and dementia likely led to an underestimation of delirium prevalence, as it removed high-risk groups from the study population. Additionally, since our study focused on patients over 65 years of age, this limits the generalizability of the findings to younger patients who may also be at risk for delirium. Furthermore, although

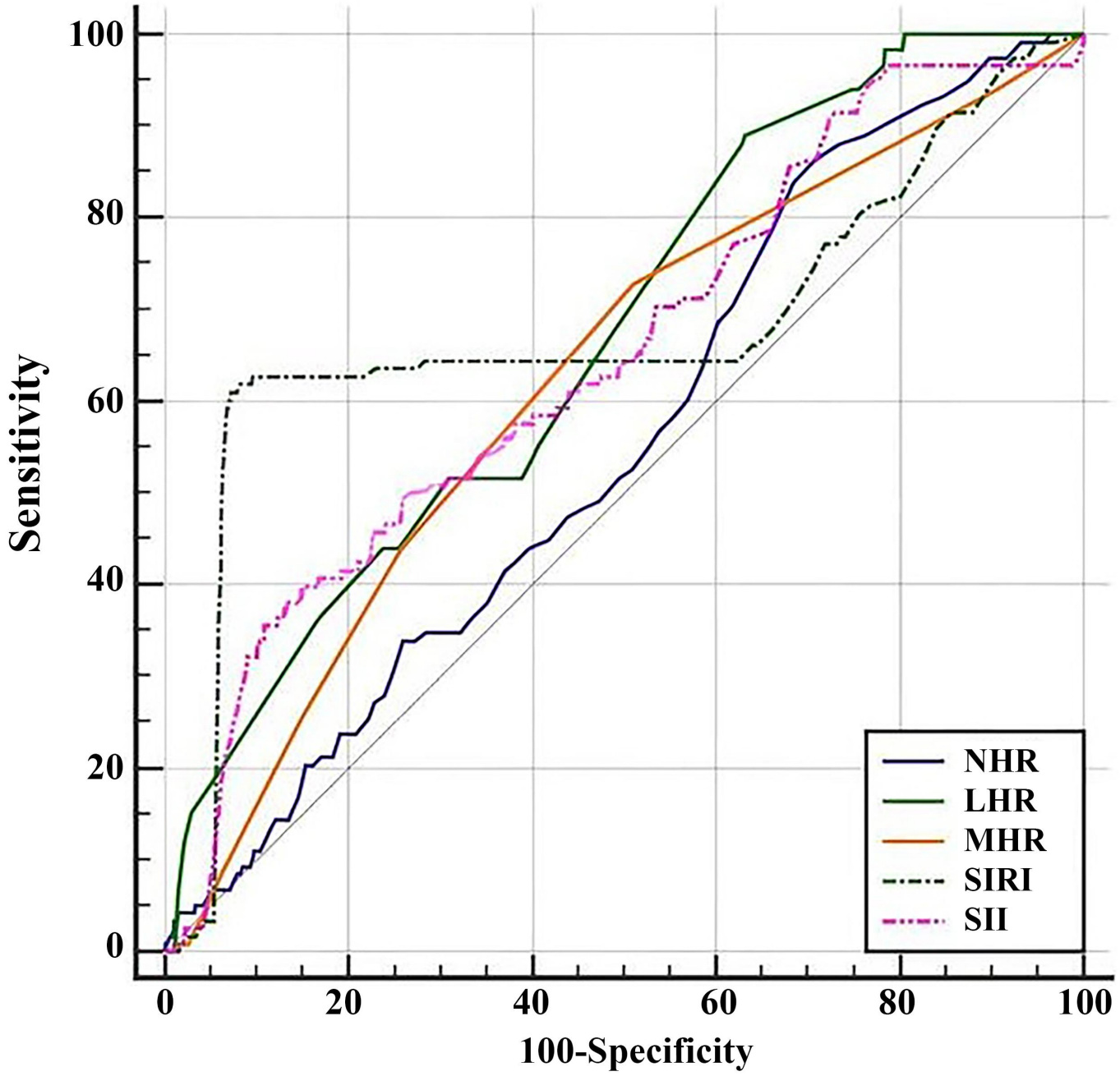

FIGURE 1. Receiver operating characteristic curves of the investigated parameters for predicting delirium. NHR: neutrophil/high-density lipoprotein; LHR: lymphocyte/high-density lipoprotein; MHR: monocyte/high-density lipoprotein; SIRI: systemic inflammatory response index; SII: systemic immune-inflammation index.

factors such as respiratory failure, shock, metabolic disorders, prolonged mechanical ventilation, pain, immobility, sedation use, and sleep disorders are known to trigger delirium [43], these parameters could not be assessed in our retrospective study. Despite these limitations, this is the first study to explore the association between SII, SIRI, NHR, LHR, MHR, and PHR levels and the development of delirium in ICU patients.

5. Conclusions

Our findings suggest that early identification of delirium risk could be possible through the use of easily accessible, cost-effective blood parameters, namely SII, SIRI, NHR, LHR, MHR, and PHR, which could potentially improve patient outcomes. Multicenter studies with larger samples that include a wider range of possible variables in patients with delirium are needed to address the limitations of the current study. Since the levels of inexpensive and applicable hemogram and biochemistry parameters used in delirium risk prediction may be elevated due to factors such as infection or trauma, we believe that considering additional inflammatory markers, such as C-reactive protein and interleukins, would be beneficial in future studies based on our findings. Furthermore, in light of our findings, we believe that standardized delirium risk scoring systems, incorporating these affordable and feasible laboratory parameters, could be developed to predict delirium in the ICU. Such systems could facilitate proactive interventions,

potentially reducing ICU mortality and morbidity rates. While promising, these inflammatory biomarkers should ideally be used in combination with other clinical assessments or standardized tools and not as stand-alone predictors.

AVAILABILITY OF DATA AND MATERIALS

The data that support the findings of this study are available upon reasonable request.

AUTHOR CONTRIBUTIONS

SY—software; resources; writing-original draft preparation; supervision; funding acquisition. MFU—investigation; writing-review and editing. BSE—formal analysis; project administration. OK—visualization. SY and MFU—conceptualization; data curation. SY and BSE—methodology. MFU, SY and OK—validation. All authors have read and agreed to the published version of the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was approved by the local ethics committee (date: 01 February 2024, number: 2024/02-09). As it is a retrospective analysis based on the hospital's electronic medical records, the requirement for informed consent was waived by Fırat University Ethics Committee.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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