

Evaluation of Complete Blood Count Parameters and Hematological Inflammatory Indices at Diagnosis in Childhood Nephrotic Syndrome

Çocukluk Çağı Nefrotik Sendromunda Tanı Anındaki Tam Kan Sayımı Parametreleri ve Hematolojik Enflamatuvar İndekslerin Değerlendirilmesi

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Keywords

Nephrotic syndrome, child, complete blood count, mean platelet volume, platelet-to-lymphocyte ratio, systemic immune-inflammation index

Anahtar kelimeler

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Abstract

Introduction: Nephrotic syndrome is associated with immune inflammatory activation and alterations in platelet-related parameters. This study aimed to compare complete blood count parameters, platelet/mean platelet volume related indicators, and hematological inflammatory indices between children with nephrotic syndrome and healthy controls, and to evaluate their relationship with steroid response and relapse frequency.

Materials and Methods: This retrospective case-control study included 72 children with nephrotic syndrome and 40 healthy controls. Laboratory data obtained at the time of diagnosis, before steroid treatment, were analyzed. Complete blood count parameters, platelet/mean platelet volume related indicators, and hematological inflammatory indices, including neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, monocyte-to-lymphocyte ratio, systemic immune inflammation index, and systemic inflammatory response index, were evaluated. Patients with nephrotic syndrome were further classified as steroid sensitive or steroid resistant. Steroid sensitive patients were also compared according to relapse frequency.

Results: Hemoglobin, white blood cell count, absolute neutrophil count, red cell distribution width, and platelet count were significantly higher in the nephrotic syndrome group than in the control group, whereas mean platelet volume was significantly lower. Neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and systemic immune inflammation index were also significantly higher in the nephrotic syndrome group. No significant differences were found between steroidsensitive and steroid resistant nephrotic syndrome groups in complete blood count parameters, platelet/mean platelet volume related indicators, hematological inflammatory indices, or biochemical parameters. Among steroid sensitive patients, platelet count, platelet-to-lymphocyte ratio, and systemic immune inflammation index were significantly higher in the frequent relapse group than in the infrequent relapse group. Correlation analyses showed limited associations, mainly between platelet count and albumin or total cholesterol levels.

Conclusion: Complete blood count derived indices may provide practical supportive information regarding inflammatory and platelet related alterations in children with nephrotic syndrome. Platelet count, mean platelet volume, platelet-to-lymphocyte ratio, and systemic immune inflammation index differed particularly in

patient control comparisons. At the same time, platelet related indices were also higher among steroid sensitive patients with frequent relapses. These parameters should be interpreted as complementary indicators rather than standalone diagnostic or prognostic markers.

Öz

Giriş: Nefrotik sendrom, immün inflamatuvar aktivasyon ve trombosit ile ilgili parametrelerdeki değişikliklerle ilişkilidir. Bu çalışmanın amacı, nefrotik sendromlu çocuklar ile sağlıklı kontrol grubu arasında tam kan sayımı parametrelerini, trombosit/ortalama trombosit hacmi ile ilgili göstergeleri ve hematolojik inflamatuvar indeksleri karşılaştırmak ve bunların steroid yanıtı ve nüks sıklığı ile ilişkisini değerlendirmektir.

Gereç ve Yöntem: Bu retrospektif vaka-kontrol çalışmasına nefrotik sendromlu 72 çocuk ve 40 sağlıklı kontrol katılımcısı dahil edildi. Tanı anında steroid tedavisi öncesinde elde edilen laboratuvar verileri analiz edildi. Tam kan sayımı parametreleri, trombosit/ortalama trombosit hacmi ile ilgili göstergeler ve nötrofil-lenfosit oranı, trombosit-lenfosit oranı, monosit-lenfosit oranı, sistemik immün inflamasyon indeksi ve sistemik inflamatuvar yanıt indeksi dahil olmak üzere hematolojik inflamatuvar indeksler değerlendirildi. Nefrotik sendromlu hastalar ayrıca steroid duyarlı veya steroid dirençli olarak sınıflandırıldı. Steroid duyarlı hastalar ayrıca nüks sıklığına göre karşılaştırıldı.

Bulgular: Hemoglobin, lökosit sayısı, mutlak nötrofil sayısı, kırmızı kan hücresi dağılım genişliği ve trombosit sayısı nefrotik sendrom grubunda kontrol grubuna kıyasla istatistiksel olarak anlamlı derecede yüksekken, ortalama trombosit hacmi ise istatistiksel olarak anlamlı derecede düşüktü. Nötrofil-lenfosit oranı, trombosit-lenfosit oranı ve sistemik immün inflamasyon indeksi de nefrotik sendrom grubunda istatistiksel olarak anlamlı derecede yüksekti. Steroid duyarlı ve steroid dirençli nefrotik sendrom grupları arasında tam kan sayımı parametreleri, trombosit/ortalama trombosit hacmi ile ilgili göstergeler, hematolojik inflamasyon indeksleri veya biyokimyasal parametreler açısından anlamlı bir fark saptanmadı. Steroid duyarlı hastalar arasında sık nüks eden grupta trombosit sayısı, trombosit-lenfosit oranı ve sistemik immün inflamasyon indeksi, seyrek nüks eden gruba kıyasla anlamlı derecede daha yüksekti. Korelasyon analizleri esas olarak trombosit sayısı ile albümin veya toplam kolesterol düzeyleri arasında sınırlı ilişkiler olduğunu gösterdi.

Sonuç: Tam kan sayımından elde edilen indeksler, nefrotik sendromlu çocuklarda inflamatuvar ve trombosit ile ilgili değişiklikler konusunda pratik ve destekleyici bilgiler sağlayabilir. Trombosit sayısı, ortalama trombosit hacmi, trombosit-lenfosit oranı ve sistemik immün inflamasyon indeksi, özellikle hasta-kontrol karşılaştırmalarında farklılık göstermiştir. Aynı zamanda, trombosit ile ilgili indeksler, sık nüks görülen steroid duyarlı hastalarda da daha yüksek bulunmuştur. Bu parametreler, tek başına tanı veya prognostik belirteçler olarak değil tamamlayıcı göstergeler olarak yorumlanmalıdır.

Introduction

Nephrotic syndrome is one of the most common glomerular diseases of childhood and is characterized by nephrotic-level proteinuria, hypoalbuminemia, edema, and, frequently, hyperlipidemia (1,2). In idiopathic nephrotic syndrome of childhood, the majority of cases are steroid-responsive, and this clinical presentation is most often associated with minimal change disease. In contrast, steroid-resistant nephrotic syndrome is less common. Focal segmental glomerulosclerosis is more commonly detected in this group, and steroid resistance is an important clinical indicator for long-term renal prognosis (3). It is believed that abnormalities in T- and B-cell responses, cytokine-mediated mechanisms, and structural and functional changes in the glomerular filtration barrier contribute to the pathogenesis of the disease. Therefore, immune and inflammatory processes are closely associated with the development and clinical course of childhood nephrotic syndrome (1,4,5). This interaction between inflammation and hemostasis has heightened interest in platelet parameters in nephrotic syndrome. Indeed, an increased risk of thromboembolism

has been identified in nephrotic syndrome, and this risk is associated with multiple mechanisms, including loss of anticoagulant factors, increased procoagulant factors, hemoconcentration, and altered platelet activation (6).

Complete blood count parameters and the hematological inflammatory indices derived from these parameters are considered practical auxiliary indicators that may reflect systemic inflammation, given their ease of access and low cost (7). Mean platelet volume is a parameter that reflects platelet size and is considered to be associated with platelet activation. Red blood cell distribution width, on the other hand, has been linked to anisocytosis, systemic inflammation, and oxidative stress (7,8). Similarly, indices derived from a complete blood count such as the neutrophil-to-lymphocyte ratio (NLR), the platelet-to-lymphocyte ratio (PLR), and the systemic immune-inflammation index (SII) are also considered as auxiliary markers that may reflect inflammatory processes. (9).

Studies have evaluated platelet indices and inflammatory markers derived from complete blood counts in childhood nephrotic syndrome. However, the findings reported in these

studies vary across different centers and patient groups (5,6,9-12). This study aimed to compare complete blood count parameters and hematological inflammatory indices at the time of diagnosis in patients followed at our clinic for nephrotic syndrome with those of a control group.

Materials and Methods

This study was conducted among pediatric patients diagnosed with nephrotic syndrome and followed up at the Pediatric Nephrology Clinic of Bursa Yüksek İhtisas Training and Research Hospital between 2016 and 2024. All patients with childhood nephrotic syndrome identified in the clinic records during the study period who had complete blood count data available at diagnosis were included, and no eligible patient was excluded. All laboratory parameters were obtained from blood samples collected at the patients' initial admission, before the initiation of any treatment, including corticosteroids, albumin infusion, or diuretic therapy. The control group consisted of cases evaluated during routine well-child examinations. When selecting control cases, care was taken to ensure they had no history of active infection, chronic disease, regular medication use, kidney disease, or hematological disease. Cases with missing baseline laboratory data or laboratory measurements taken at times other than the time of diagnosis were excluded from the study. Nephrotic-range proteinuria was defined as 24-hour urinary protein excretion $\geq 1,000$ mg/m²/day (≥ 40 mg/m²/h). Complete remission was defined as negative or trace proteinuria on urine dipstick for three consecutive days. SSNS was defined as complete remission within four weeks of standard-dose corticosteroid treatment, whereas SRNS was defined as failure to achieve complete remission within four weeks (2,3).

Data Collection

Data were obtained retrospectively by reviewing patient records and the hospital information system. For each case, age, sex, and study group were recorded. In patients with nephrotic syndrome, the age at diagnosis, response to steroid therapy, and disease subtype were also assessed. At the time of diagnosis, the following complete blood count parameters were recorded: hemoglobin (Hb), white blood cell count (WBC), absolute neutrophil count (ANC), absolute lymphocyte count (ALC), platelet count (PLT), mean corpuscular volume (MCV), red blood cell distribution width (RDW), and mean platelet volume (MPV). Since monocyte counts were present only in the nephrotic syndrome group, the monocyte-to-lymphocyte ratio (MLR) and the systemic inflammatory

response index (SIRI) were not included in the case-control comparison. In patients with nephrotic syndrome, serum albumin, creatinine, blood urea nitrogen (BUN), total protein, sodium, potassium, total cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), very low-density lipoprotein cholesterol (VLDL), erythrocyte sedimentation rate (ESR), and 24-hour urinary protein excretion were recorded. Hematological inflammatory indices were calculated using complete blood count components. In this context, NLR, PLR, MLR, SII, and SIRI were evaluated. SII was calculated using the formula $PLT \times ANC / ALC$, while SIRI was calculated using the formula $ANC \times \text{monocyte count} / ALC$. The platelet-to-MPV ratio was also calculated as a platelet- and MPV related indicator.

Statistical Analysis

The study size was determined by the number of eligible patients available in the clinic records during the study period. Therefore, no a priori sample size calculation was performed. Statistical analysis of the data was performed using SPSS. The normality of continuous variables was assessed using the Shapiro-Wilk test. Variables that followed a normal distribution were presented as mean $\pm$ standard deviation, while those that did not follow a normal distribution were presented as median and interquartile range (IQR). Categorical variables were expressed as counts and percentages. The main comparison in the study was made between the nephrotic syndrome group and the healthy control group. In secondary analyses, the SSNS and SRNS groups were compared. Within the SSNS subgroup, patients with frequent and infrequent relapses were evaluated separately.

For comparisons between the two groups, the Student's t-test was used for continuous variables that followed a normal distribution, and the Mann-Whitney U test was used for continuous variables that did not follow a normal distribution. For comparisons of categorical variables, the chi-square test was used, or Fisher's exact test was used when the expected cell counts were insufficient. In the correlation analyses, the Pearson or Spearman correlation coefficient was calculated based on the variables' distributional characteristics. Effect sizes were calculated as Hedges' g for comparisons performed using the independent-samples t-test, r for Mann-Whitney U tests, and the Phi coefficient for 2×2 categorical comparisons. A p-value of <0.05 was considered statistically significant.

Ethics Committee Approval

Approval for this study was obtained from the Ethics Committee of Bursa Specialized Training and Research Hospital (No. 2011-KAEK-25-2020/10-04, date: 23.11.2011). Due to the retrospective design, data were obtained from patient charts and hospital records. All patient data were anonymized prior to analysis. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Results

A total of 112 children were included in the study. Of these, 72 were in the nephrotic syndrome group, and 40 were in the control group. When the nephrotic syndrome group was evaluated based on steroid response, 57 patients were classified as SSNS and 15 as SRNS. In the SSNS group, based on relapse frequency, 25 patients were classified as frequent relapsers and 32 as infrequent relapsers.

Demographic Characteristics

The mean age in the nephrotic syndrome group was 11.12 ± 4.05 years, and in the control group, 9.37 ± 3.62 years. There was a statistically significant difference in age between the groups ($p=0.025$). The gender distribution was 25 girls and 47 boys in the nephrotic syndrome group and 14 girls and 26 boys in the control group. There was no significant difference in gender distribution between the groups. The median age at diagnosis in the nephrotic syndrome group was 4.00 (3.00–6.00) years. Demographic characteristics are presented in Table 1.

Comparison of Complete Blood Count Parameters

A comparison of complete blood count parameters between the nephrotic syndrome group and the control group is presented in Table 2. The between-group effect was moderate for hemoglobin ($r = 0.36$), small for WBC, ANC, and RDW ($r = 0.25$ - 0.28), and large for platelet count and MPV (Hedges' $g = 1.12$ and -0.92 , respectively).

Table 1. Demographic characteristics of the study groups

Nephrotic syndrome vs control			
Variable	Nephrotic syndrome (n=72)	Control (n=40)	p
Age (years)	11.12 ± 4.05	9.37 ± 3.62	0.025
Sex, Female/Male (n)	25/47	14 / 26	0.976
Age at diagnosis (years)	4.00 (3.00-6.00)		
SSNS and SRNS subgroups			
Variable	SSNS (n=57)	SRNS (n=15)	p
Age (years)	11.03 ± 4.09	11.47 ± 4.05	0.713
Sex, Female/Male (n)	23/34	2/13	0.069

Data are presented as mean $\pm$ standard deviation, median (interquartile range), or number. SSNS: steroid-sensitive nephrotic syndrome; SRNS: steroid-resistant nephrotic syndrome

Table 2. Complete blood count parameters in the nephrotic syndrome and control groups

Variable	Nephrotic syndrome	Control	p
Hemoglobin (g/dL)	13.30 (11.95-14.05)	12.0 (11.02-12.97)	<0.001
WBC (mm ³)	10100 (7710-13125)	8400 (7020-9915)	0.003
Neutrophil (mm ³)	5600 (3890-7790)	4230 (2580-5145)	0.008
Lymphocyte (mm ³)	3060 (2425-4375)	3082 (2362-4395)	0.949
Platelet (mm ³)	408704 ± 123927	281712 ± 89493	<0.001
MCV (fL)	78.57 ± 5.15	77.48 ± 4.37	0.262
RDW (%)	14.00 (13.30-14.80)	13.43 (12.61-13.98)	0.005
MPV (fL)	8.37 ± 1.14	9.36 ± 0.93	<0.001
Platelet/MPV ratio	46188 (39892-58918)	26820 (22868-36448)	<0.001

Data are presented as mean $\pm$ standard deviation or median (interquartile range), according to distribution. WBC: white blood cell count; MCV: mean corpuscular volume; RDW: red cell distribution width; MPV: mean platelet volume

In the nephrotic syndrome group, hemoglobin, WBC, ANC, RDW, and platelet count were significantly higher than in the control group. However, MPV was significantly lower in the nephrotic syndrome group. The p-values were as follows: $p < 0.001$ for hemoglobin, $p = 0.003$ for WBC count, $p = 0.008$ for ANC count, $p = 0.005$ for RDW, and $p < 0.001$ for both platelet count and MPV. The platelet-to-MPV ratio was also significantly higher in the nephrotic syndrome group compared to the control group ($p < 0.001$). The platelet-to-MPV ratio also showed a large effect size ($r = 0.60$).

Hematological Inflammatory Indices

A comparison of hematological inflammatory indices between the nephrotic syndrome and control groups is presented in Table 3. The NLR was significantly higher in the nephrotic syndrome group compared to the control group ($p = 0.034$). Similarly, PLR and SII values were also significantly higher in the nephrotic syndrome group ($p < 0.001$ for both). The effect size was small for NLR ($r = 0.20$) and moderate for PLR and SII ($r = 0.34$ and $r = 0.35$, respectively). Since monocyte data were not available for the control group, MLR and SIRI were not included in the patient-control comparison and were reported only in the nephrotic syndrome subgroup analyses.

Comparison of the SSNS and SRNS Subgroups

The SSNS ($n = 57$) and SRNS ($n = 15$) groups were compared for demographic characteristics, complete blood count parameters, platelet- and MPV related indicators, hematological inflammatory indices, and biochemical parameters. There were no significant differences between the groups in age, age at diagnosis, or gender distribution. Hemoglobin, WBC, neutrophil, lymphocyte, monocyte, and platelet counts, as well as MCV, RDW, and MPV values, were similar between the two groups. No significant differences were observed in platelet or MPV related indicators or in hematological inflammatory indices, including NLR, PLR, MLR, SII, and SIRI. Serum albumin, total protein, lipid profile, creatinine, and other biochemical parameters were similar between the groups (Table 4). The corresponding effect sizes were predominantly negligible or small.

Comparison of Frequent Relapses in the SSNS Group

SSNS patients were compared between those with frequent relapses ($n = 25$) and those with infrequent relapses ($n = 32$). In the frequent relapse group, platelet count, PLR, and SII values were significantly higher. The effect size was moderate for platelet count and SII (Hedges' $g = 0.56$ and $r = 0.30$, respectively) and large for PLR (Hedges' $g = 0.83$). No significant differences were observed between the groups in terms of other complete blood count parameters, MPV, NLR, MLR, SIRI, MPV/platelet ratio, and the evaluated biochemical parameters (Table 5).

Correlation Analyses

In the nephrotic syndrome group, the relationships between hematological markers and disease parameters were evaluated using Spearman's correlation analysis. A significant negative correlation was found between platelet count and serum albumin ($\rho = -0.36$; $p = 0.002$). A significant positive correlation was found between platelet count and total cholesterol ($\rho = 0.30$; $p = 0.012$). There was a significant positive correlation between the MPV/platelet ratio and serum albumin ($\rho = 0.36$; $p = 0.002$). No significant correlations were found between NLR, PLR, SII, SIRI, and MPV values and serum albumin, 24-hour urinary protein excretion, total cholesterol, and erythrocyte sedimentation rate (Supplementary Table 1).

Discussion

In this retrospective case-control study, hematological changes at the time of diagnosis in childhood nephrotic syndrome were evaluated using platelet- and MPV related markers, as well as inflammatory indices derived from the complete blood count. Our findings indicate that in patients with nephrotic syndrome, platelet-related markers particularly platelet count, PLR, and SII are higher than in healthy controls, whereas MPV is lower. However, the evaluated hematological and biochemical parameters showed no significant differences between the SSNS and SRNS subgroups.

Table 3. Hematological inflammatory indices in the nephrotic syndrome and control groups

Variable	Nephrotic syndrome	Control	p
NLR	1.96 (0.91-3.26)	1.29 (0.80-1.93)	0.034
PLR	125 (89-181)	84 (67-109)	<0.001
SII $\times 10^9/L$	750.2 (310.5-1318.3)	355.2 (187.0-541.6)	<0.001

Data are presented as median (interquartile range). NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; SII: systemic immune-inflammation index

The higher platelet count, PLR, and SII observed in frequent relapsers within the SSNS group may represent a preliminary pattern; however, given the small subgroup size, this finding requires confirmation in larger prospective studies. In correlation analyses, however, the fact that only certain platelet-based parameters show a limited association with albumin and lipid profiles suggests that these indicators should not be considered, on their own, as strong markers of disease activity or severity.

It has long been recognized that nephrotic syndrome is associated with immune-mediated mechanisms, particularly within the spectrum of steroid-responsive and minimal change disease. Impaired podocyte integrity, abnormalities in T- and B-cell responses, circulating permeability factors, and anti-nephrin autoantibodies which have been identified in recent years are among the primary mechanisms involved in this pathogenesis (13). Studies have shown that childhood nephrotic syndrome is associated with changes in the CD4/

Table 4. Comparison of demographic, hematological, inflammatory, and biochemical parameters between the SSNS and SRNS subgroups

Variable	SSNS (n=57)	SRNS (n=15)	p
Demographic			
Age (years)	11.03 ± 4.09	11.47 ± 4.05	0.713
Age at diagnosis (years)	4.00 (3.00-6.00)	3.50 (2.50-4.50)	0.345
Complete blood count			
Hemoglobin (g/dL)	13.15 (12.23-14.03)	13.4 (11.4-13.9)	0.882
WBC (mm ³)	10100 (7780-13088)	10600 (7655-13105)	0.794
Neutrophil (mm ³)	5600 (3930-7890)	5570 (3102-6830)	0.983
Lymphocyte (mm ³)	2835 (2408-4400)	3240 (2730-3905)	0.632
Monocyte (mm ³)	530 (408-792)	630 (415-770)	0.905
Platelet (mm ³)	409071 ± 128228	407333 ± 110414	0.962
MCV (fL)	78.38 ± 5.35	79.27 ± 4.41	0.557
RDW (%)	14.00 (13.38-14.80)	13.70 (13.15-14.40)	0.356
MPV (fL)	8.34 ± 1.10	8.50 ± 1.32	0.627
Platelet/MPV related			
Platelet/MPV ratio	48000 (39950-61666)	45567 (39716-51772)	0.529
Inflammatory indices			
NLR	2.04 (0.98-3.32)	1.61 (0.83-2.38)	0.451
PLR	126 (88-180)	114 (95-180)	0.784
MLR	0.19 (0.13-0.27)	0.16 (0.12-0.20)	0.490
SII ×10 ⁹ /L	766.5 (385.6-1272.3)	532.5 (279.7-1215.6)	0.730
SIRI×10 ⁹ /L	1072 (485-1785)	899 (421-2592)	0.719
Biochemical			
Albumin (g/dL)	1.80 (1.50-2.32)	2.00 (1.57-2.05)	0.632
Total protein (g/dL)	4.49 ± 0.97	4.75 ± 0.69	0.339
Total cholesterol (mg/dL)	352 ± 127	356 ± 93	0.919
Triglyceride (mg/dL)	179 (134-243)	168 (132-309)	0.510
LDL (mg/dL)	213 (166-307)	235 (139-342)	0.707
HDL (mg/dL)	65.8 (52.5-87.5)	79.5 (53.3-91.7)	0.769
VLDL (mg/dL)	38.00 (27.40-49.75)	33.7 (25.02-53.75)	0.559
Creatinine (mg/dL)	0.39 (0.28-0.51)	0.39 (0.35-0.51)	0.464

Data are presented as mean ± standard deviation or median (interquartile range), according to distribution. WBC: white blood cell count; MCV: mean corpuscular volume; RDW: red cell distribution width; MPV: mean platelet volume; NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; MLR: monocyte-to-lymphocyte ratio; SII: systemic immune-inflammation index; SIRI: systemic inflammatory response index; SSNS: steroid-sensitive nephrotic syndrome; SRNS: steroid-resistant nephrotic syndrome

Table 5. Comparison of hematological, inflammatory, and biochemical parameters according to relapse frequency within the SSNS group

Variable	Frequent relapse (n=25)	Infrequent relapse (n=32)	p
Hemoglobin (g/dL)	13.5 (12.7-14.2)	13.0 (11.8-13.9)	0.167
WBC (mm ³)	10085 (7780-13012)	10100 (7838-13268)	0.947
Neutrophil (mm ³)	6000 (4330-8202)	4975 (3895-7722)	0.389
Lymphocyte (mm ³)	2630 (2272-3685)	3315 (2500-4772)	0.070
Platelet (mm ³)	449542 ± 137562	378719 ± 113637	0.040
MPV (fL)	8.41 ± 1.07	8.28 ± 1.14	0.674
RDW (%)	14.00 (13.70-14.38)	14.00 (13.17-15.12)	0.974
NLR	2.41 (1.19-3.98)	1.90 (0.93-2.44)	0.081
PLR	186 ± 106	117 ± 60	0.003
SII×10 ⁹ /L	1259.5 ± 868.6	1169.6 (423.5-1858.1)	0.025
SIRI×10 ⁹ /L	1345 (703-1861)	939 (468-1657)	0.271
MLR	0.20 (0.14-0.27)	0.17 (0.12-0.26)	0.436
MPV/Platelet (×10 ³)	0.02 (0.02-0.02)	0.02 (0.02-0.03)	0.156
Albumin (g/dL)	1.88 ± 0.54	1.96 ± 0.59	0.631
Cholesterol (mg/dL)	391 ± 120	324 ± 125	0.051
24-hour protein (mg/day)	1180 (625-3056)	1049 (792-1930)	0.813

Data are presented as mean ± standard deviation or median (interquartile range), according to distribution. WBC: white blood cell count; RDW: red cell distribution width; MPV: mean platelet volume; NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; MLR: monocyte-to-lymphocyte ratio; SII: systemic immune-inflammation index; SIRI: systemic inflammatory response index; SSNS: steroid-sensitive nephrotic syndrome

CD8 ratio, CD19+ B lymphocytes, and natural killer (NK) cells, supporting the notion that the disease develops against a background of immune dysregulation (5, 14). For this reason, inflammation indices derived from peripheral blood cells have become a focus of interest in nephrotic syndrome. NLR, PLR, MLR, SII, and SIRI provide indirect information about the systemic inflammatory response. These indices do not require additional testing and are easily calculated from a complete blood count. Their low cost has led to their widespread use in research on various inflammatory diseases.

In our study, NLR, PLR, and SII were higher in the nephrotic syndrome group than in the control group. However, in the absence of CRP data and a case-control comparison of ESR, these indices cannot be interpreted as reflecting inflammation alone. They may represent overlapping processes, including inflammation, hemoconcentration, and hematological changes associated with hypoalbuminemia and hyperlipidemia. This finding is consistent with observations reporting increased leukocyte and neutrophil counts in children with nephrotic syndrome, as well as with studies suggesting that NLR and PLR may be associated with relapse or an adverse clinical course in steroid-responsive nephrotic syndrome (9,11). However, because no monocyte data were

available for the control group, the MLR and SIRI indices could not be included in the case-control comparison. Therefore, these two indices were interpreted only within the context of subgroup analyses within the nephrotic syndrome group.

The platelet-related findings in our study are largely consistent with the literature. Previous clinical studies have consistently shown that platelet counts are elevated in children with nephrotic syndrome. This finding may be associated with platelet hyperactivity, an increased tendency toward aggregation, and increased activation dependent surface markers (4,6,8,15). This increase may be associated with multifactorial mechanisms, including plasma protein loss, hyperlipidemia, and hemoconcentration, that are observed in nephrotic syndrome. However, the causal relationship between platelet changes and thromboembolic events remains unclear (6).

Our findings regarding mean platelet volume reflect the heterogeneity in the literature. In our study, MPV was lower in the nephrotic syndrome group. While Gulleroğlu et al. (15) reported similarly low MPV during the active phase, Gökner et al. (4) found higher MPV in children with nephrotic syndrome than in the control group. The fact that MPV may increase or decrease in inflammatory conditions suggests that this parameter may be influenced by the type and stage

of the disease, as well as by platelet production dynamics (8). For this reason, it is difficult to explain the low MPV findings in our study by a single mechanism.

The marked differences in platelet count and MPV were also reflected in the ratios derived from these two parameters. In our study, the platelet-to-MPV ratio was higher in the nephrotic syndrome group. Nickavar et al. (10) reported higher platelet counts in children with steroid-resistant nephrotic syndrome and suggested that certain platelet indices may be associated with steroid resistance. In contrast, our study found no significant difference in platelet count or MPV between the SSNS and SRNS groups. This finding may be related, in particular, to the limited number of patients in the SRNS group. In our study, RDW was higher in the nephrotic syndrome group. It has been reported that RDW may have prognostic value in systemic inflammation and various clinical conditions (7,8). However, this increase in RDW should not be interpreted as a finding specific to nephrotic syndrome.

No significant differences were found between the steroid-sensitive and steroid-resistant subgroups of nephrotic syndrome in complete blood count parameters, platelet- and MPV related markers, and hematological inflammatory indices. This finding indicates that these parameters do not distinguish the steroid response phenotype in the current patient group. However, the literature has reported that platelet count and certain platelet indices may be associated with steroid resistance (4,10,11).

These differences may stem from variations in subgroup definitions, patient characteristics, and sample size. In our study the SRNS group comprising only 15 patients limits the statistical power of the subgroup comparisons. Therefore, the failure to detect a difference between the SSNS and SRNS groups should not be interpreted as indicating that hematological indices at the time of diagnosis are entirely inadequate for distinguishing the steroid-response phenotype.

In our study, platelet count, PLR, and SII were higher in patients with frequent relapses within the SSNS group. Although this pattern is consistent with previous studies (9,12), the limited subgroup size precludes considering it a confirmed association with relapse tendency. This preliminary observation should be explored in larger prospective studies.

Correlation analyses should be considered supporting findings rather than the study's main message. NLR, PLR, MLR, SII, SIRI, and MPV did not show significant correlations with albumin, 24-hour proteinuria, total cholesterol, or

erythrocyte sedimentation rate. In contrast, platelet count was negatively correlated with albumin and positively correlated with total cholesterol. This finding suggests that an increase in platelet count may be associated with a nephrotic syndrome characterized by hypoalbuminemia and hyperlipidemia (15). However, due to the limited magnitude of the correlation coefficients and the possibility of multiple comparisons, these data are insufficient to draw definitive conclusions.

Among the strengths of the study are the focus on laboratory parameters at the time of diagnosis before treatment and the joint evaluation of numerous indices derived from the complete blood count within the same patient group. The separate analysis of platelet and MPV related indicators, combined with the examination of clinically meaningful subgroups such as steroid-sensitive/resistant and frequent/infrequent relapsers, lends the findings a stronger clinical context.

Study Limitations

The main limitations of the study are its retrospective, single-center design, limited sample size, and, in particular, the small number of patients in the SRNS group. The lack of monocyte data in the control group prevented the evaluation of MLR and SIRI in a case-control comparison. CRP data were unavailable, and ESR data were not available for the control group; therefore, these hematological indices could not be directly compared with conventional inflammatory markers in the case-control analysis. Certain platelet indices, such as PDW and plateletcrit, are also missing from the dataset. The significant age difference between the patient and control groups represents a potential confounding factor, particularly because hemoglobin, WBC, and RDW may vary with age, and this effect could not be fully controlled for because of the retrospective design. Additionally, complete blood count parameters can be influenced by infection, hydration status, time of sample collection, and technical factors. Because the study covered an eight-year period, possible changes in hematology analyzers, reagent lots, or laboratory reference ranges may have introduced measurement variability, particularly for instrument-dependent parameters such as MPV and RDW.

Conclusion

In conclusion, indices derived from a complete blood count may provide practical information about hematological changes in children with nephrotic syndrome, but they should not be interpreted as specific measures of

inflammation. Our findings indicate that platelet and MPV related indicators, in particular, showed differences in the patient-control comparison. However, these indices should not be evaluated as diagnostic or prognostic markers on their own; they should be interpreted alongside clinical findings and standard laboratory parameters.

Ethics

Ethics Committee Approval: Approval for this study was obtained from the Ethics Committee of Bursa Specialized Training and Research Hospital (approval number: 2011-KAEK-25-2020/10-04, date: 23.11.2011).

Footnotes

Conflict of Interest: No conflict of interest was declared by the authors.

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Supplementary Table 1: <https://d2v96fxpocvx.cloudfront.net/51ec7646-9122-48c7-a1d9-90e9cb16981b/content-images/c14e01df-6a4b-49cf-ae09-99e5223469c1.pdf>

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