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Systemic Immune-Inflammation Index (SII) as a Predictor of Treatment Response in Primary Immune Thrombocytopenia

Primer İmmün Trombositopenide Tedavi Yanıtının Öngördürücüsü Olarak Sistemik İmmün-İnflamasyon İndeksi (SII)

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Abstract: Primary immune thrombocytopenia (ITP) is an autoimmune disorder characterized by isolated thrombocytopenia resulting from immune-mediated platelet destruction and impaired platelet production. Although corticosteroids and intravenous immunoglobulin (IVIG) are standard first-line therapies, many patients fail to achieve or maintain an adequate response, emphasizing the need for early predictors of treatment resistance. This study aimed to identify clinical and laboratory factors associated with unresponsiveness to corticosteroid and IVIG therapy in primary ITP and to explore the predictive value of systemic immune-inflammation index (SII). This retrospective study included 109 adults newly diagnosed with primary ITP between January 2008 and December 2023. Demographic, clinical, and laboratory data were collected from patient records, and SII was calculated for each patient. Receiver operating characteristic (ROC) analysis determined the optimal SII cut-off for predicting treatment response, while logistic regression identified independent predictors of corticosteroid and IVIG resistance. The mean age was 51.48 ± 16.9 years, and 72.5% were female. All patients received systemic steroids, and 32.1% also received IVIG. The complete response rate to steroids was 50%, while 31.3% were non-responders; the IVIG non-response rate was 45.7%. ROC analysis identified an optimal SII cut-off of 48.33, with lower SII associated with significantly higher response rates to both steroids and IVIG ($p < 0.05$). Multivariate analysis confirmed low SII as an independent predictor of IVIG responsiveness (OR = 8.25, 95% CI 1.15–59.00; $p = 0.036$). In conclusion, SII at the time of diagnosis independently predicts response to first-line therapy, and early assessment may facilitate timely second-line interventions.

Keywords: Primary immune thromboytopenia (ITP), Systemic immune inflammation index (SII), Intravenous immunoglobulin (IVIG), Corticosteroids

Özet: Primer immün trombositopeni (İTP), immün aracılı trombosit yıkımı ve trombosit üretiminde azalma sonucu gelişen izole trombositopeni ile karakterize otoimmün bir hastalıktır. Kortikosteroidler ve intravenöz immünoglobulin (IVIG) standart birinci basamak tedaviler olmasına rağmen, birçok hastada yeterli veya kalıcı yanıt elde edilememekte, bu da tedavi direncini erken öngörebilecek belirteçlerin önemini ortaya koymaktadır. Bu çalışmanın amacı, primer İTP hastalarında kortikosteroid ve IVIG tedavisine yanıtsızlıkla ilişkili klinik ve laboratuvar faktörleri belirlemek ve sistemik immün-inflamasyon indeksinin (SII) prognostik değerini araştırmaktır. Bu retrospektif çalışmaya Ocak 2008 - Aralık 2023 arasında primer İTP tanısı alan 109 erişkin hasta dahil edilmiştir. Demografik, klinik ve laboratuvar veriler hasta dosyalarından elde edilerek her hasta için SII değeri hesaplanmıştır. Tedavi yanıtını öngörmede optimal SII kesim değeri ROC analizi ile belirlenmiş, lojistik regresyon analizi ile kortikosteroid ve IVIG direncini etkileyen bağımsız faktörler saptanmıştır. Hastaların yaş ortalaması 51,5 ± 16,9 yıl olup, %72,5'i kadındır. Tüm hastalara birinci basamak tedavide sistemik steroid uygulanmış olup, %32,1'ine ek olarak IVIG uygulanmıştır. Steroid tedavisine tam yanıt oranı %50, yanıtsızlık oranı %31,3; IVIG tedavisine yanıtsızlık oranı ise %45,7 olarak saptanmıştır. ROC analizi sonucunda optimal SII kesim değeri 48,33 olarak bulunmuştur. Düşük SII düzeyine sahip hastalarda her iki tedaviye yanıt oranlarının anlamlı olarak daha yüksek olduğu bulunmuştur ($p < 0,05$). Çok değişkenli analiz, düşük SII'nin IVIG yanıtını bağımsız olarak öngördüğünü göstermiştir (OR = 8,25, %95 GA 1,15–59,00; $p = 0,036$). Sonuç olarak, tanı anındaki SII değeri birinci basamak tedavi yanıtını öngören bağımsız bir belirteçtir ve erken değerlendirilmesi, dirençli olguların erken dönemde ikinci basamak tedaviye yönlendirilmesine olanak sağlayacaktır.

Anahtar Kelimeler: Primer immün trombositopeni (İTP), Sistemik immün inflamasyon indeksi (SII), İntravenöz immünoglobulin (IVIG), Kortikostreoidler

Ethics Committee Approval: The study was approved by the Clinical Research Ethics Committee of the Bursa Uludag University Faculty of Medicine (Approval no: 2023-24/16, Approval date: 21.11.2023).

Authorship Contributions: Study Conception/Design: FÇH, HÖ, VÖ, FÖ, Data Collection/ Processing: FÇH, KAÜ, İEP, VG ,Analysis or Interpretation: FÇH, TE, HÖ ,Literature Search: FÇH, KAÜ, HÖ , Writing: FÇH, FÖ, VÖ

Informed Consent: The authors declared that it was not considered necessary to get consent from the patients because the study was a retrospective data analysis.

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1. Introduction

Primary immune thrombocytopenia (ITP) is an acquired autoimmune disease that develops as a result of immune-mediated destruction of platelets and in some cases impaired production of platelets (1). Its prevalence in adults is 9-20 per 100,000. Although it is seen more frequently in women of reproductive age, its incidence peaks a second time after the age of 60 (2,3). Most patients are asymptomatic. The main clinical features of symptomatic cases include thrombocytopenia (platelet count $<100*10^9$/L), mucosal bleeding such as petechiae, purpura and ecchymosis as well as in some cases, life-threatening organ bleeding (intracranial haemorrhage, gastrointestinal bleeding) and a decrease in quality of life. During the diagnostic process, secondary pathologies that could affect platelet production and consumption need to be excluded. After diagnosis, there are three temporally distinct subtypes; newly diagnosed (first 3 months), persistent (3-12 months), and chronic (over 12 months) (4,5).

The primary objective in managing newly diagnosed cases of ITP is to achieve hemostatic control and elevate the platelet count to a clinically safe threshold. In addition to platelet count, comorbidities significantly influence bleeding tendencies. Nonetheless, the prevailing consensus is to initiate treatment when the platelet count is less than $30*10^9$/L (6). Corticosteroids are the primary treatment for cases of ITP with the initial dosage generally being 1 mg/kg of prednisone or 40 mg/day of dexamethasone. In cases where prednisone is initiated, the starting dose should be administered for 2 weeks and then the steroid treatment should be gradually tapered and discontinued within 6-8 weeks to prevent side effects. In cases where dexamethasone is preferred, treatment is administered at 40 mg/day for 4 days, up to a maximum of 3 cycles (7,8). Another initial treatment option that can be used in life-threatening situations, such as intracranial haemorrhage or major gastrointestinal bleeding or in situations where platelet counts need to be rapidly increased, such as before surgery, is intravenous immunoglobulins (IVIG). The standard dosage is 1 g/kg administered for a maximum duration of 2 days (9,10). In approximately 80% of patients receiving IVIG, platelet levels increase to a safe range; however, approximately 20% of cases exhibit no response. Similarly, an initial response is observed in 60-80% of cases treated with corticosteroids and about half of these patients maintain a long-term treatment response. However, 10-20% of cases do not respond to initial steroid treatment and similar to IVIG non-responders, are classified as refractory ITP cases. These cases have a poorer prognosis compared to standard cases due to both the side effects associated with prolonged corticosteroid use and the complications arising from bleeding (10,11).

While existing literature includes studies focused on the early identification of refractory ITP cases, a standardized scoring system is not currently in use. Since both the humoral and cellular immune systems are active in the pathogenesis of ITP cases, it is not always possible to determine which pathway is predominant in a given case or which second-line treatment will be beneficial. In cases where initial treatment proves ineffective, early identification is essential to enhance the prognosis. This study aimed to identify clinical and laboratory factors associated with resistance to first-line therapies (systemic corticosteroids and IVIG) in patients with primary ITP in order to determine potential early predictors of treatment unresponsiveness.

2. Materials and Methods

The study included 109 adult patients newly diagnosed with primary ITP who were followed at the Hematology Clinic of Bursa Uludag University between January 2008 and December 2023. Only newly diagnosed primary ITP cases were included, while patients with secondary ITP, those with chronic ITP under follow-up, organ transplant recipients and HIV-positive individuals were excluded from the study. The study flowchart is presented in Figure 1.

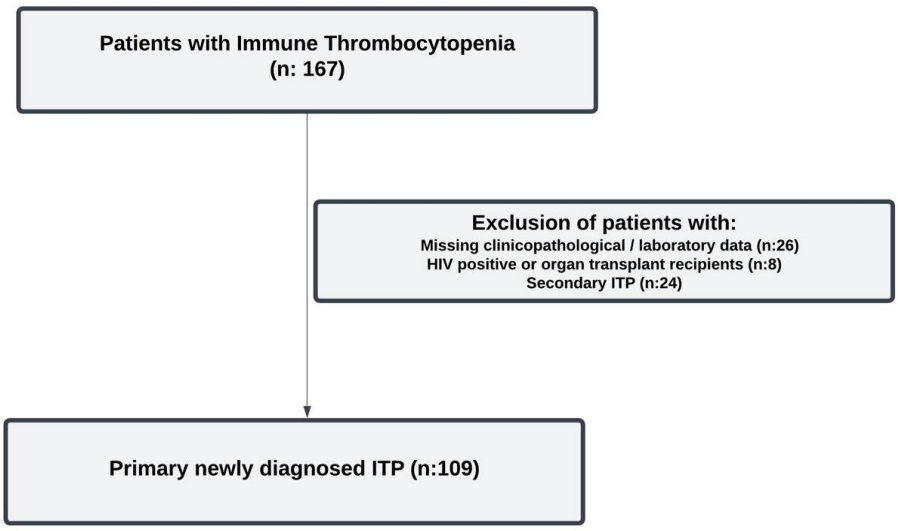

Figure 1. *Flowchart of the Study*

Demographic characteristics, comorbidities, clinicopathological features, laboratory parameters and imaging findings at the time of diagnosis were retrospectively obtained from patient files and the hospital information system. As part of the diagnostic work-up, all patients routinely underwent peripheral smear evaluation, coagulation profile, serum vitamin B12 and folate levels, liver function tests, C-reactive protein (CRP), lactate dehydrogenase (LDH), antinuclear antibody (ANA), antiphospholipid antibodies, lupus anticoagulant, viral serologies and thyroid function tests. Patients with suspected malignancy at baseline were evaluated with computed tomography (CT) and, when indicated, positron emission tomography–CT (PET-CT) to exclude secondary ITP. Bone marrow biopsy was performed in patients aged over 60 years at diagnosis and in those unresponsive to standard ITP therapies (corticosteroids, IVIG, or eltrombopag) to confirm the diagnosis and rule out myelodysplastic syndrome. The neutrophil-to-lymphocyte ratio (NLR) was calculated by dividing the neutrophil count (10^9/L) by the lymphocyte count (10^9/L), and the lymphocyte-to-monocyte ratio (LMR) was calculated by dividing the lymphocyte count (10^9/L) by the monocyte count (10^9/L). The systemic immune-inflammation index (SII) was calculated as (platelet count [10^9/L] × neutrophil count [10^9/L]) / lymphocyte count (10^9/L), while the systemic inflammation response index (SIRI) was calculated as (neutrophil count [10^9/L] × monocyte count [10^9/L]) / lymphocyte count (10^9/L). The EASIX score was defined as (LDH [U/L] × creatinine [mg/dL]) / platelet count (10^9/L), and the modified EASIX (mEASIX) as (LDH [U/L] × CRP [mg/L]) / platelet count (10^9/L). The neutrophil-to-ferritin ratio (NFR) was calculated as neutrophil count (10^9/L) / ferritin (µg/L), and the CALLY index as (albumin [g/dL] × lymphocyte count [10^9/L]) / CRP [mg/L].

In newly diagnosed ITP cases, the indication for treatment was defined as a platelet count ≤20×10^9/L or ≤30×10^9/L in the presence of bleeding. All patients received systemic corticosteroid therapy (prednisone 1 mg/kg/day) as initial treatment. IVIG was added to steroid therapy in cases of life-threatening bleeding or when a rapid increase in platelet count was required. A complete response (CR) was defined as a sustained platelet count ≥100×10^9/L on at least two consecutive measurements, while a partial response (PR) was defined as an increase in platelet count from 20–50×10^9/L to 50–100×10^9/L or from <20×10^9/L to above 20×10^9/L on two consecutive measurements (12,13). To establish a definition of CR or PR, it was necessary to obtain at least two distinct platelet counts, with a minimum interval of seven days between measurements, for confirmation (14). Patients who achieved either CR or PR were classified as treatment responders, whereas treatment non-responsiveness (NR) was defined as failure to meet the criteria for CR or PR. The study was approved by the Clinical Research Ethics Committee of the Bursa Uludag University Faculty of Medicine (Approval no: 2023-24/16, Approval date: 21.11.2023) and conducted in accordance with the Declaration of Helsinki.

3. Statistical Analysis

Data analysis was conducted utilizing SPSS version 29.0 (IBM, Armonk, NY, USA). Descriptive statistics for categorical variables were expressed as counts and percentages. For continuous variables,

the mean ± standard deviation was reported for data following a normal distribution, while the median with minimum-maximum values was used for non-normally distributed data, as determined by the Shapiro–Wilk test. Categorical variables were compared using the chi-square test. Receiver operating characteristic (ROC) curve analysis was employed to ascertain the optimal cutoff values for the SII index. Binary logistic regression analysis, utilizing the backward LR method, was conducted for multivariate analysis, incorporating factors with a p-value below 0.2 in the univariate analysis. The Spearman rank correlation analysis was performed to evaluate the associations between the variables. A p-value of less than 0.05 was considered indicative of statistical significance in the multivariate analysis.

4. Results

The demographic, clinical and laboratory characteristics of the 109 patients included in the study are presented in Table 1. The mean age was 51.48 ± 16.9 years and 72.5% of the patients were female. Diabetes mellitus was the most common comorbid condition, observed in 9.2% of the patients. The median platelet count at diagnosis was 11×10^9/L.

Table 1. General Patient Characteristics

	n:	**109**
Age, years (mean ± SD)	51.48	± 16.94
Sex, female (%)	79	72.5
Comorbidities		
Diabetes Mellitus, (%)	10	9.2
Coronary Artery Disease, (%)	6	5.5
Chronic Kidney Disease, (%)	5	4.6
Hypertension, (%)	4	3.7
Presence of H. Pylori, (%)	2	1.8
Presence of ANA, (%)	3	2.7
Total Leukocyte, 10^9/L (median)	7.9	(2.7-23.5)
Neutrophil, 10^9/L (median)	5	(1.1-18.1)
Lymphocyte, 10^9/L (median)	1.9	(0.1-6)
Monocyte, 10^9/L (median)	0.56	(0.1-2.3)
Hemoglobin, g/dL (mean ± SD)	12.7	± 2.18
Platelets, 10^9/L (median)	11	(1.6-36.2)
Serum Creatinine, mg/dl (median)	0.76	(0.5-9.5)
Serum LDH, IU/L (median)	218	(143-562)
Serum Ferritin, µg/L (median)	62	(3-2371)
CRP, mg/dL (median)	2	(0-88)
ESR, mm/h (median)	14	(0-80)
Serum Albumin, gr/dl (median)	4.2	(2.8-5.3)
NLR, (median)	2.47	(0.84-97.02)
LMR, (median)	3.32	(0.12-22.50)
SII, (median)	30.7	(1.99-637.41)
SIRI, (median)	1.36	(0.13-44.92)
EASIX, (median)	15.53	(2.84-353.55)
mEASIX, (median)	48.42	(1.30-2850.34)
CALLY, (median)	36.67	(0.61-1408.50)
NFR, (median)	88.91	(1.94-1780)

SD: Standard deviation, H.Pylori: Helicobacter Pylori, ANA: Anti-nuclear antibody, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, NLR: Neutrophil–lymphocyte ratio, LMR: Lymphocyte-monocyte ratio, SII: Systemic immune-inflammatory index, SIRI: Systemic inflammation response index, EASIX: Endothelial activation and stress index, mEASIX: Modified endothelial activation and stress index, CALLY: CRP-albumin-lymphocyte index, NFR: Neutrophil-ferritin ratio.

The distribution of agents utilized in the study group for initial and second-line treatment, as well as the overall treatment responses are presented in Table 2. While all patients received systemic steroids as initial treatment, the rate of patients who received concurrent IVIG therapy was found to be 32.1%. The CR rate to steroid treatment in the whole group was 50%, while NR was observed in 31.3% of patients. In patients who received IVIG, the NR rate was 45.7%. Among second-line treatments, the most commonly preferred agent was eltrombopag; at least a PR was achieved in 55% of patients who received eltrombopag, while NR was observed in 45% of patients. Rituximab was administered to seven cases as second-line treatment, and CR was observed in three patients.

Table 2. Agents Used in Initial Treatment of ITP and Treatment Responses

Therapeutic Agents	**n**	**%**
First-line treatment		
Systemic corticosteroids	109	100
Intravenous immunoglobulin (IVIG)	35	32.1
Second-line treatment		
Eltrombopag	20	18.3
Rituximab	7	6.4
Treatment Responses		
Systemic Corticosteroids		
Complete Response	50	45.8
Partial Response	25	22.9
Non-response	34	31.3
IVIG		
Complete Response	15	42.9
Partial Response	4	11.4
Non-response	16	45.7
Eltrombopag		
Complete Response	5	25
Partial Response	6	30
Non-response	9	45
Rituximab		
Complete Response	3	42.8
Partial Response	-	-
Non-response	4	57.2

ROC curve analysis was used to determine the optimal cut-off value of the SII score for predicting first-line treatment response, as shown in Figure 2. Analysis results revealed that the optimal cut-off value was 48.33, and the power of this value in predicting steroid and IVIG therapy response is shown in Table 3. Patients with an SII of < 48.33 were categorized as $SII^{low,}$ and those with an SII of ≥ 48.33 were categorized as SII^{high}.

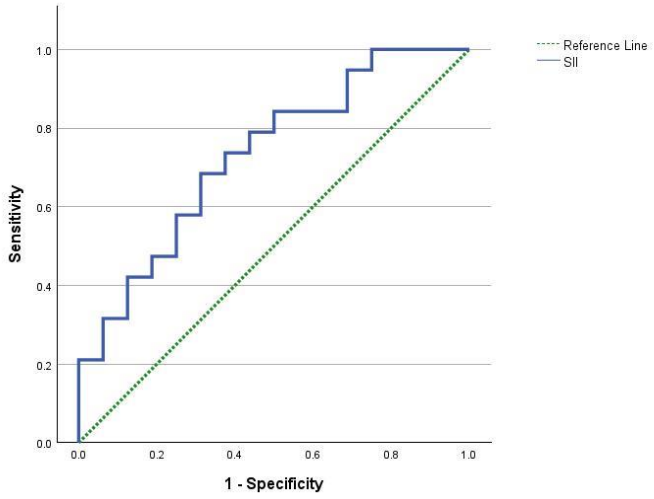

Figure 2. *ROC Curve Analysis of SII Score*

Table 3. ROC Analysis of SII for Predicting Treatment Response to Steroid and IVIG

SII cut-off: 48.33	**AUC**	**95% CI**	**Sensitivity (%)**	**Specificity (%)**	**p-value**
Response to Steroid Therapy	0.627	0.516-0.738	76	47.1	**0.025**
Response to IVIG Therapy	0.730	0.564-0.897	78.9	56.2	**0.007**

SII: Systemic immune-inflammatory index, AUC: Area under the curve, CI: Confidence interval, IVIG: Intravenous immunoglobulin.

The distribution of treatment modalities and treatment responses according to SII score is shown in Table 4. In both groups, all patients initially received systemic steroids as first-line treatment, and there was no significant difference between the two groups in terms of the rate of IVIG administration or the types of agents used in second-line treatment. In the SII^{low} group, the treatment responses to both systemic steroids and IVIG were found to be significantly higher compared to the SII^{high} group (76% vs 52.9%, 68.2% vs 30.8%, $p<0.05$). There was no significant difference between the two groups in terms of response to agents used in second-line treatment ($p =0.406$, $p = 0.999$).

Table 4. Comparison of Treatment Modalities and Responses According to SII Groups

Therapeutic Agents	**SII^{low} n:75**	**SII^{high} n:34**	**p-value**
First-line treatment			
Systemic corticosteroids, (%)	75 (100)	34 (100)	0.999 χ^2
IVIG, (%)	22 (29.3)	13 (38.2)	0.356 χ^2
Second-line treatment			
Eltrombopag, (%)	11 (14.7)	9 (26.5)	0.140 χ^2
Rituximab, (%)	3 (4)	4 (11.8)	0.201 χ^2

Treatment Responses			
Systemic Corticosteroids			
Responder	57 (76)	18 (52.9)	**0.016** χ^2
Nonresponder	18 (24)	16 (47.1)	
IVIG			
Responder	15 (68.2)	4 (30.8)	**0.032** χ^2
Nonresponder	7 (31.8)	9 (69.2)	
Eltrombopag			
Responder	5 (45.5)	6 (66.7)	0.406 χ^2
Nonresponder	6 (54.5)	3 (33.3)	
Rituximab			
Responder	1 (33.3)	2 (50)	0.999 χ^2
Nonresponder	2 (66.7)	2 (50)	

SII: Systemic immune-inflammatory index, IVIG: Intravenous immunoglobulin, χ2: Chi-squared test.

The results of the binary logistic regression analysis conducted to identify factors affecting the response to IVIG treatment are shown in Table 5. According to the multivariate analysis, a low SII score at the beginning of treatment was identified as an independent predictor of response to IVIG treatment (OR: 8.25, CI: 1.15–59.00; p=0.036). In the correlation analysis performed to evaluate the relationship between inflammatory markers, no statistically significant correlation was found between the SII index and either CRP or Ferritin levels (p > 0.05).

Table 5. Multivariate Analysis of Factors Asssociated with Treatment Response

Factor		**Univariate Analysis**				**Multivariate Analysis**			
		OR	**95% Cl**		**p-value**	**OR**	**95% Cl**		**p-value**
			Lower	Upper			Lower	Upper	
Gender	*Male [RC] vs Female*	0.359	0.061	2.106	0.256				
Age (years)		1.002	0.966	1.039	0.922				
Comorbidities	*Absent [RC] vs Present*	0.680	0.429	1.080	0.102				
H. Pylori	*Absent [RC] vs Present*	0.999	0.001	1.930	0.999				

Leukocyte (10^9/L)		1.076	0.905	1.279	0.409				
Hemoglobin (g/dl)		1.120	0.767	1.635	0.557				
Platelets (10^9/L)		0.933	0.855	1.017	0.115				
Serum LDH (IU/L)		0.993	0.984	1.003	0.191				
Ferritin (µg/L)		0.995	0.981	1.010	0.514				
CRP (mg/L)		1.034	0.953	1.122	0.423				
ESR (mm/h)		1.064	0.961	1.177	0.231				
Albumin (gr/dl)		1.063	0.889	1.271	0.503				
NLR		0.834	0.666	1.043	0.111				
LMR		1.280	0.893	1.835	0.179				
SIRI		0.842	0.635	1.116	0.232				
EASIX		0.996	0.983	1.009	0.520				
mEASIX		1.000	0.999	1.002	0.599				
CALLY		1.000	0.997	1.003	0.976				
NFR		1.003	0.996	1.009	0.392				
SII	*High [RC] vs Low*	3.429	0.818	14.369	0.092	8.250	1.154	59.003	**0.036**

OR: Odds ratio, CI: Confidence interval, RC: Reference category, H. Pylori: Helicobacter pylori, LDH: Lactate dehydrogenase, CRP: C-Reactive protein, ESR: Erythrocyte sedimentation rate, NLR: Neutrophil-lymphocyte ratio, LMR: Lymphocyte-monocyte ratio, SIRI: Systemic inflammation response index, EASIX: Endothelial activation and stress index, mEASIX: Modified endothelial activation and stress index, CALLY: CRP-albumin-lymphocyte index, NFR: Neutrophil ferritin ratio, SII: Systemic immune-inflammatory index.

5. Discussion

Early identification of cases potentially refractory to standard initial treatment in ITP is crucial for both preventing acute complications and mitigating side effects associated with prolonged steroid use (15). Although existing literature endeavors to facilitate early identification of such cases, a standardized scoring system is currently lacking (16). Our study has identified an elevated SII score (≥ 48.33) at diagnosis as a potential marker for early detection of unresponsiveness to both steroid and IVIG treatments. In instances where a high SII score is observed at the commencement of treatment, the early integration of second-line therapies may facilitate a rapid treatment response and aid in the prevention of complications.

In the literature, studies conducted in both pediatric and adult populations with ITP have highlighted the role of inflammatory markers in predicting the response to corticosteroid and IVIG therapy (17). In a study evaluating secondary ITP cases, elevated SII levels were found to correlate with lower treatment response rates (18). Similarly, investigations in pediatric ITP cohorts demonstrated that higher SII levels at diagnosis were associated with an increased risk of disease chronicity and poorer initial treatment outcomes (19). Moreover, among the components of the SII, elevated neutrophil counts and lymphopenia have also been linked to poor corticosteroid responsiveness in ITP patients (18,20). Consistent with previous reports, our study likewise revealed that patients with high SII values had significantly higher inflammatory scores and lower treatment response rates. However, it is important to distinguish the nature of the inflammation reflected by the SII in this context. In our analysis, we observed no significant correlation between SII and conventional acute-phase reactants such as CRP or ferritin. Given that the median levels of these markers were within normal ranges in our cohort, this lack of correlation suggests that SII likely represents the cellular component of immune

dysregulation—specifically the neutrophil-lymphocyte imbalance—rather than a generalized systemic acute-phase response.

In patients with ITP, multiple immunopathogenic pathways contribute to disease development and treatment resistance. Studies focusing on refractory ITP have demonstrated that alterations in humoral, cellular, and innate immune responses play a critical role in determining therapeutic outcomes (17). Dysregulation of T-cell homeostasis, particularly increased activation of T-helper 17 (Th17) cells accompanied by suppression of Th2 and regulatory T (Treg) cells, has been associated with poor treatment responses (21,22). Elevated levels of Th17-related cytokines such as IL-17 and IL-21, along with decreased concentrations of anti-inflammatory cytokines like IL-10, have been shown to possess prognostic significance (23). Beyond adaptive immunity, activation of the NOD-like receptor pyrin domain-containing protein 3 (NLRP3) inflammasome and the subsequent release of proinflammatory cytokines have been implicated in both disease pathogenesis and treatment resistance. NLRP3 activation enhances Th17 responses and triggers neutrophil-mediated immune mechanisms (24,25). Additionally, TNF receptor–associated factor 6 (TRAF6) has been shown to contribute to disease progression through IL-1 and CD40-mediated immune activation, with elevated TRAF6 levels correlating with poor corticosteroid and IVIG responsiveness (26). Considering these immunopathogenic mechanisms, early assessment of inflammatory indices before initiating treatment may help identify refractory patients at diagnosis and potentially improve clinical outcomes. However, it is important to acknowledge that specific cytokines and Th17 levels were not directly measured in this study. Therefore, the proposed mechanistic link between elevated SII and these specific immunological pathways remains hypothetical and requires confirmation in future translational studies.

The retrospective design, inclusion of a limited number of patients from a single center and the lack of internal or external validation for the determined cut-off value are among the limitations of our study. Consequently, the specific SII cut-off reported here should be considered preliminary and further validation in larger, multicenter cohorts is required to establish its clinical utility. Additionally, the lack of evaluation of lymphocyte subgroups and inflammatory cytokine levels that could contribute to a detailed assessment of the immune system represents another limitation.

6. Conclusions

In our study, the SII score calculated at the time of diagnosis suggests a potential association with the response to standard first-line therapy (systemic corticosteroids and IVIG) in patients with primary ITP. Early evaluation of the SII score may help clinicians identify potentially refractory cases at the time of diagnosis. Although further validation is needed, this marker could contribute to risk stratification and support clinical decision-making processes. Future studies with larger patient cohorts and comprehensive immunological analyses are needed to further clarify the prognostic value of SII and other inflammatory markers in the management of ITP.

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