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RESEARCH ARTICLES

Changes in hematological and micronutrient parameters and their relationship with glycemic control in pediatric patients with type 1 diabetes

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ABSTRACT

Aim: Disturbances in hematological indices and micronutrient status are frequently encountered during the routine follow-up of children with type 1 diabetes mellitus (T1DM). In clinical practice, these alterations often parallel poor glycemic control. Therefore, this study was designed to evaluate hematological parameters and micronutrient levels in pediatric patients with T1DM and to investigate their relationship with metabolic control.

Materials and Methods: This retrospective analysis included 159 children and adolescents with T1DM followed at the Pediatric Endocrinology Clinic of Düzce University Faculty of Medicine, alongside 160 age- and sex-matched healthy controls. Laboratory data were obtained from medical records and included complete blood count parameters, lipid profile, ferritin, vitamin B_{12}, and vitamin D levels. Glycemic control was classified as "good" for HbA1c <8.5% and "poor" for HbA1c ≥8.5%. Statistical analyses were performed using SPSS version 22.0, with $p<0.05$ considered statistically significant.

Results: In the study cohort, children with T1DM exhibited significantly higher mean platelet volume (MPV), white blood cell count (WBC), neutrophil-to-lymphocyte ratio (NLR), systemic immune-inflammation index (SII), and systemic inflammation response index (SIRI). In contrast, platelet count and vitamin B_{12} levels were significantly lower. Multivariate analysis demonstrated that MPV, hemoglobin, hematocrit, high-density lipoprotein (HDL) cholesterol, vitamin B_{12}, SIRI, and NLR were independently associated with the presence of T1DM. In the ROC analysis, the area under the curve (AUC) for NLR was 0.791 (95% CI: 0.742-0.839), with a sensitivity of 71.1% and a specificity of 72.5% at a cutoff value of 1.46. When patients were stratified according to metabolic control, those with HbA1c ≥8.5% were older, had higher glucose levels, and had a higher proportion of females, whereas hematocrit levels were lower.

Conclusion: Hematological alterations and inflammatory indices appear to be closely associated with metabolic control in pediatric T1DM. Elevated MPV, SIRI, and NLR values suggest that hyperglycemia, particularly during adolescence, disrupts hematological homeostasis. In this context, the combined evaluation of hematological and inflammatory parameters may be clinically meaningful for identifying the presence of T1DM and delineating the burden of chronic low-grade inflammation. Supported by prospective studies, these findings may help guide individualized treatment strategies.

Keywords: Type 1 diabetes, pediatric patients, HbA1c, hematological parameters, inflammation, biomarkers

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INTRODUCTION

Type 1 diabetes mellitus (T1DM) is one of the most common endocrine disorders encountered during childhood and adolescence (1,2). It results from the immune-mediated destruction of pancreatic beta cells triggered by environmental factors in genetically susceptible individuals (3,4). Although the disease often manifests early in life, its consequences extend beyond childhood, leading to an increased risk of microvascular complications, macrovascular disease, and long-term cardiovascular morbidity.

The clinical course and severity of diabetes-related complications in children are shaped by multiple interacting factors, including disease duration, the level of metabolic control, genetic predisposition, and environmental exposures. In clinical practice, T1DM imposes a substantial psychosocial and economic burden not only on pediatric patients but also on their families and healthcare systems. This burden is particularly evident in developing regions where regular follow-up is limited.

Routine hematological parameters obtained from complete blood count analysis provide practical and readily accessible means for evaluating inflammatory activity and endothelial dysfunction associated with diabetic complications. Alterations in erythrocyte indices, white blood cell counts, and platelet morphology have been associated with metabolic syndrome, insulin resistance, and vascular risk in adult diabetic populations (5-14). Whether similar patterns occur in children with T1DM remains a focus of interest in pediatric research.

In pediatric populations, anemia most commonly occurs in the setting of iron, vitamin B_{12}, or folate deficiency, as these micronutrients are essential for effective hemoglobin synthesis. In patients with T1DM, nutritional insufficiency represents an important cause, but it is rarely the sole factor. Acute metabolic disturbances, dietary restrictions, coexisting autoimmune diseases, and socioeconomic challenges may further increase the risk. In poorly controlled diabetes, chronic hyperglycemia can sustain a low-grade inflammatory state that disrupts hematological homeostasis (15).

Early recognition of iron deficiency is of major clinical importance. Timely correction of anemia in children with diabetes contributes not only to reduced morbidity but also to improved physical performance, cognitive function, and psychosocial development (16). Nevertheless, data regarding iron, vitamin B_{12}, folate, and vitamin D status in pediatric populations with T1DM remain limited. This may partly reflect the assumption that children with diabetes who receive regular medical follow-up and nutritional counseling are protected against anemia.

Within this context, the present study was designed to comprehensively evaluate hematological parameters and micronutrient levels in pediatric patients with T1DM, to determine the prevalence and potential causes of anemia, and to examine the relationship between these variables and glycemic control.

MATERIALS AND METHODS

Study Design and Ethical Approval

This retrospective study was conducted to evaluate the epidemiological and laboratory data of pediatric patients with T1DM followed in the Pediatric Endocrinology Department of XXXX University Faculty of Medicine. Participant information was obtained retrospectively from the hospital's electronic database. The study was approved by the Ethics Committee of XXXX University Faculty of Medicine (approval number: 2025/284; date: November 10, 2025).

Sample Selection and Inclusion Criteria

The study included adolescent patients diagnosed with T1DM who regularly attended their three-month and annual follow-up visits and had received education on diabetes management and nutrition. Patients with systemic diseases that could cause anemia or micronutrient deficiencies, malnutrition, gastrointestinal malabsorption, or abnormal uterine bleeding, as well as those with uncontrolled hypothyroidism or adrenal insufficiency, were excluded from the study.

Data Collection and Laboratory Measurements

Data from annual follow-up examinations were used to record complete blood count parameters [hemoglobin, hematocrit, red blood cells (RBC), mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), white blood cells (WBC), and platelet count], along with serum iron, total iron-binding capacity (TIBC), ferritin, folic acid, vitamin B_{12}, and vitamin D levels. Hemoglobin and MCV values were evaluated based on age-specific reference ranges (6). Anemia was defined according to age- and sex-specific hemoglobin reference ranges, in accordance with World Health Organization (WHO) criteria (11,13,15). Vitamin B_{12} deficiency was defined as serum B_{12} <200 pg/mL (16-19). All reference ranges used in this study were consistent with the standards of the institutional laboratory.

Calculation of Inflammatory Indices

Hemogram-based inflammatory markers were calculated using the following formulas:

- NLR (Neutrophil-to-Lymphocyte Ratio) = Neutrophil / Lymphocyte
- SII (Systemic Immune-Inflammation Index) = (Platelet × Neutrophil) / Lymphocyte
- SIRI (Systemic Inflammatory Response Index) = (Neutrophil × Monocyte) / Lymphocyte

These indices are considered reliable markers that reflect the peripheral inflammatory response and are widely used in clinical research.

Classification and Statistical Analysis

Age, sex, disease duration, and metabolic control are key variables influencing both hematological and biochemical profiles in children with type 1 diabetes. Therefore, participants in our study were stratified according to age (10-14.9 years and 15-18.9 years), sex (female/male), duration of diabetes (<3 years or ≥3 years), and level of glycemic control.

Glycemic control was defined as "good" for HbA1c <8.5% and "poor" for HbA1c ≥8.5%. This cutoff value was deliberately selected. In clinical practice, standard HbA1c categories (<7.0%, 7.0-8.5%, and >8.5%) often result in uneven subgroup sizes, particularly in adolescent populations. Because HbA1c values in our study cohort were not homogeneously distributed across these categories, an HbA1c cutoff of 8.5% was used to achieve balanced subgroup sizes and adequate statistical power. Hematological and biochemical parameters were compared according to this classification.

Correlation analyses were performed to examine the relationship between HbA1c, as a marker of long-term glycemic exposure, and other clinical and laboratory variables. Pediatric patients were evaluated within two glycemic control subgroups, allowing for the analysis of both categorical differences and continuous associations.

Data analysis was performed using the Statistical Package for the Social Sciences (SPSS), version 22.0. The normality of distribution was assessed using the Shapiro-Wilk test. For descriptive statistics, normally distributed variables were expressed as mean ± standard deviation, whereas non-normally distributed variables were presented as median and interquartile range (IQR).

Categorical variables were compared using the chi-square test, with Fisher's exact test applied when expected cell counts were low. For comparisons of continuous variables between groups, the independent-samples t-test was used for normally distributed data, and the Mann-Whitney U test was used for non-normally distributed data. When more than two independent groups were compared, one-way ANOVA was applied for normally distributed variables, and the Kruskal-Wallis test was used for non-normally distributed variables.

Associations between continuous variables were assessed using Pearson's correlation coefficient for normally distributed parameters and Spearman's rank correlation coefficient for non-normally distributed parameters. A two-sided p-value of <0.05 was considered statistically significant for all analyses.

RESULTS

A total of 319 pediatric patients were included in this study, comprising 159 patients with T1DM and 160 healthy controls. The mean age of the T1DM group was significantly higher than that of the control group ($p<0.05$). No significant difference was found between the groups in terms of sex distribution ($p>0.05$). The demographic, hematological, and biochemical characteristics of the study population are presented in Table 1.

In the comparative analysis of hematological and biochemical parameters, patients with T1DM demonstrated significantly higher levels of mean platelet volume (MPV), neutrophil-to-lymphocyte ratio (NLR), systemic inflammatory indices (SII and SIRI), white blood cell count (WBC), hemoglobin, hematocrit, red blood cell count (RBC), triglycerides, high-density lipoprotein (HDL), and total cholesterol compared with healthy controls (all $p<0.05$). In contrast, platelet count and vitamin B_{12} levels were significantly lower in the T1DM group ($p<0.05$). No statistically significant

Table 1. Demographic, hematological, and biochemical characteristics of the study population

Characteristic	Min-Max	Median	Mean ± SD or n (%)
Age	5.0 - 21.0	15	14.4 ± 2.9
Gender	Female		177 (55.5%)
	Male		142 (44.5%)
BMI kg/m²	13.8 - 38.6	20.3	20.8 ± 3.6
HbA1c %	5.0 - 16.3	5	7.3 ± 2.7
Platelets (10^3/µL)	125.0 - 779.0	313	313.9 ± 83.1
MPV (fL)	6.9 - 11.1	8.8	8.8 ± 0.9
Glucose (mg/dL)	21.6 - 632	98.6	150.0 ± 95.2
RBC (10^3/µL)	3.9 - 6.5	4.8	4.8 ± 0.4
Hemoglobin (g/dL)	8.8 - 17.5	13	13.1 ± 1.4
Hematocrit (%)	31 - 51.3	38.2	38.8 ± 4.2
WBC (10^3/µL)	3.4 - 24.1	6.6	6.8 ± 1.9
Triglyceride (mg/dl)	28.0 - 1112.0	82.9	105.1 ± 97.1
LDL (mg/dl)	31.5 - 220.3	85	89.7 ± 28.3
HDL (mg/dl)	30.9 - 107.1	51	54.3 ± 13.2
TSH (mIU/L)	0.3 - 9.5	2.1	2.3 ± 1.3
Total Cholesterol (mg/dl)	100 - 759.4	153.4	159.9 ± 49.3
D Vitamin (ng/mL)	2.0 - 56.7	16.2	18.0 ± 9.1
B12 Vitamin (pg/mL)	120.2 - 1553.0	334.8	395.0 ± 201.9
NLR	0.4 - 13.6	1.4	1.8 ± 1.6
SII	82.3 - 5515.9	431.5	564.7 ± 520
SIRI	0.1 - 22.5	0.8	1.2 ± 1.8
Group	Healthy Controls		177 (55.5%)
	Type 1 Diabetes		142 (44.5%)

Continuous variables are presented as mean ± standard deviation (SD), and categorical variables are presented as number and percentage [n (%)].

differences were observed between the groups with respect to low-density lipoprotein cholesterol (LDL), thyroid-stimulating hormone (TSH), or vitamin D levels (p>0.05; Table 2).

As shown in Table 3, univariate analysis indicated that age, MPV, RBC count, hemoglobin, hematocrit, WBC count, triglyceride, HDL, total cholesterol, vitamin B_{12}, NLR, SIRI, and SII were significantly associated with T1DM (p<0.05). Among these variables, NLR (OR=5.057; 95% CI: 3.299-7.754; p<0.001) and SIRI (OR=7.299; 95% CI: 4.039-13.190; p<0.001) demonstrated the strongest associations with the presence of T1DM.

In the multivariate forward logistic regression (LR) model, MPV, hemoglobin, hematocrit, HDL, vitamin B_{12}, NLR, and SIRI remained independently associated with T1DM (p<0.05). Increased MPV (OR=1.509; 95% CI: 1.021-2.232; p=0.039), hemoglobin (OR=2.041; 95% CI: 1.506-2.767; p<0.001), HDL (OR=1.046; 95% CI: 1.014-1.078; p=0.004), NLR (OR=5.158; 95% CI: 2.980-8.926; p<0.001), and SIRI (OR=6.438; 95% CI: 1.269-32.660; p=0.025) were identified as independent risk factors, whereas hematocrit exhibited a protective association (OR=0.437; 95% CI: 0.308-0.621; p<0.001). SII did not retain statistical significance in the multivariate model (p=0.680).

Table 2. Comparison of hematological and biochemical parameters between children and adolescents with T1DM and healthy controls

		Healthy Controls Group (n:160)		Type 1 Diabetes Group (n:159)		p	
		Mean±sd / n (%)	Median	Mean±sd / n (%)	Median		
Age		13.9 ± 2.9	14	14.9 ± 2.7	15	**0.003**	m
Gender	Female	86 (53.8%)		91 (57.2%)		0.531	X^2
	Male	74 (46.3%)		68 (42.8%)			
BMI kg/m²		20.4 ± 3.5	20	21.2 ± 3.7	20.4	0.063	m
HbA1c %		5.0 ± 0.0	5	9.5 ± 2.1	9.3	**0.000**	m
Platelets (10^3/μL)		322.5 ± 82.0	316.5	305.2 ± 83.5	306	**0.037**	m
MPV (fL)		8.7 ± 0.9	8.7	9.0 ± 0.9	9	**0.007**	m
RBC (10^6/μL)		4.7 ± 0.4	4.7	4.8 ± 0.4	4.8	**0.037**	m
Hemoglobin (g/dL)		12.8 ± 1.3	12.8	13.5 ± 1.4	13.4	**0.000**	m
Hematocrit %		37.8 ± 3.2	37.8	39.92 ± 4.09	39.6	**0.000**	m
WBC (10^3/μL)		6.3 ± 1.5	6	7.4 ± 2.2	7.1	**0.000**	m
Triglyceride mg/dl		92.2 ± 56.0	79.5	118.1 ± 124.3	89.6	**0.019**	m
LDL (mg/dl)		91.4 ± 32.1	90	87.8 ± 29.6	81	0.167	m
HDL (mg/dl)		50.0 ± 11.2	50	56.8 ± 15.8	55	**0.000**	m
TSH (mIU/L)		2.4 ± 1.2	2.1	2.3 ± 1.3	2.1	0.696	m
Total Cholesterol (mg/dl)		146.9 ± 27.4	145	172.0 ± 62.8	160	**0.000**	m
D Vitamin (ng/mL)		17.4 ± 8.4	16	18.6 ± 9.8	16.9	0.293	m
B12 Vitamin (pg/mL)		429.9 ± 246.1	352.8	359.8 ± 136.4	323.8	**0.034**	m
NLR		1.2 ± 0.5	1.1	2.4 ± 2.0	2	**0.000**	m
SIRI		0.67 ± 0.35	0.59	1.81 ± 1.76	1.12	**<0.001**	m
SII		389.06 ± 207.13	315.2	741.54 ± 662.02	576.2	**<0.001**	m

Table 3. Presents the results of univariate and multivariate logistic regression analyses evaluating hematological, biochemical, and inflammatory parameters associated with the presence of T1DM in pediatric patients

	Univariate Model			Multivariate Model		
	OR	**%95 GA**	**p**	**OR**	**%95 GA**	**p**
Age	1.14	1.049 - 1.231	0.002			
Platelets (10^3/μL)	1	0.995 - 1.000	0.064			
MPV (fL)	1.44	1.111 - 1.863	0.006	1.51	1.021 - 2.232	0.039
RBC (10^6/μL)	1.68	1.006 - 2.812	0.048			
Hemoglobin (g/dL)	1.5	1.249 - 1.792	0.000	2.04	1.506 - 2.767	0.000
Hematocrit %	0.78	0.706 - 0.857	0.000	0.44	0.308 - 0.621	0.000
WBC (10^3/μL)	1.43	1.235 - 1.660	0.000			
Triglyceride (mg/dl)	1	1.000 - 1.008	0.028			
HDL (mg/dl)	1.04	1.020 - 1.058	0.000	1.05	1.014 - 1.078	0.004
Total Cholesterol (mg/dl)	1	0.997 - 0.999	0.003			
B12 Vitamin (pg/mL)	1.02	1.012 - 1.028	0.000	1	0.995 - 1.000	0.021
NLR	5.06	3.299 - 7.754	0.000	5.16	2.980 - 8.926	0.000
SIRI	7.3	4.039 - 13.190	<0.001	6.44	1.269 - 32.660	0.025
SII	1	1.002 - 1.004	<0.001	1	0.995 - 1.003	0.68

Univariate and multivariate logistic regression analyses were performed using the forward likelihood ratio (Forward LR) method. Variables with p<0.05 in univariate analysis were entered into the multivariate model. Odds ratios are presented with 95% confidence intervals. A p-value <0.05 was considered statistically significant.

Table 4. ROC analysis of hemogram-based inflammatory indices for distinguishing pediatric patients with Type 1 diabetes mellitus from healthy controls

Parameter	**AUC**	**95% CI**	**Cut-off value**	**Sensitivity (%)**	**Specificity (%)**	**PPV (%)**	**NPV (%)**	**p-value**
NLR	0.791	0.742-0.839	1.46	71.1	72.5	72.0	71.6	<0.001
SIRI	0.768	0.716-0.820	0.97	60.4	83.8	78.7	68.0	<0.001

AUC: Area Under the Curve; CI: Confidence Interval; NLR: Neutrophil-to-Lymphocyte Ratio; SIRI: Systemic Inflammatory Response Index; PPV: Positive Predictive Value; NPV: Negative Predictive Value; ROC: Receiver Operating Characteristic.

The discriminative power of the NLR parameter between pediatric patients with T1DM and healthy controls was statistically significant (AUC=0.791; 95% CI: 0.742-0.839; p<0.001). The cutoff value of 1.46 for NLR yielded a sensitivity of 71.1%, specificity of 72.5%, positive predictive value of 72.0%, and negative predictive value of 71.6%, indicating moderate diagnostic performance. Similarly, the systemic inflammatory response index (SIRI) showed significant discriminatory performance, with an AUC of 0.768 (95% CI: 0.716-0.820; p<0.001). At a cutoff value of 0.97, SIRI provided a sensitivity of 60.4%, specificity of 83.8%, positive predictive value of 78.7%, and negative predictive value of 68.0%.

Overall, both NLR and SIRI exhibited moderate diagnostic accuracy in differentiating pediatric patients with T1DM from healthy controls, as summarized in Table 4.

The discriminative performance of hemogram-based inflammatory indices was further evaluated using receiver operating characteristic (ROC) curve analysis. The ROC-derived parameters for NLR and SIRI are summarized in Table 4, while the corresponding ROC curves are illustrated in Figure 1. The optimal cutoff value for the neutrophil-to-lymphocyte ratio (NLR) is illustrated in Figure 2.

In Table 5, demographic, hematological, and biochemical parameters were compared according to glycemic control status (HbA1c <8.5% vs. ≥8.5%) in pediatric patients with Type 1 diabetes mellitus. The group with HbA1c ≥8.5% had a significantly higher mean age and a higher proportion of female patients ($p<0.05$). In the same group, fasting blood glucose levels were significantly higher, while hematocrit values were significantly lower ($p<0.05$). No significant differences were observed between the groups in terms of body mass index, MPV, hemoglobin, WBC count, lipid profile, TSH, vitamin B_{12}, vitamin D, NLR, SII, or SIRI ($p>0.05$).

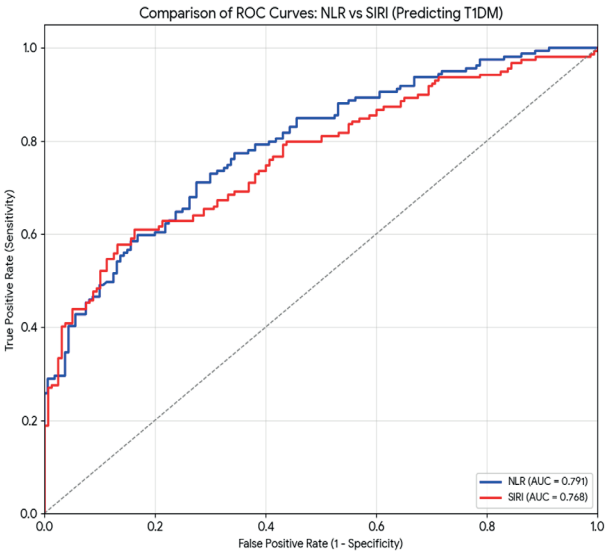

Figure 1. Receiver operating characteristic (ROC) curve analysis comparing the neutrophil-to-lymphocyte ratio (NLR) and systemic inflammatory response index (SIRI) for distinguishing pediatric patients with T1DM.

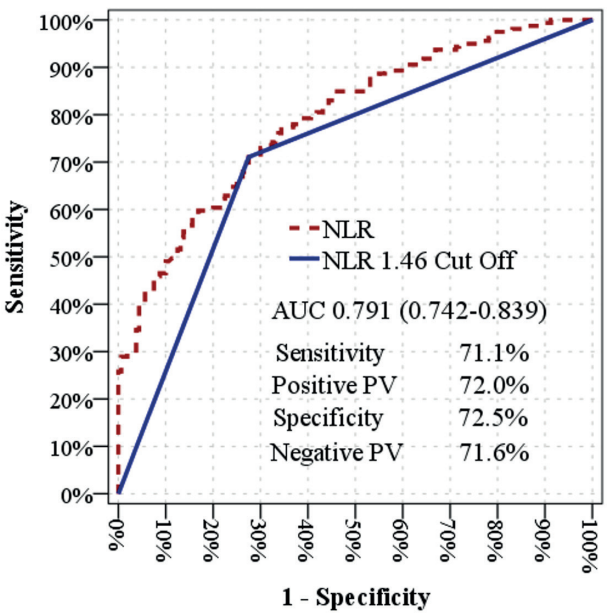

Figure 2. ROC curve of neutrophil-to-lymphocyte ratio (NLR) showing the optimal cut-off value of 1.46 with corresponding sensitivity and specificity for distinguishing children with Type 1 diabetes mellitus from healthy controls.

DISCUSSION

Evidence linking hematological alterations with metabolic control in type 1 diabetes mellitus (T1DM) remains limited. In our study cohort, distinct differences in hematological profiles were identified between children with T1DM and their healthy peers. We believe these differences are not incidental but convey important clinical information; they parallel glycemic control and suggest that hematological balance in pediatric diabetes is closely related to metabolic status.

In our clinical practice, persistently elevated HbA1c levels are often accompanied by changes in blood parameters. In the present study, increased MPV, WBC, NLR, SII, and SIRI values, together with decreased platelet count and vitamin B_{12} levels, indicate a disruption of hematological homeostasis under chronic hyperglycemic conditions. Similar findings have been reported by Tihić Kapidžić et al. in Bosnian children with T1DM (20), supporting both our observations and the notion that these alterations may be present across different ethnic pediatric populations.

Tablo 5. Comparison of demographic, hematological, and biochemical parameters according to glycemic control (HbA1c <8.5% vs ≥8.5%) in children and adolescents with T1DM

Type 1 Diabetes		HbA1c<8.5 (n:61)		HbA1c≥8.5 (n:98)		p	
		Mean±sd / n (%)	Median	Mean±sd / n (%)	Median		
Age		14.2 ± 2.8	14	15.4 ± 2.6	16	0.009	m
Gender	Female	26 (42.6%)		65 (66.3%)		**0.003**	X^2
	Male	35 (57.4%)		33 (33.7%)			
BMI kg/m²		21.1 ± 4.3	20.1	21.2 ± 3.2	21	0.271	m
Platelets (10^3/μL)		307.6 ± 90.9	307	303.7 ± 79.1	305	0.911	m
MPV (fL)		9.1 ± 0.8	9.1	8.9 ± 0.9	8.9	0.2	m
Glucose (mg/dL)		194.0 ± 170.6	190	301.5 ± 235.6	243	0.003	m
RBC (10^6/μL)		4.9 ± 0.4	4.9	4.8 ± 0.4	4.8	0.24	m
Hemoglobin (g/dL)		13.6 ± 1.3	13.6	13.4 ± 1.5	13.3	0.598	t
Hematocrit %		40.22 ± 3.86	39.8	39.76 ± 4.22	39.4	0.493	t
WBC (10^3/μL)		7.4 ± 2.7	6.9	7.4 ± 1.8	7.2	0.559	m
Triglyceride (mg/dl)		105.55 ± 63.47	92	125.10 ± 147.71	88.7	0.991	m
LDL (mg/dl)		89.1 ± 27.2	81	87.0 ± 31.1	80.5	0.581	m
HDL (mg/dl)		55.6 ± 17.6	52.7	57.6 ± 14.6	55.6	0.321	m
TSH		2.5 ± 1.4	2.2	2.2 ± 1.3	2	0.161	m
Total Cholesterol (mg/dl)		181.3 ± 87.4	159	166.2 ± 40.2	162.5	0.745	m
D Vitamin (ng/mL)		18.7 ± 8.7	17.6	18.6 ± 10.5	16.4	0.586	m
B12 Vitamin (pg/mL)		371.1 ± 147.1	346.2	352.7 ± 129.5	320.5	0.568	m
NLR		2.6 ± 2.4	2	2.3 ± 1.8	2	0.791	m
SIRI		2.05 ± 3.48	1.16	1.73 ± 2.57	1.1	0.936	m
SII			581.6	704.83 ± 505.04	573.9	0.772	m

t: Independent Samples t test; m: Mann-whitney u test; X^2: Chi-square test.
Pediatric patients were categorized according to the International Society for Pediatric and Adolescent Diabetes (ISPAD) guidelines. HbA1c <8.5% represents suboptimal but stable control for this cohort's distribution, while HbA1c ≥8.5% represents high-risk glycemic control.

Mean platelet volume (MPV) is of particular importance. Elevated MPV reflects increased platelet activation and is associated with a higher risk of microvascular complications (21,22). The higher MPV values observed in our diabetic group suggest that chronic hyperglycemia adversely affects platelet morphology and function. This finding is consistent with the results of Çoban et al. (23), who associated increased MPV with vascular involvement in pediatric diabetes. Hyperglycemia enhances non-enzymatic glycation and platelet membrane reactivity, exerting a prothrombotic effect that leads to an increase in MPV (24).

In multivariate analysis, MPV, hemoglobin, hematocrit, HDL, vitamin B_{12}, SIRI, and NLR emerged as independent factors distinguishing children with T1DM from healthy controls. When considered together, these findings demonstrate that the disease is not confined to disturbances in glucose metabolism alone but exerts broader systemic effects (25,26).

Inflammatory indices derived from the hemogram provide clinicians with an additional perspective. The elevated NLR, SII, and SIRI values observed in our study reflect the autoimmune and inflammatory nature of T1DM. These indices should not be regarded as primary

diagnostic tools; rather, they should be interpreted as indicators of chronic low-grade inflammation accompanying autoimmune beta-cell destruction and metabolic dysregulation. Previous studies have shown that such indices may reflect subclinical immune activation even before overt vascular complications develop (27,28). From this viewpoint, increased NLR, SII, and SIRI values are not diagnostic per se but are informative markers of inflammatory burden.

Age-related effects were also clinically relevant. Children in the HbA1c ≥8.5% group were relatively older, indicating that glycemic control becomes increasingly difficult during adolescence. Rising levels of growth hormone and sex steroids during puberty contribute to increased insulin resistance (29-33). Adolescence itself represents a physiological period characterized by changes that may influence hematological parameters and should therefore be considered a potential confounding factor. The higher proportion of females in the poor glycemic control group is consistent with the literature reporting lower insulin sensitivity and higher HbA1c levels in adolescent girls compared with boys (34,35).

Treatment adherence represents another important consideration. Adolescence is frequently associated with irregular insulin use, dietary non-adherence, increased fast-food consumption, and psychosocial stressors, all of which complicate glycemic regulation (31-33). Current ADA guidelines recommend targeting an HbA1c level below 7.5% in pediatric patients; however, achieving this goal under real-life conditions is often challenging (36).

The lower vitamin B_{12} levels observed in children with T1DM in our study are consistent with previous reports indicating an increased risk of deficiency in this population. Potential contributing factors include coexisting autoimmune conditions such as autoimmune gastritis and celiac disease, inadequate dietary intake, malabsorption, and diabetes-related gastrointestinal motility disorders (37,38). These findings support the need for routine monitoring of vitamin B_{12} levels, particularly in children with longer disease duration or suboptimal metabolic control. Regular nutritional counseling and support for treatment adherence constitute essential components of comprehensive diabetes care.

In our ROC analysis, NLR differed significantly between diabetic and healthy groups but demonstrated only moderate discriminative power. Although a cutoff value of 1.46 provided acceptable sensitivity and specificity, these values do not support its use as a standalone diagnostic marker. Rather, NLR should be considered a biomarker reflecting inflammatory activity associated with T1DM, without directly predicting clinical outcomes or complications (39-41). Details of its diagnostic performance are presented in Figure 2.

Our study has several limitations. Its retrospective design precludes causal inference, and its single-center nature limits generalizability. In addition, detailed data on dietary intake and physical activity were unavailable, and long-term complications were not assessed prospectively. Nevertheless, the inclusion of a well-matched control group and the evaluation of emerging indices such as SII and SIRI enhance the clinical relevance of our findings.

CONCLUSION

Hematological alterations, inflammatory indices, and micronutrient status are closely associated with metabolic regulation in children with T1DM. Elevated MPV, NLR, SII, and SIRI values, together with reduced vitamin B_{12} levels, demonstrate the detrimental effects of hyperglycemia on hematological balance.

Poor glycemic control, increasing age, and puberty-related hormonal changes—particularly in females—further accentuate metabolic deterioration during adolescence. These observations highlight the importance of age- and sex-specific, individualized treatment and nutritional strategies in pediatric diabetes management.

We believe that readily accessible hematological parameters such as MPV and NLR can provide useful insights into subclinical inflammatory activity in T1DM. In addition, regular assessment of vitamin B_{12} levels and continuous nutritional education are important for long-term metabolic control.

In conclusion, the combined evaluation of hematological and metabolic parameters may offer clinicians a practical and informative approach for assessing inflammatory burden and for planning individualized treatment strategies in pediatric patients with type 1 diabetes mellitus.

Ethical approval

This study has been approved by the Düzce University Non-Interventional Health Research Ethics Committee (approval date 10.11.2025, number 2025/284). Written informed consent was obtained from the participants.

Author contribution

Surgical and Medical Practices: ŞÖ; Concept: ŞÖ; Design: ŞÖ, İlknur Arslanoğlu; Data Collection or Processing: ŞÖ; Analysis or Interpretation: ŞÖ, İA; Literature Search: ŞÖ; Writing: ŞÖ. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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