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POLISH GYNECOLOGY
GINEKOLOGIA POLSKA
ORGAN POLSKIEGO TOWARZYSTWA GINEKOLOGICZNEGO
THE OFFICIAL JOURNAL OF THE POLISH GYNECOLOGICAL SOCIETY

ISSN: 0017-0011

e-ISSN: 2543-6767

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DOI: 10.5603/gpl.100739

Article type: Research paper

Submitted: 2024-05-17

Accepted: 2024-10-05

Published online: 2025-02-15

Articles in "Ginekologia Polska" are listed in PubMed.

ORIGINAL PAPER / OBSTETRICS

Prognostic evaluation of systemic immune inflammatory index and hematological parameters in postpartum hemorrhage: a retrospective analysis

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ABSTRACT

Objectives: Postpartum hemorrhage (PPH) is a significant global health risk for mothers. This study investigated the predictive capacity of the systemic immune inflammatory index (SII) to assess the risk of PPH. The SII, which is predicated on cell types of integral to inflammatory processes, correlates with high values of increased inflammatory activity and potentially adverse prognoses.

Material and methods: This retrospective cohort study included female patients aged 15–49 diagnosed with PPH who continued to bleed post-treatment, received transfusions of four or more units of erythrocyte suspension, or underwent laparotomy/re-laparotomy.

Results: The study found that Hemoglobin, hematocrit, platelet, and SII values were significantly lower, and lymphocyte counts were elevated in the PPH group. Both univariate and

multivariate analyses identified hemoglobin and SII levels as significant determinants of PPH. An SII cutoff value of 915 proved to be an effective predictor of PPH. In subjects with an SII ≥ 915, leukocyte, platelet, and neutrophil values were higher, and lymphocyte counts were lower. Furthermore, the rates of PPH and Intensive Care Unit admissions increased in this cohort.
Conclusions: The findings suggest that the SII is a potentially significant marker for PPH risk prediction. Elevated SII levels beyond the threshold of 915 were associated with heightened PPH risk of PPH.
Keywords: postpartum hemorrhage; systemic immune-inflammatory index; hematological parameters; massive transfusion; multidisciplinary approach

INTRODUCTION

Postpartum hemorrhage (PPH) is a global health issue that poses a serious threat to maternal health. According to the World Health Organization, PPH is a leading cause of maternal death, particularly in developing countries, and continues to be a significant health concern even in developed nations [1]. According to the American College of Obstetricians and Gynecologists, early postpartum hemorrhage is defined as a total blood loss of at least one thousand (1000) mL within the first twenty-four hours after delivery, or blood loss accompanied by symptoms and signs of hypovolemia. [2]. Effective management of PPH is critical to reduce maternal mortality and morbidity [3] Despite advancements in the early diagnosis and management of modern obstetric practices, challenges persist due to unexpected bleeding events that can occur even in patients without risk factors, highlighting the importance of a multidisciplinary approach in PPH management [4, 5]

The decline in postpartum hematocrit levels has been known to correlate poorly with the severity of acute blood loss, thus not providing a clinically useful definition in an emergency [6]. Therefore, the use of various laboratory and clinical parameters is recommended for managing emergencies, such as PPH. Notably, initial fibrinogen levels in emergency department patients with primary PPH were independently associated with the need for massive transfusion [7]. Lactate concentration may play a critical role in the management of PPH, especially in rapidly determining the need for massive transfusion [8]. It is important to remember that clinical findings in addition to laboratory tests should be considered. This multifaceted approach is necessary for effective PPH management and contributes to the safeguarding of maternal health.

A high shock index is generally regarded as an indicator of significant blood loss and entry into hypovolemic shock, necessitating rapid life-saving interventions by health professionals, such as blood transfusion, fluid replacement, or other emergency measures [9, 10].

The systemic immune-inflammation index (SII), defined by Hu et al. in 2014 and calculated using the formula “SII = Platelets x Neutrophils/Lymphocytes,” is a marker based on the roles of these three cell types in inflammatory processes [11]. Platelets and neutrophils accumulate in areas of active inflammation in the body, while lymphocytes play a critical role in regulating the immune response [12]. A high SII value has been utilized as a prognostic factor, particularly in patients with cancer, and various studies have demonstrated that high SII values are associated with disease progression and mortality [13]. However, a meta-analysis conducted in 2022 on a large cohort of 18,609 patients with ischemic stroke reported that a high SII significantly predicted poor outcomes, such as mortality and hemorrhagic transformation [14]. This finding suggests that SII could potentially be used as a tool for predicting hemorrhagic events. It is conceivable that the SII may also have prognostic value in acute bleeding conditions, such as PPH. Nevertheless, further research is required to determine the diagnostic accuracy and optimal threshold values of these indices [15]. Our study, aiming to fill the existing gap in the literature, is, to our knowledge, the first to explore the relationship between PPH and SII and seeks to make a significant contribution to this field.

This study investigated the use of SII to predict the risk and severity of PPH. The efficacy of SII in forecasting clinical outcomes, such as the need for post-bleeding transfusion, the necessity for laparotomy, and admission to the intensive care unit, is being evaluated.

MATERIAL AND METHODS

Study design

This retrospective cohort study included female patients aged 15-49 who were diagnosed with postpartum hemorrhage at Başakşehir Çam and Sakura City Hospital’s Obstetrics and Gynecology Clinic between April 1, 2020, and October 20, 2023, who continued to bleed despite treatment, received four or more units of red blood cell suspension transfusion, or underwent laparotomy or re-laparotomy. The primary hypothesis of this study was that the SII can predict postpartum hemorrhage and anticipate the need for post-bleeding transfusion, laparotomy, and intensive care requirements.

Study population

A total of 270 patients meeting the selection criteria constituted the study population. Patient demographic information, obstetric histories, and laboratory results were retrospectively reviewed. The patient group consisted of women who experienced postpartum hemorrhage after 34 normal deliveries and 101 cesarean sections. The control group included 34 normal delivery and 101 cesarean section patients who did not experience postpartum hemorrhage.

Exclusion criteria

Those 15 or over 49 years of age, with a hemoglobin value below 8, placental adhesion and placement anomalies, experiencing resistant bleeding due to non-obstetric reasons, who gave birth at a gestational age of < 28 weeks, using drugs that could affect bleeding or coagulation, with a history of resistant postpartum hemorrhage, and those who had multiple pregnancies such as twins or triplets were excluded from the study.

Data collection

The age of the patients, number of births (parity), and modes of delivery were recorded. Blood samples taken six and twenty-four hours prior to delivery were analyzed for leukocyte, hemoglobin, hematocrit, neutrophil, platelet, and lymphocyte levels. Data was then transferred to Microsoft Excel.

Inflammatory indices

Inflammatory indices were calculated using the following formulas:

SII = Neutrophil × Platelet/Lymphocyte.

Potential limitations

Potential limitations of the study include the inability to definitively establish causality due to the retrospective cohort design and limited study population.

Ethical approval

The study was initiated with approval number E-96317027-514.10-227839520 from the Başakşehir Çam and Sakura City Hospital Ethics Committee, and all procedures were conducted in accordance with the Declaration of Helsinki.

Statistical method

Descriptive statistics of the data included mean, standard deviation, median, lowest, highest, frequency, and ratio values. The distribution of variables was measured

using the Kolmogorov-Smirnov and Shapiro-Wilk tests. The Mann-Whitney U test was used to analyze quantitative independent data. The chi-squared test was used for the analysis of independent qualitative data. The effect level and cutoff values were investigated using the ROC curve. The effect level was investigated using univariate and multivariate logistic regression analyses. The SPSS 28.0 program was used for all analyses.

RESULTS

Our study showed that age and mode of delivery did not have a significant impact on PPH ($p > 0.05$), whereas hemoglobin, hematocrit, platelet counts, and SII values were lower in patients with PPH ($p < 0.05$), and lymphocyte counts were higher ($p < 0.05$). This suggests that these parameters may play a significant role in the development of PPH (Tab. 1).

In the univariate model, significant efficacy of hemoglobin, hematocrit, platelet, lymphocyte, and SII values was observed in distinguishing between patients with and without PPH ($p < 0.05$). This indicates that these parameters play an important role in determining the PPH. In the multivariate model, significant and independent efficacy of hemoglobin and SII values was observed in distinguishing between patients with and without PPH ($p < 0.05$). This demonstrates that these two parameters have an independent effect on PPH even when other potential influencing factors are controlled (Tab. 2).

In our study, the SII value showed significant efficacy in distinguishing patients with and without PPH. The area under the curve was 0.653 (0.587–0.719), indicating that the SII value plays a significant role in determining the PPH. Additionally, an SII cut-off value of 915 showed significant efficacy in distinguishing between patients with and without PPH. The area under the curve was 0.663 (0.598–0.728), indicating that the SII cutoff value of 915 plays a significant role in determining PPH. At an SII cut-off value of 915, the sensitivity was 55.6%, positive predictive value, specificity, and negative predictive value were 63.4% 70.8%, 77.0 patients, and without PPH. This demonstrates that an SII cut-off value of 915 is an effective tool for determining PPH (Tab. 3, Fig. 1).

In our study, the sensitivity and specificity were compared based on the SII values. No significant differences were found in age, mode of delivery, and parity number between the groups with SII < 915 and SII ≥ 915 ($p > 0.05$ and $p > 0.05$). This indicates that these factors do not play a significant role in determining SII values (Tab. 4).

No significant difference was found in hemoglobin and hematocrit values between the groups with SII < 915 and SII ≥ 915 ($p > 0.05$). However, leukocyte, platelet, and neutrophil values were significantly higher in the group with an SII ≥ 915 than in the group with an SII < 915 ($p < 0.05$). This indicates that these parameters increase when the SII value exceeds 915.
Furthermore, the lymphocyte count was significantly lower in the group with an SII ≥ 915 than in the group with an SII < 915 ($p < 0.05$). This indicated that the lymphocyte level decreased when the SII value was above 915.
No significant difference was found in the rate of laparotomy between groups with SII < 915 and SII ≥ 915 ($p > 0.05$). However, the rates of PPH and intensive care unit (ICU) admissions were significantly higher in the group with an SII ≥ 915 than in the group with an SII < 915 ($p < 0.05$). This indicated that the rates of PPH and ICU admissions increased when the SII value was above 915 (Tab. 4).

DISCUSSION

SII is based on a combination of lymphocyte, neutrophil, and platelet counts in the peripheral blood samples. This index is a comprehensive indicator of the patient's immunological status and inflammatory activity in the body [16]. An increase in the neutrophil count or neutrophilia is typically indicative of a body's fight against an infection or inflammatory condition.
Lymphocytes, which form the memory of the immune system, respond more quickly and effectively in secondary immune responses. As the fundamental cells of the specific immune response, they are critical in defense against pathogens through antibody production [17].
Platelets play significant roles in inflammatory processes, not only in hemostasis but also by interacting with the immune system and influencing adaptive immune responses [18]. A high SII usually indicates increased neutrophil, and platelet counts with a low lymphocyte count, which may signal high inflammatory activity and potential immune suppression in the body. The SII is defined as a new inflammatory index that can more comprehensively represent a patient's immune and inflammatory status [19]. This index is used to assess the prognosis of various diseases and monitor inflammatory conditions.
In obstetric and gynecological pathologies, the potential of SII as a prognostic indicator has been examined in current research. In cases of preeclampsia, a significant increase in the SII has been observed, and SII values measured in the first trimester have been determined to be effective in

predicting preeclampsia [20, 21]. High SII values during delivery are noteworthy [22]. In the case of placenta previa, the SII has been shown to be useful in predicting the spectrum of placenta accreta [23]. Moreover, the SII is emphasized as an important marker for predicting the inflammatory status and possible miscarriage risk in ongoing pregnancies [24].

However, studies examining the predictive role of these indices in patients with postpartum hemorrhage are limited. Accurately predicting the risk of postpartum hemorrhage could be significant in clinical practice by supporting the management of certain cases and contributing to the prevention of adverse outcomes. This study aimed to evaluate the usability and effectiveness of the SII in predicting the risk of postpartum hemorrhage.

In the human reproductive system, neutrophils play a critical role in processes, such as follicle development and ovulation, even in the absence of infection. Dysfunction of these cells, which is effective in regulating endometrial function, can lead to abnormal bleeding [25]. In cases of resistant postpartum hemorrhage following cesarean section, histological detection of inflammation in the uterine body and isthmus has led to the consideration of acute myometritis as a potential cause of postpartum hemorrhage in non-infectious etiologies [26, 27]. Women who have experienced postpartum hemorrhage have been observed to have increased plasma inflammatory cytokine levels compared with the control groups [28]. In a study conducted by Kong, T., and colleagues, inflammatory indices such as the delta neutrophil index have been shown to be usable in predicting the need for massive transfusion after postpartum hemorrhage [29]. Additionally, changes in platelet count and volume before delivery in women with pathological pregnancy complications have been shown to be useful in predicting the risk of postpartum hemorrhage [30, 31]. These fin blood and local inflammatory mediators in the uterus in predicting the occurrence and severity of postpartum hemorrhage.

Our research revealed that the SII and other hematological parameters are significant in predicting the risk of PPH. In patients with PPH, lymphocyte counts were significantly higher, whereas no difference was observed between leukocyte and neutrophil levels. Hemoglobin, hematocrit, and platelet values were also determined to be important in identifying the risk of PPH. These findings highlight the necessity of a comprehensive analysis to assess PPH risk. Furthermore, the high sensitivity and specificity rates of the SII above the 915-cut-off value indicate that it could be an important prognostic tool for determining PPH risk.

The current literature emphasizes the importance of the SII as a potential indicator for predicting hemorrhagic events and their outcomes. In cardiothoracic surgery, high SII levels after aortic valve replacement have been associated with an increased risk of bleeding [32]. However, there is no study in the obstetric field on this subject; therefore, this study could be the first to examine the usability of the SII in predicting the risk of PPH. These results suggest that the SII could play a significant role in evaluating inflammatory processes and the risk of PPH.

Findings in the literature support that the SII is an effective indicator for predicting hospital mortality and adverse outcomes in various bleeding conditions and acute intracerebral hemorrhage cases. The SII has been observed to be a strong discriminator for poor clinical outcomes through ROC analysis [33]. Additionally, studies using the systemic inflammatory response index have been useful for predicting the necessity of surgical intervention in cases of abdominal trauma [34]. However, studies examining the prognostic value of SII for laparotomy after cesarean or vaginal delivery are limited in the literature, presenting new research opportunities to explore the potential of SII in this area [35].

Our research has revealed that in patients with SII value above 915, there is an increase in the rates of PPH and admission to the intensive care unit. This suggests that high SII values could be a strong indicator of not only PPH but also the need for intensive care. However, the SII alone was not sufficient to predict the need for laparotomy. This implies that the SII may have limited prognostic utility, especially in determining the need for surgical intervention.

These results underscore the importance of a multifaceted approach in the management of PPH rather than relying on a single indicator. In assessing the risk of PPH, the integrated use of specific inflammatory markers, such as SII, along with other hematological parameters, such as hemoglobin, hematocrit, and platelets, can allow for a more accurate evaluation of the patient's condition.

Our study has aimed to comprehensively examine the clinical potential and limitations of SII, establishing a foundation for future research. Our findings underscore the importance of utilizing the SII in conjunction with other hematological parameters to predict the risk of PPH. However, validation of these results in larger patient cohorts and prospective studies will reinforce the role of these parameters in clinical decision-making processes. **We would like to note that ferritin levels were not analyzed; this reflects the laboratory capabilities of our hospital and**

indicates that this parameter was not routinely measured during the period our study was conducted. This limitation should be considered when interpreting the results of our study.

Article information and declarations

Data availability statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Ethics statement

Ethical Approval: The study was initiated with approval number E-96317027-514.10-227839520 from the Başakşehir Çam and Sakura City Hospital Ethics Committee, and all procedures were conducted in accordance with the Declaration of Helsinki.

Author contributions

Emrullah Akay and Gizem Şirin Donbalıoğlu played a significant role in the design and implementation, while Ali Selçuk Yeniocak, Emrah Dağdeviren, and Can Tercan were instrumental in the analysis of the results and the writing of the manuscript. Emrullah Akay and İbrahim Polat conceived the original idea and supervised the project.

Funding

There are no institutions or organizations that support or finance this study.

Acknowledgments

We extend our heartfelt gratitude to all women who participated in our study at the Department of Obstetrics and Gynecology, İstanbul Başakşehir Çam, and Sakura City Hospital. Your contributions are invaluable to our research.

Conflict of interest

The authors declare that they have no conflict of interest.

Supplementary material

None.

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Table 1. Comparison of demographic and laboratory parameters of patients according to PPH status

	PPH (-)		PPH (+)		p
	Mean ± SD / n – %	Median	Mean ± SD / n – %	Median	
Age	29.9 ± 6.2	31.0	31.2 ± 6.0	31.0	0.082 [m]

Table 1. Comparison of demographic and laboratory parameters of patients according to PPH status

Mode of birth	Cesarean	101	74.8%		101	74.8%		1.000	x^2
	Vaginal Birth	34	25.2%		34	25.2%			
Parity		2.91	± 1.65	3.00	2.76	± 1.40	3.00	0.659	m
Leukocyte		10.6	± 2.3	10.5	11.5	± 4.3	10.9	0.362	m
Hemoglobin		11.8	± 1.6	12.0	11.3	± 1.2	11.5	0.006	m
Hematocrit		34.4	± 3.9	34.7	33.6	± 3.2	33.5	0.009	m
Platelet		236.3	± 64.6	228.0	211.8	± 69.8	211.0	0.001	m
Neutrophil		8.26	± 2.22	8.10	9.28	± 6.93	7.89	0.866	m
Lymphocyte		1.48	± 0.62	1.40	2.50	± 6.58	1.70	0.000	m
SII		1528.4	± 853.6	1277.2	1187.9	± 907.4	832.0	0.000	m
Laparotomy	(-)	135	100.0%		103	76.3%		0.000	x^2
	(+)	0	0.0%		32	23.7%			
ICU Admission	(-)	135	100.0%		97	71.9%		0.000	x^2
	(+)	0	0.0%		38	28.1%			

[m] Mann-Whitney u test; [x^2] Chi-square test

PPH — postpartum hemorrhage; SII — systemic immune inflammatory index

Table 2. Univariate and multivariate model analysis of hematological and inflammatory parameters in the presence and absence of PPH

	Univariate model				Multivariate model			
	OR	95% GA		p	OR	95% GA		p
Hemoglobin	0.799	0.673	– 0.949	0.010	0.763	0.639	– 0.911	0.003
Hematocrit	0.931	0.869	– 0.998	0.043				
Platelet	0.995	0.991	– 0.998	0.004				
Lymphocyte	2.019	1.394	– 2.924	0.000				
SII	1.000	0.999	– 1.000	0.002	0.999	0.999	– 1.000	0.001

Logistic Regression (Forward LR); PPH — postpartum hemorrhage; SII – systemic immune inflammatory index

Table 3. ROC analysis of the efficacy of SII value in predicting the presence of PPH

		Area under the curv		95% Confidence interva		p
SII		0.653		0.587	– 0.719	0.000
SII 915 cut off		0.663		0.598	– 0.728	0.000
		PPH (–)	PPH (+)			%
SII	< 915	31	75	Sensitivity		55.6%
	≥ 915	104	60	Positive predictive value		70.8%
				Specificity		77.0%

Table 3. ROC analysis of the efficacy of SII value in predicting the presence of PPH

Negative predictive value	63.4%

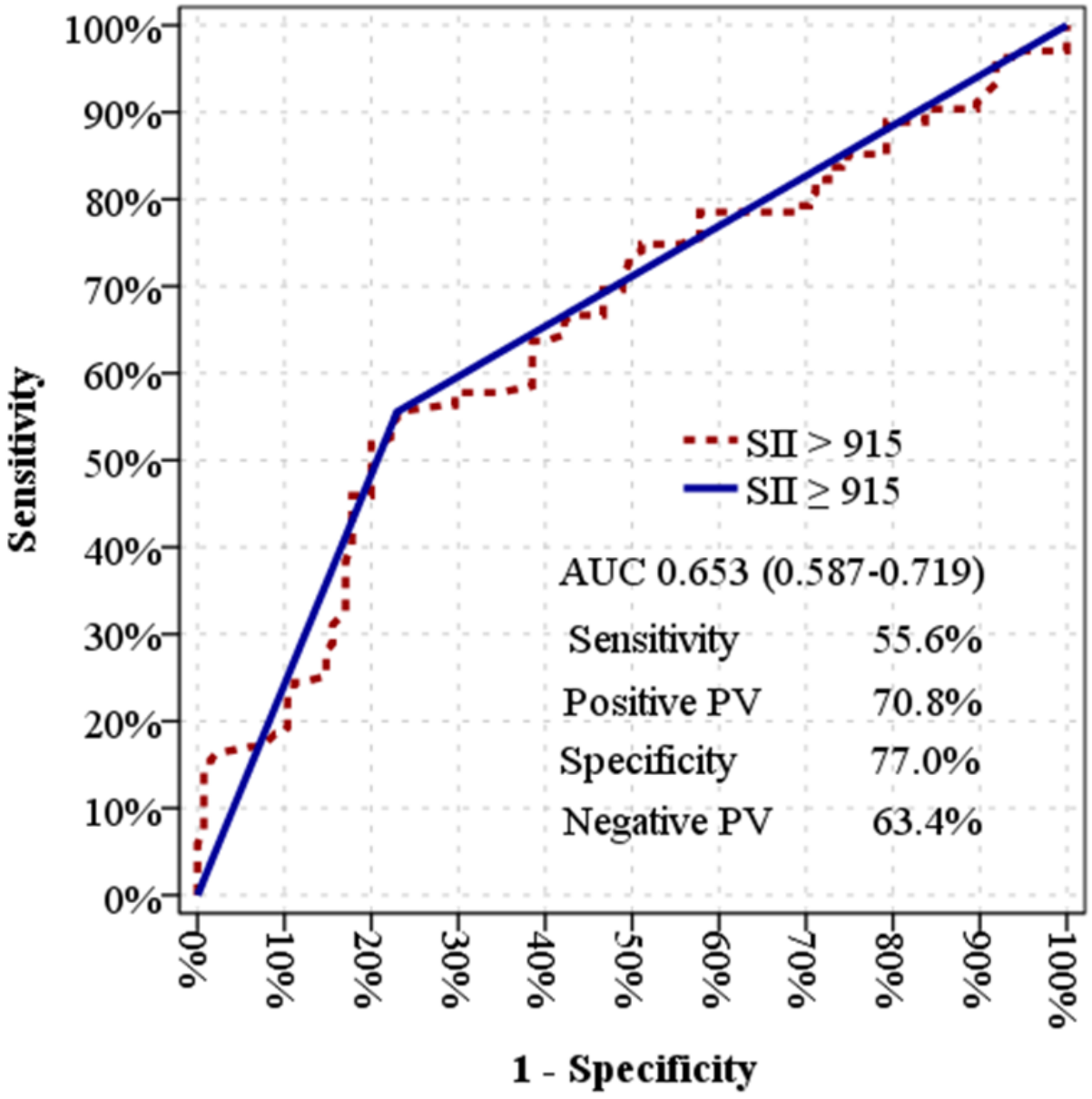
ROC Curve

PPH — postpartum hemorrhage; SII — systemic immune inflammatory index

Table 4. Comparison of parameters according to SII values in the presence and absence of PPH

		SII < 915				SII ≥ 915				p	
		Mean ± SD/n – %			Median	Mean ± SD/n – %			Median		
Age		30.2	±	5.8	29.0	30.8	±	6.3	31.0	0.410	m
Mode of birth	Cesarean	83		78.3%		119		72.6%		0.289	X^2
	Vaginal birth	23		21.7%		45		27.4%			
Parity		2.76	±	1.34	3.00	2.88	±	1.64	3.00	0.887	m
Leukocyte		9.88	±	3.25	9.77	11.78	±	3.40	10.90	0.000	m
Hemoglobin		11.7	±	1.5	11.9	11.5	±	1.4	11.6	0.283	m
Hematocrit		34.5	±	3.5	34.3	33.7	±	3.5	34.2	0.265	m
Platelet		189.1	±	55.3	188.0	246.7	±	66.3	234.0	0.000	m
Neutrophil		7.03	±	2.77	6.64	9.90	±	5.98	8.56	0.000	m
Lymphocyte		2.73	±	7.22	1.92	1.51	±	1.47	1.32	0.000	m
Laparotomy	(–)	92		86.8%		146		89.0%		0.580	X^2
	(+)	14		13.2%		18		11.0%			
PPH	(–)	31		29.2%		104		63.4%		0.000	X^2
	(+)	75		70.8%		60		36.6%			
ICU Admission	(–)	83		78.3%		149		90.9%		0.004	X^2
	(+)	23		21.7%		15		9.1%			

[m] Mann-Whitney u test; [X^2] Chi-square test; ICU — intensive care unit, PPH — postpartum hemorrhage; SII — systemic immune inflammatory index



SII — systemic immune inflammatory index

Figure 1. Comparison of sensitivity and specificity according to SII values. This graph illustrates how sensitivity and specificity vary according to SII values. Sensitivity and specificity values for cases with SII > 915 are represented by a dotted line, while cases with SII ≤ 915 are shown with a solid line. The AUC value is 0.653, indicating the overall performance of the model. Sensitivity

is 55.6%, positive predictive value is 70.8%, specificity is 77.0%, and negative predictive value is 63.4%. These values help us understand how the model performs across different SII values