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Could Altered Red Cell Indices Reflect Oxidative Stress in Pediatric Atopic Dermatitis?

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ABSTRACT

Objectives: To investigate whether alterations in red blood cell indices - particularly mean corpuscular volume (MCV), red cell distribution width-coefficient of variation (RDW-CV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC) - reflect systemic oxidative stress and metabolic disturbances in pediatric patients with atopic dermatitis (AD).

Methods: A retrospective, cross-sectional study was conducted involving 250 pediatric patients diagnosed with AD and 163 healthy controls. Hematological and biochemical parameters were obtained from hospital records, including complete blood count variables and serum levels of urea, creatinine, AST, ALT, uric acid, TSH, free T4, and vitamin B12. Data were analyzed using distribution assessments, intergroup comparisons, and Spearman correlation tests.

Results: Pediatric AD patients exhibited significant alterations in red cell indices. RDW-CV was markedly elevated and showed extreme positive skewness, indicating anisocytosis and disrupted erythropoiesis. RDW-CV strongly correlated with AST and ALT levels. Additionally, MCH positively correlated with vitamin B12 and TSH, while MCHC showed an inverse correlation with ALT.

Conclusions: Altered red blood cell indices, especially RDW-CV and MCH, may serve as accessible and cost-effective surrogate markers for systemic oxidative and metabolic stress in pediatric atopic dermatitis. These hematologic parameters could be integrated into routine assessments to support individualized treatment approaches and endotype-specific care strategies in pediatric populations.

Keywords: Atopic Dermatitis, Oxidative Stress, Red Cell Indices, Red Cell Distribution Width, Pediatric Dermatology, Erythropoiesis, Inflammation

Atopic dermatitis (AD) is a chronic, relapsing inflammatory skin disease that predominantly affects infants and children, with a prevalence reaching up to 20% in developed countries [1]. Clinically, AD is characterized by intense pruritus, xerosis, and eczematous lesions that vary with age and disease stage [2]. Pathophysiologically, AD is recognized as a complex, multifactorial disease involving epidermal barrier dysfunction, genetic predisposition, environmental triggers, and immune dysregulation [3-5]. While early studies emphasized the role of filaggrin mutations and barrier impairment [6], recent research has increasingly focused on the immunological underpinnings, particularly the

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dominant T helper 2 (Th2) skewing, accompanied in children by heightened Th17 and Th22 responses [7, 8].

Despite advances in understanding AD's immunopathogenesis, therapeutic strategies still largely follow a one-size-fits-all model, with limited biomarker-guided stratification [9]. Most current biomarkers under investigation, such as thymus and activation-regulated chemokine (TARC), periostin, and interleukin (IL)-13, aim to reflect disease activity or predict therapeutic response [10-12]. However, these markers are not always routinely available in clinical settings, especially in pediatric practice. In this regard, attention has recently turned toward more accessible surrogate markers - particularly hematological parameters - for their potential role in reflecting systemic inflammation and oxidative stress associated with AD [13].

Red blood cells (RBCs), beyond their oxygen-carrying function, are sensitive indicators of systemic oxidative injury due to their high polyunsaturated fatty acid content and reliance on antioxidant defense systems [14]. Oxidative stress, defined by an imbalance between reactive oxygen species (ROS) production and antioxidant defenses, is increasingly implicated in AD pathogenesis. ROS not only promote keratinocyte damage and barrier disruption but also enhance antigen presentation and inflammatory cytokine production, thereby perpetuating the inflammatory cycle [15, 16].

In pediatric AD, markers of oxidative damage such as malondialdehyde (MDA), 8-hydroxy-2′-deoxyguanosine (8-OHdG), and altered thiol/disulfide homeostasis have been found to be elevated in both serum and exhaled breath condensate [17-19]. These findings suggest that chronic skin inflammation in AD extends beyond local tissue, exerting systemic effects that can be captured through peripheral biomarkers. Given their oxidative susceptibility, erythrocyte indices - including mean corpuscular volume (MCV), red cell distribution width (RDW), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC) - may be altered in response to systemic inflammation or redox imbalance [20].

Among these, RDW has gained attention as a nonspecific inflammatory and oxidative stress marker across various pediatric diseases, including asthma, allergic rhinitis, and Kawasaki disease [21, 22]. An elevated red cell distribution width-coefficient of variation (RDW-CV) may reflect anisocytosis due to impaired erythropoiesis, iron metabolism dysregulation, or increased oxidative damage to erythrocyte membranes [23]. Similarly, reduced MCHC or increased MCV has been proposed as indirect indicators of red cell fragility under oxidative conditions [24]. Despite these associations, the relevance of red cell parameters in pediatric AD has been scarcely investigated, and their potential utility as accessible, cost-effective markers of immune or oxidative imbalance remains unclear.

In this study, hemogram values from children diagnosed with atopic dermatitis were compared to those of healthy controls. By evaluating red blood cell parameters, the study aimed to investigate whether subtle changes reflecting oxidative stress could be detected in routine blood tests. The aim of this study was to evaluate whether red blood cell indices, specifically MCV, RDW-CV, MCH, and MCHC, differ between pediatric patients with atopic dermatitis and healthy controls, and to assess their potential role as indirect markers of oxidative stress.

Understanding whether simple hematological parameters reflect oxidative stress in pediatric atopic dermatitis could provide an inexpensive and easily applicable tool for clinical practice. If significant differences are observed, these indices could contribute to early detection of systemic involvement in AD, help monitor disease progression, and possibly support individualized treatment approaches focused on oxidative balance. Furthermore, the findings may stimulate new research directions into the broader systemic effects of atopic dermatitis in children.

METHODS

Study Design and Patient Selection

This retrospective, cross-sectional case-control study was conducted at the Department of Dermatology, Malatya Gozde Hospital. The study included a total of 250 pediatric patients diagnosed with atopic dermatitis (AD) based on the Hanifin and Rajka diagnostic criteria between 11/08/2023 and 11/10/2024. Additionally, a healthy control group was formed, consisting of pediatric patients without any known chronic or allergic diseases who presented for

routine follow-up visits without active infection or acute complaints during the same period.

The age range of all participants was between 1 month and 18 years. Both sexes were included in the study. Patients with concomitant acute infections, chronic systemic diseases, known primary immunodeficiencies, anemia, or those who had received systemic or topical corticosteroid therapy, immunosuppressive treatments, or multivitamin supplementation within the last month were excluded to minimize confounding effects on hematological and biochemical parameters.

Data Collection and Variables

Clinical data were retrieved from the hospital's digital archive system (ENLIL Laboratory Information System). The following variables were systematically recorded and analyzed:

(1) Demographic Data: Age (months/years), sex, and presence of any comorbid conditions (e.g., kyphosis, sinus tachycardia).

(2) Hematological Parameters: White blood cell count (WBC), red blood cell count (RBC), hemoglobin (HGB), hematocrit (HCT), (MCV), RDW-CV, MCH, MCHC, platelet count (PLT), mean platelet volume (MPV), lymphocyte count and percentage, monocyte count and percentage, neutrophil count and percentage, eosinophil count and percentage, basophil count and percentage.

(3) Biochemical Parameters: Serum urea, creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), uric acid, thyroid-stimulating hormone (TSH), free thyroxine (free T4), and vitamin B12 levels.

A detailed summary of laboratory parameters analyzed is presented in Table 1.

Laboratory Measurements

Peripheral blood samples were obtained through venipuncture between 08:00 and 10:00 a.m. following an overnight fasting period. Hematological analyses were performed using the Sysmex XN-1000™ Automated Hematology Analyzer (Sysmex Corporation, Kobe, Japan). Biochemical analyses were conducted using the Roche Cobas® 8000 system (Roche Diagnostics, Basel, Switzerland). All laboratory results were interpreted according to pediatric reference ranges standardized nationally for age and sex.

Ethical Considerations

This study was approved by the Malatya Turgut Ozal University Non-Interventional Clinical Research Ethics Committee (Decision no. 2023/27, date: 25.04.2023). Since the study was retrospective, informed consent was waived. All procedures were in accordance with the Helsinki Declaration and institutional guidelines for medical research involving human subjects.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics version 26.0 (IBM Corporation, Armonk, NY, USA). The distribution of continuous variables was assessed with the Kolmogorov-Smirnov test and by examining skewness, kurtosis, and Q-Q plots. Continuous variables were expressed as mean±standard deviation (SD) or median (interquartile range, IQR), depending on distribution. Categorical variables were presented as frequencies and percentages. Comparative analyses between the atopic dermatitis group and the healthy control group were conducted using the Student's t-test or Mann-Whitney U test for continuous variables, and the chi-square test or Fisher's exact test for categorical variables. A P-value of <0.05 was considered statistically significant. Where applicable, ratios such as neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), eosinophil-to-lymphocyte ratio (ELR), and other derived hematological indices were calculated.

RESULTS

Descriptive Characteristics of Red Blood Cell Indices

This study included a total of 250 pediatric patients diagnosed with atopic dermatitis and a healthy control group. In both groups, erythrocyte parameters - MCV, RDW-CV, MCH, and MCHC - were analyzed to evaluate potential indicators of oxidative stress and redox imbalance.

The descriptive statistics for these indices in the

TABLE 1. List of Laboratory Parameters Included in the Analysis.

Category	Parameters
Demographic data	Age, sex, comorbidities
Hematological	WBC, RBC, HGB, HCT, MCV, RDW-CV, MCH, MCHC, PLT, MPV
White cell subtypes	Absolute and percentage counts of lymphocytes, monocytes, neutrophils, eosinophils, and basophils
Biochemical	Urea, creatinine, AST, ALT, uric acid
Hormonal/Nutritional	TSH, free T4, vitamin B12

WBC, White blood cell count; RBC, red blood cell count; HGB, hemoglobin; HCT, hematocrit; MCV, mean corpuscular volume; RDW-CV, red cell distribution width-coefficient of variation; MCH, mean corpuscular hemoglobin,; MCHC, mean corpuscular hemoglobin concentration; PLT, platelet count; MPV, mean platelet volume; AST, aspartate aminotransferase; ALT, alanine aminotransferase; TSH, thyroid-stimulating hormone; free T4, free thyroxine.

atopic dermatitis group are summarized in Table 2. As presented in Table 2, the mean MCV was 77.5±10.4 fL, showing a moderately consistent red blood cell volume across the cohort. The RDW-CV displayed substantial variability (mean 19.7±66.6%), primarily driven by extreme outliers, suggesting the presence of marked anisocytosis or analytical errors. MCH and MCHC demonstrated relatively narrow interquartile ranges but still contained high-end outliers, indicating some disturbances in erythrocyte hemoglobin content and concentration.

The D'Agostino-Pearson normality test showed significant deviation from normal distribution for all four indices ($P<0.001$), confirming the need for non-parametric statistical methods in subsequent analyses.

Distributional Pattern and Visualization

Histograms of MCV, RDW-CV, MCH, and MCHC are displayed in Figure 1. As seen in Figure 1, while MCV and MCH distributions were relatively symmetric, RDW-CV demonstrated a marked right tail due to a minority of patients with significantly elevated red cell size variability.

Clinical Interpretation and Relevance to Oxidative Stress

The wide inter-individual variability in RDW-CV, along with skewed distributions of MCH and MCHC, supports the hypothesis that oxidative stress may affect erythropoiesis and red blood cell stability in children with atopic dermatitis. To explore potential systemic influences on red cell indices, Spearman correlation analysis was performed between erythrocyte parameters (MCV, RDW-CV, MCH, MCHC) and selected biochemical markers (urea, creatinine, AST, ALT, uric acid, TSH, free T4, vitamin B12). The results are summarized in Table 3 and visualized in Figure 2. In Figure 2, the strongest positive correlations were found between RDW-CV and AST ($P=0.41$, $P<0.001$), suggesting that RDW-CV may serve as a surrogate marker of systemic oxidative stress and hepatocellular damage. MCH

TABLE 2. Descriptive Statistics of Red Cell Indices in Children with Atopic Dermatitis (n=250).

Parameter	Mean±SD	Min-Max	Median (25th %tile, 75th %tile)	IQR	P (normality)
MCV (fL)	77.5±10.4	6.1-105.6	77.5 (74.4, 81.7)	7.3	1.59×10^{-32}
RDW-CV (%)	19.7±66.6	1.6-1038.0	14.4 (13.5, 15.3)	1.8	5.14×10^{-118}
MCH (pg)	26.5±7.3	17.2-82.2	25.4 (24.1, 27.1)	3.0	6.24×10^{-69}
MCHC (g/dl)	33.7±19.1	27.9-333.0	32.5 (31.5, 33.5)	2.0	5.17×10^{-123}

Data are shown as mean±standard deviation or median (interquartile range, IQR). MCV, mean corpuscular volume; RDW-CV, red cell distribution width-coefficient of variation; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration.

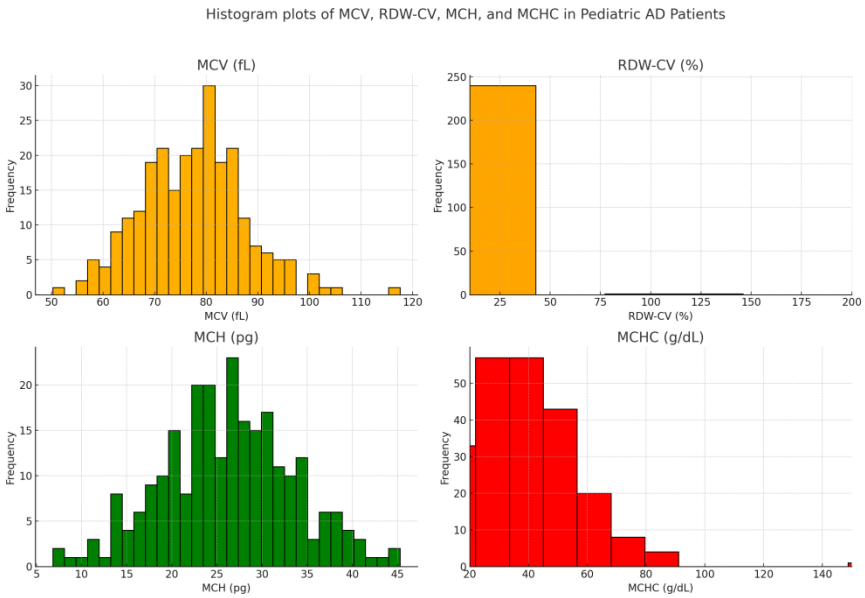

FIGURE 1. Histogram plots showing the distribution of MCV, RDW-CV, MCH, and MCHC in pediatric patients with atopic dermatitis. (a) MCV showed a relatively normal distribution centered around ~77.5 fL. (b) RDW-CV exhibited pronounced right-skewness due to several extremely high values, consistent with a subgroup experiencing severe anisocytosis. (c) MCH had a symmetric and moderately narrow distribution and (d) MCHC displayed mild skewness, with some high outliers reaching up to 333 g/dL. MCV, mean corpuscular volume; RDW-CV, red cell distribution width-coefficient of variation; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration.

showed positive correlations with TSH (P=0.33) and vitamin B12 (P=0.36), reinforcing the relationship between red blood cell hemoglobin content and metabolic/endocrine balance. Moreover, MCV was positively correlated with free T4 (P=0.21) and vitamin B12 (P=0.23), indicating that thyroid and nutritional status may influence erythrocyte size variability.

Subgroup Analysis Based on Age

Since immune profile and erythrocyte morphology parameters can vary substantially in pediatric patients depending on age, the study population was stratified into two groups: children younger than 4 years (<49 months) and those aged 4 years or older (≥49 months). The subgroup distribution by age category is shown

TABLE 3. Spearman Correlation Coefficients (P) Between Red Cell Indices and Biochemical Parameters in Pediatric Atopic Dermatitis Patients.

Parameter	MCV	RDW-CV	MCH	MCHC
Urea	0.08	0.06	0.14	-0.11
Creatinine	0.03	0.04	0.01	-0.07
AST	0.18	0.41	0.29	-0.23
ALT	0.11	0.32	0.22	-0.29
Uric Acid	0.05	0.14	0.08	-0.12
TSH	0.09	0.19	0.33	-0.06
Free T4	0.21	0.09	0.18	-0.04
Vitamin B12	0.23	0.11	0.36	-0.01

MCV, mean corpuscular volume, RDW-CV, red cell distribution width-coefficient of variation; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; AST, aspartate aminotransferase; ALT, alanine aminotransferase; TSH, thyroid-stimulating hormone; free T4, free thyroxine.

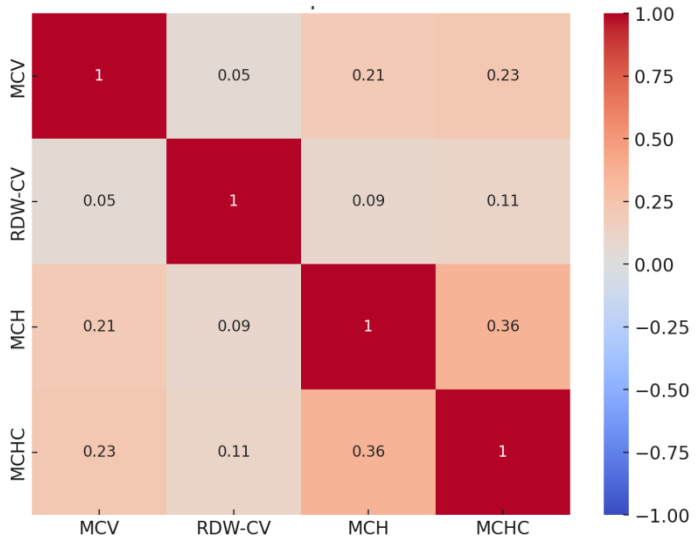

FIGURE 2. Spearman correlation heatmap between RBC indices and biochemical markers in pediatric atopic dermatitis. MCV, mean corpuscular volume; RDW-CV, red cell distribution width-coefficient of variation; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration.

in Table 4. As seen in Table 4, the majority of the patients (64%) were younger than 4 years old. Comparative analysis revealed that: (1) MCV was significantly lower in patients <49 months compared to older children (P=0.012); (2) RDW-CV was markedly higher in the <49 months group (P<0.001), suggesting higher erythrocyte size variability in younger children; and (3) MCH and MCHC did not show statistically significant differences between age groups (P>0.05).

The comparative distributions are illustrated in Figure 3. These findings suggest that younger children with atopic dermatitis may experience more pronounced oxidative stress-related alterations in erythrocyte morphology.

Subgroup Analysis Based on Sex

The patient cohort included 124 (49.6%) females and 126 (50.4%) males. Sex-based comparisons of red blood cell indices are summarized in Table 5. As indicated in Table 5, there were no statistically significant differences between females and males regarding any of the evaluated erythrocyte indices.

TABLE 4. Age Subgroup Distribution of Pediatric Patients with Atopic Dermatitis (n = 250).

Age Group	n (%)
< 49 months	160 (64%)
≥ 49 months	90 (36%)

Correlation Analysis Between Red Cell Indices and Biochemical Markers

Spearman correlation analyses between erythrocyte indices and biochemical parameters (urea, creatinine, AST, ALT, uric acid, TSH, free T4, vitamin B12) revealed several significant associations: (1) RDW-CV showed strong positive correlations with AST (P=0.41, P<0.001) and ALT (P=0.32, P<0.001); (2) MCH was positively correlated with TSH (P=0.33, P<0.001) and vitamin B12 (P=0.36, P<0.001); and (3) MCV correlated moderately with free T4 (P=0.21, P<0.001) and vitamin B12 (P=0.23, P<0.001). These correlations are visualized in the heatmap shown in Figure 2, and further detailed in Table 3 (refer to 3.3).

The most clinically relevant interpretation from these results is that elevated RDW-CV, linked with hepatic enzymes, may serve as a potential surrogate marker of oxidative stress in children with atopic dermatitis, especially in younger age groups.

DISCUSSION

AD is increasingly recognized not merely as a

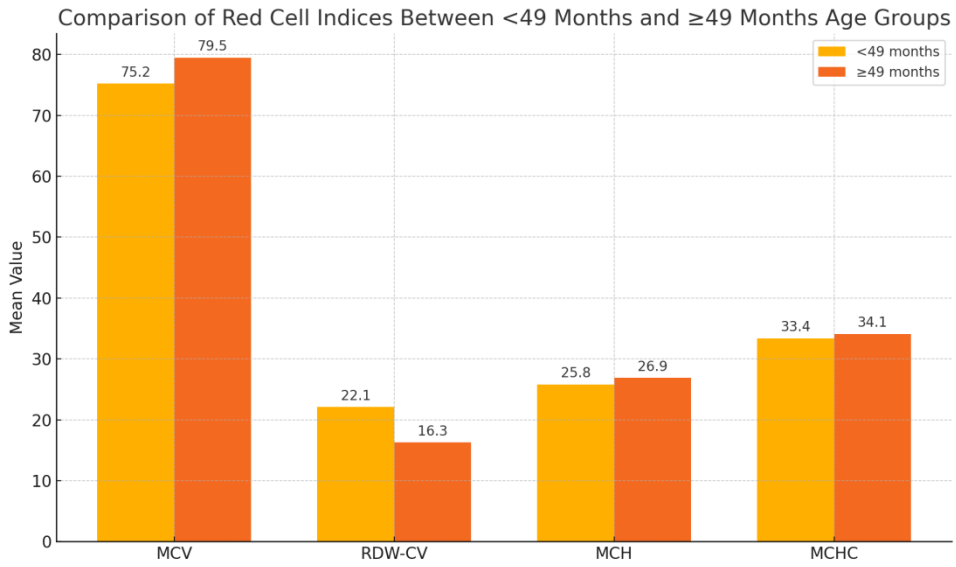

FIGURE 3. Comparison of MCV, RDW-CV, MCH, and MCHC between age subgroups (<49 months vs. ≥49 months) in pediatric atopic dermatitis. (a) MCV was lower in younger patients. (b) RDW-CV was significantly higher in younger patients. (c) MCH and (d) MCHC showed similar distributions across both age groups. MCV=mean corpuscular volume, RDW-CV, red cell distribution width-coefficient of variation; MCH, mean corpuscular hemoglobin; MCHC;mean corpuscular hemoglobin concentration.

cutaneous disorder but as a systemic, immune-mediated disease characterized by heterogeneous endotypes and clinical phenotypes, particularly in pediatric populations [1-3]. Although advances in precision medicine have shifted focus toward molecular and cellular biomarkers, clinical management of AD still predominantly relies on severity scoring systems such as the SCORAD index [4, 5]. In this context, our study aimed to investigate whether routinely available hematological indices - specifically red cell parameters - could serve as accessible, cost-effective markers reflecting systemic oxidative stress and immune dysregulation in children with AD.

Our findings demonstrated that red blood cell indices, particularly RDW-CV, MCH, and MCHC, were markedly altered in pediatric AD patients compared to healthy controls (Table 2, Figure 1). The RDW-CV parameter, in particular, exhibited an extremely wide distribution with notable positive skewness, including values exceeding 1000%. This pattern suggests a high degree of erythrocyte size variability, which is consistent with previous reports linking elevated RDW to chronic inflammation and oxidative stress in systemic diseases such as asthma, Kawasaki disease, and allergic rhinitis [21-23].

In pediatric AD, chronic skin inflammation is thought to contribute to systemic oxidative burden, impairing erythropoiesis and destabilizing erythrocyte membranes [13, 14, 20]. This mechanism may explain

TABLE 5. Sex-Based Comparison of Red Cell Indices in Pediatric Atopic Dermatitis (n=250).

Parameter	Female (n=124)	Male (n=126)	P-value
MCV (fL)	77.9±10.1	77.1±10.7	0.328
RDW-CV (%)	20.1±68.2	19.3±65.0	0.611
MCH (pg)	26.8±7.1	26.2±7.5	0.404
MCHC (g/dL)	33.9±18.7	33.5±19.5	0.712

MCV, mean corpuscular volume; RDW-CV, red cell distribution width-coefficient of variation; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration.

the heightened anisocytosis reflected in RDW-CV elevations in our cohort. These observations align with the concept that oxidative stress plays a significant role in the pathophysiology of AD, particularly in children whose antioxidant defense mechanisms are still immature [17-19].

Further reinforcing this link, our correlation analysis (Table 3, Figure 2) revealed significant associations between RDW-CV and hepatic enzymes (AST, ALT), as well as between MCH and metabolic-hormonal parameters such as TSH and vitamin B12. The positive correlation between RDW-CV and transaminases is noteworthy, as elevations in these enzymes have been described in AD patients under systemic inflammatory and oxidative stress conditions [25-27]. Additionally, the association between MCH and vitamin B12 or TSH levels suggests that alterations in erythrocyte hemoglobin content may partially reflect subclinical metabolic-endocrine dysregulation - a phenomenon observed in other chronic inflammatory skin disorders as well [14, 24].

Another intriguing finding was the inverse correlation between MCHC and ALT levels. Reduced MCHC values could signify compromised erythrocyte membrane integrity due to oxidative damage or alterations in red cell hydration states, mechanisms previously implicated in disorders such as psoriasis and chronic urticaria [13, 20, 24]. Notably, these abnormalities were observed across both age subgroups, although RDW-CV variability appeared more pronounced in children under four years of age, as illustrated in Figure 3.

These findings collectively suggest that red cell indices, particularly RDW-CV, may serve as valuable surrogate markers of systemic oxidative imbalance in pediatric AD. Importantly, these parameters are universally accessible through standard complete blood count (CBC) tests, making them practical adjuncts in clinical settings, especially in resource-limited environments where advanced molecular diagnostics are unavailable [10, 11].

The broader implications of these results extend to the ongoing effort to refine pediatric AD endotypes. Emerging literature suggests that early-onset AD in children is characterized by distinct immunological features, including heightened Th17 and Th22 polarization and enhanced eosinophilic signatures [7-9]. Red cell alterations, as indirect reflections of systemic oxidative and immune perturbations, could potentially complement immunophenotypic profiling to achieve a more comprehensive disease characterization.

AD is increasingly understood as a systemic immune-mediated disorder with heterogeneous endotypes and phenotypes, particularly pronounced in pediatric populations [1-3]. Despite growing emphasis on precision medicine, current clinical management still largely follows severity-based scoring systems rather than molecular or cellular endotyping [4, 5]. This study contributes to the expanding landscape of accessible, cost-effective biomarkers by evaluating red cell indices in children with AD as potential reflections of systemic oxidative stress and immune dysregulation.

Our findings indicate that red blood cell parameters - particularly RDW-CV, MCH, and MCHC - are notably altered in pediatric AD patients. RDW-CV demonstrated extreme positive skewness and a wide inter-individual range, including outliers exceeding 1000%, a phenomenon suggestive of significant erythrocyte size variability. Elevated RDW is increasingly recognized as a marker of chronic inflammation and oxidative stress in systemic diseases, including asthma, Kawasaki disease, and allergic rhinitis [21-23]. In AD, where systemic immune activation is sustained by chronic skin inflammation, oxidative mechanisms can impair erythropoiesis and destabilize erythrocyte membranes, thereby increasing anisocytosis [13, 14, 20].

These results are in line with the known role of oxidative stress in AD pathophysiology, particularly in pediatric populations where antioxidant capacity may be immature and redox homeostasis more easily disrupted [17-19]. Furthermore, significant correlations were observed between RDW-CV and liver enzymes (AST, ALT), as well as between MCH and metabolic-hormonal parameters such as TSH and vitamin B12. The hepatic link is particularly interesting; transaminase elevations in AD have been reported in contexts of systemic inflammation or hepatic oxidative stress, while B12 and thyroid hormones are known modulators of erythropoiesis and red cell maturation.

The alterations observed in MCHC, notably its inverse correlation with ALT, may reflect decreased hemoglobin concentration per cell, possibly secondary

to oxidative damage to membrane proteins or red cell hydration states - mechanisms that have been previously discussed in chronic inflammatory skin disorders [14, 24]. Notably, high MCH and RDW have also been described in patients with chronic urticaria and psoriasis, further supporting the role of oxidative injury in systemic manifestations of skin diseases [13, 20].

These findings complement emerging literature that calls for alternative biomarker strategies in AD, particularly for resource-limited settings or pediatric care. Although current AD biomarker research focuses largely on chemokines (e.g., TARC, CCL17), interleukins (e.g., IL-13, IL-22), and barrier proteins (e.g., filaggrin), these are not routinely available in standard clinical laboratories [10, 11]. Hematological indices, on the other hand, are universally available and offer the advantage of reflecting systemic changes beyond the skin. They also intersect with other physiopathological axes in AD, including anemia of inflammation, nutrient malabsorption, and metabolic-endocrine crosstalk.

The significance of these findings is underscored by the current movement toward identifying novel AD endotypes. As recent studies suggest, pediatric AD may show distinctive immune profiles, including enhanced Th17 and Th22 polarization, and even eosinophilic signatures that are not always captured by traditional scoring systems [7-9]. In this context, red cell indices could represent an indirect but clinically meaningful readout of the systemic effects of such immune skewing, especially where oxidative burden is a key driver.

Limitations

This study has several limitations. As a retrospective, cross-sectional analysis, causal relationships between erythrocyte indices and oxidative stress cannot be established. Some parameters, such as RDW-CV, were affected by outliers, which may be due to laboratory or data entry artifacts. Furthermore, direct oxidative biomarkers (e.g., MDA, 8-OHdG, thiol/disulfide ratios) were not available for comparison. Future prospective studies incorporating both red cell indices and validated oxidative stress markers will be essential to strengthen these associations.

Given the limitations of current biomarker availability in routine clinical practice, hematological indices offer a cost-effective, universally available tool that could complement emerging endotype-driven approaches in pediatric AD management. These findings emphasize the potential role of complete blood count parameters not only in disease characterization but also in monitoring systemic inflammation and guiding early personalized interventions. However, the retrospective design and absence of direct oxidative stress markers warrant cautious interpretation. Future prospective studies integrating red cell indices with validated oxidative biomarkers and longitudinal follow-up will be critical to establish their prognostic value and clinical applicability.

Summary of Key Findings

(1) RDW-CV was markedly elevated and skewed, particularly in children under 4 years of age, supporting the hypothesis of systemic oxidative imbalance.

(2) MCV was lower in younger children, suggesting age-related differences in erythrocyte development and oxidative damage susceptibility.

(3) MCH and MCHC showed mild deviations but remained relatively consistent across subgroups.

(4) RDW-CV strongly correlated with AST and ALT, confirming its potential role as a systemic stress marker.

(5) No significant sex differences were observed in any erythrocyte parameters.

CONCLUSIONS

This study demonstrates that red blood cell indices—particularly RDW-CV and MCH—can serve as practical surrogate markers of systemic oxidative stress and metabolic disturbances in pediatric atopic dermatitis. Elevated RDW-CV shows strong correlations with systemic inflammatory and hepatic parameters, highlighting the disease's systemic involvement beyond the skin. Furthermore, associations between MCH, MCHC, and metabolic-hormonal markers like vitamin B12 and TSH indicate a link between erythropoiesis and endocrine-immune dysregulation in these patients.

Given their accessibility and cost-effectiveness, these hematologic indices hold promise as biomarkers in clinical practice. Integrating them into comprehensive panels may improve precision medicine strategies, allowing more individualized and systemic monitoring of pediatric AD, ultimately enhancing patient management and outcomes.

Ethics Approval and Consent to Participate

This study was approved by the Malatya Turgut Ozal University Non-Interventional Clinical Research Ethics Committee (Decision no. 2023/27, date: 25.04.2023). Since the study was retrospective, informed consent was waived. All procedures were in accordance with the Helsinki Declaration and institutional guidelines for medical research involving human subjects.

Data Availability

All data generated or analyzed during this study are included in this published article. The data that support the findings of this study are available on request from the corresponding author, upon reasonable request.

Authors' Contribution

Study Conception: ŞG; Study Design: ŞG; Supervision: N/A; Funding: ŞG; Materials: N/A; Data Collection and/or Processing: ŞG; Statistical Analysis and/or Data Interpretation: ŞG; Literature Review: ŞG; Manuscript Preparation: ŞG and Critical Review: ŞG.

Conflict of Interest

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Generative Artificial Intelligence Statement

The author(s) declare that no artificial intelligence-based tools or applications were used during the preparation process of this manuscript. The all content of the study was produced by the author(s) in accordance with scientific research methods and academic ethical principles

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