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Article

The Role Of Systemic Inflammatory Indices In Predicting Cardiovascular Involvement In Children With Duchenne Muscular Dystrophy

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Highlights

What are the main findings?

- Hemoglobin levels were significantly higher in DMD patients compared to controls, while common inflammatory markers (NLR, PLR, MLR, SIRI, SII, PIV) did not differ significantly between groups.
- A strong positive correlation was found between Pro-BNP levels and PLR values ($r = 0.86$, $p < 0.05$), highlighting a potential link between cardiac stress and systemic inflammation.

What is the implication of the main finding?

- Cardiac involvement in DMD may occur early, even before symptoms appear, underscoring the need for routine ECG and echocardiographic screening in all patients.
- The observed correlation between Pro-BNP and PLR suggests that inflammatory markers might reflect cardiac stress and could have prognostic value when combined with cardiac biomarkers.
- Although inflammatory markers did not differ overall between DMD patients and controls, further research is needed to explore their role in specific patient subgroups or stages of disease progression.

Abstract

Background: Duchenne Muscular Dystrophy (DMD) is an X-linked recessive neuromuscular disorder that leads to progressive muscle weakness and cardiomyopathy, with cardiovascular complications being a primary cause of morbidity and mortality. Recent interest has emerged in the role of systemic inflammatory indices as potential predictors of cardiovascular involvement. This study aimed to evaluate the prognostic value of inflammatory markers—NLR, PLR, MLR, SIRI, SII, and PIV—in children with DMD and to explore their association with cardiac findings. **Methods:** In this retrospective study, 25 male patients diagnosed with DMD and 25 age-matched healthy male controls were evaluated between January 2021 and July 2024. Demographic and clinical data, hematologic and biochemical parameters, and inflammatory indices were recorded. Cardiovascular involvement was assessed using electrocardiography (ECG) and transthoracic echocardiography (TTE). Group comparisons were conducted using independent t-tests, while ROC and Pearson correlation analyses were used for diagnostic performance and associations. **Results:** Pathological Q waves were the most frequent ECG abnormality (24%), and 16% of patients had echocardiographic abnormalities. While most systemic inflammatory indices (NLR, MLR, SIRI, SII, PIV) did not significantly distinguish cardiovascular involvement, PLR demonstrated a strong positive correlation with Pro-BNP levels ($r = 0.86$, $p < 0.05$), suggesting a potential link between systemic inflammation and subclinical cardiac stress. **Conclusions:** Although the overall diagnostic utility of inflammatory indices in predicting cardiovascular complications in DMD was limited, PLR emerged as a promising marker. Its significant correlation with Pro-BNP highlights its potential role in identifying early cardiovascular risk, warranting further investigation in prospective studies.

Keywords: Duchenne Muscular Dystrophy; cardiomyopathy; electrocardiography; echocardiography; inflammatory indices; Pro-BNP

1. Introduction

Duchenne Muscular Dystrophy (DMD) is an X-linked inherited disorder characterized by progressive muscle weakness and degeneration, primarily observed in male children. The etiology of DMD is linked to a genetic defect resulting in absent or dysfunctional production of the protein dystrophin. This deficiency leads to muscle fiber damage and subsequent loss of muscle function. However, DMD is not limited to skeletal muscle involvement; its systemic effects also contribute to impairment of the cardiovascular system. In particular, cardiac function in individuals with DMD typically deteriorates in parallel with muscle weakness, significantly affecting patients' quality of life and prognosis [1].

Cardiovascular involvement is a frequently overlooked but critical component of DMD. Most children with DMD develop cardiac muscle weakness (cardiomyopathy) that becomes more pronounced with advancing age. This cardiomyopathy mainly manifests as left ventricular dysfunction, which can eventually progress to heart failure [2]. Additionally, arrhythmias and other electrophysiological abnormalities play a significant role in disease progression and contribute to increased mortality rates in these patients [3].

Non-invasive diagnostic tools such as electrocardiography (ECG) enable early detection of cardiovascular involvement in DMD. ECG provides valuable information on cardiac status; commonly observed abnormalities in children with DMD include QRS complex widening, PR interval prolongation, T-wave inversions, and pathological Q waves [4].

Recently, systemic inflammatory indices have gained prominence as novel markers for predicting cardiovascular disease prognosis and quantifying inflammation. Indices such as neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), platelet-to-lymphocyte ratio (PLR), systemic inflammatory response index (SIRI), systemic immune-inflammation index (SII), and pan-immune inflammation value (PIV) are simple, low-cost parameters derived from routine blood tests that reflect the extent of systemic inflammation. Their prognostic values have been demonstrated in various cardiovascular, neurovascular, oncological, and metabolic disorders [5–7].

Early identification and management of cardiovascular complications in children with Duchenne Muscular Dystrophy may improve disease prognosis. In this context, further research is required to clarify whether systemic inflammatory indices can serve as predictors of cardiovascular involvement in this population. This study aims to investigate the cardiovascular effects and electrocardiographic findings of DMD and to evaluate the potential utility of novel inflammatory indices in guiding cardiac monitoring and treatment strategies.

2. Materials and Methods

This retrospective study evaluated data from 25 patients diagnosed with Duchenne Muscular Dystrophy between January 1, 2021, and July 1, 2024. Sample size calculations were performed to ensure a minimum statistical power of 80% and a Type I error rate of 5% for each variable analyzed. The control group consisted of an equal number of healthy male children aged 2 to 18 years, randomly selected from individuals presenting to the pediatric outpatient clinic who had undergone complete blood counts.

The variables assessed included patient age, age at diagnosis, wheelchair dependence, tracheostomy status, treatment regimens, hematological parameters, neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), platelet-to-lymphocyte ratio (PLR), systemic inflammatory response index (SIRI: neutrophils \times monocytes / lymphocytes), systemic immune-inflammation index (SII: neutrophils \times platelets / lymphocytes), pan-immune inflammation value

(PIV: neutrophils \times monocytes \times platelets / lymphocytes), and electrocardiographic (ECG) and echocardiographic (ECHO) parameters.

Statistical Analysis

All statistical analyses were performed using SPSS for Windows, version 26 (IBM Corp., Armonk, NY, USA), with statistical significance set at $p < 0.05$. The normality of continuous variables was assessed using the Kolmogorov-Smirnov test and skewness-kurtosis measures. Since the data were normally distributed, parametric tests were applied.

Descriptive statistics were presented as mean, standard deviation, count (n), and percentage (%). Independent samples t-test was used for comparisons between groups. Receiver operating characteristic (ROC) curve analysis was conducted to determine optimal cut-off values for variables within the patient group, calculating area under the curve (AUC), sensitivity, and specificity.

Pearson correlation coefficient was employed to evaluate relationships between continuous variables.

3. Results

3.1. Demographic and Clinical Characteristics

In this retrospective study, clinical data from 25 patients diagnosed with Duchenne Muscular Dystrophy (DMD) were analyzed. All patients were male. The median age was 12 years (range: 5–18), with a mean age of 11.2 ± 4.3 years. The mean age at diagnosis was 4.8 ± 2.6 years, with a median age of 4 years (range: 2–10 years). Wheelchair dependence was observed in 16% of the patients. None of the patients required home mechanical ventilation or tracheostomy during the study period.

Among the DMD patients, three cases were receiving cardiac treatment due to cardiovascular involvement. Of these, one patient was treated with an angiotensin-converting enzyme (ACE) inhibitor, one with a combination of beta-blocker and ACE inhibitor, and one with digoxin, diuretics, and ACE inhibitor. Descriptive statistics for other measured parameters are presented in Table 1.

Table 1. Descriptive Statistics of Categorical Variables in the Patient Group (n=25).

			N	%
Disability (Wheelchair Use)	Status	Yes	4	16%
		No	21	84%
Cardiac Treatment		ACE Inhibitor (ACEI)	0	0,0%
		Beta Blocker	1	4%
		ACE Inhibitor + Beta Blocker	1	4%
		Digoxin + Diuretic + ACE Inhibitor	1	4%
Home Ventilation	Mechanical	No	25	100,0%
Tracheostomy		No	25	100,0%

3.2. Electrocardiographic and Echocardiographic Findings

Electrocardiographic (ECG) abnormalities were detected in 9 (36%) of the patients. The most common ECG abnormality was pathological Q waves observed in the V5–V6 leads in 6 patients (24%) (Figure 1). Other abnormalities included T-wave inversion in the inferior leads in one patient (Figure 2), right bundle branch block in another, and supraventricular tachycardia in a third patient. Among these 9 patients with ECG abnormalities, transthoracic echocardiography (TTE) was normal in 6 (66.7%). Of the remaining three patients, one had left ventricular systolic dysfunction, another

presented with both left ventricular dysfunction and dilated cardiomyopathy, and the third was diagnosed with mitral valve prolapse accompanied by mitral regurgitation. All three patients who received cardiac treatment were among those with echocardiographic abnormalities. Two of these patients exhibited pathological Q waves on ECG, while one patient (25%) showed T-wave inversion. Echocardiographic and electrocardiographic abnormalities of the patients are summarized in Table 2.

Table 2. Echocardiographic and Electrocardiographic Findings in the Patient Group.

Electrocardiography (ECG) Findings	Normal	21	84,0%
	Mitral Valve Prolapse + Mitral Regurgitation (MVP + MR)	1	4,0%
	Left Ventricular Systolic Dysfunction	1	4,0%
	Left Ventricular Systolic Dysfunction + Dilated Cardiomyopathy	1	4,0%
	Tricuspid Regurgitation	1	4,0%
Electrocardiography (ECG) Findings	Pathological Q Wave	6	24,0%
	T negatifliği (İnferior Derivasyonlarda)	1	4,0%
	Normal	16	64,0%
	Right Bundle Branch Block (RBBB)	1	4,0%
	Supraventricular Tachycardia (SVT)	1	4,0%

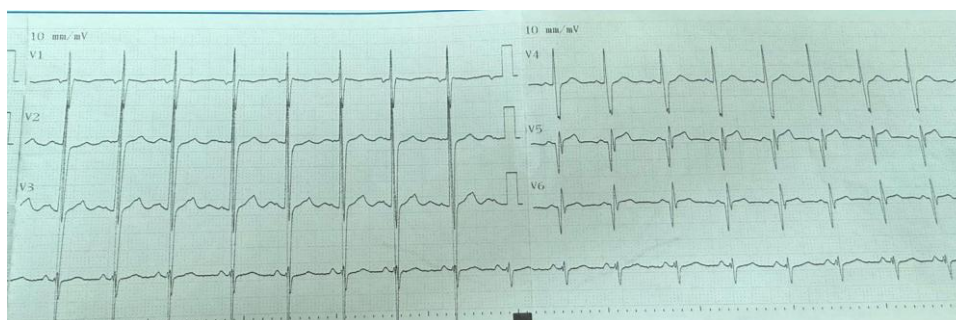


Figure 1. 5 mm Q Waves in Leads V5 and V6.

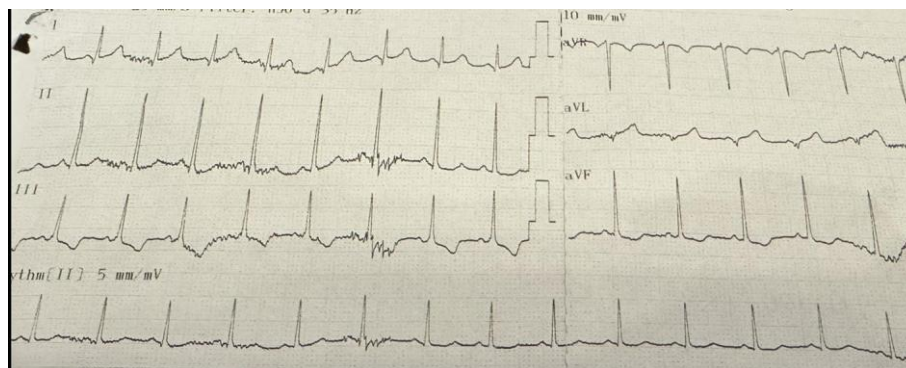


Figure 2. T-Wave Inversion in Inferior Leads.

When comparing hematological parameters, hemoglobin levels were found to be significantly higher in patients with Duchenne Muscular Dystrophy (DMD) compared to the control group. The

mean hemoglobin level in the DMD group was 13.46 ± 1.11 g/dL, whereas in the control group it was 12.65 ± 0.84 g/dL. This difference between the two groups was statistically significant ($p = 0.006$), indicating a notable increase in hemoglobin levels in DMD patients relative to controls.

No statistically significant differences were observed between groups for other hematological parameters. Although white blood cell (WBC), lymphocyte, neutrophil, monocyte, and platelet (PLT) counts appeared slightly elevated in the patient group compared to controls, these differences did not reach statistical significance (Table 3).

Table 3. Comparison of Other Hematological Parameters Between the Groups.

	Control (n=25)		Patient (n=25)		* <i>p.</i>
	Mean	Std. Dev.	Mean	Std. Dev.	
Hemoglobin	12,652	,842	13,461	1,114	,006
White Blood Cell (Lökosit)	8278,400	2241,084	9157,826	3643,207	,315
Lymphocyte	2912,400	1260,632	3200,000	1058,979	,399
Neutrophil	4456,000	2316,610	5033,913	3465,274	,497
Monocyte	560,400	199,885	579,565	349,876	,815
Platelet	293600,00	75365,77	297347,82	73297,40	,862

* Significance levels based on independent samples *t*-test results.

3.4. Inflammatory Marker Levels

Key inflammatory markers were examined in patients with Duchenne Muscular Dystrophy. The mean neutrophil-to-lymphocyte ratio (NLR) was 2.00 ± 2.28 , showing high inter-individual variability. Platelet-to-lymphocyte ratio (PLR) was measured at 102.63 ± 46.92 , while monocyte-to-lymphocyte ratio (MLR) was low at 0.21 ± 0.15 . The systemic inflammatory response index (SIRI) and systemic immune-inflammation index (SII) demonstrated considerable variation within the patient group, with mean values of 0.14 ± 0.19 and 592.8 ± 659.16 , respectively. The pan-immune inflammation value (PIV) was 502.84 ± 103.66 .

Comparison of these inflammatory markers between the patient and control groups revealed no statistically significant differences for NLR, PLR, MLR, SIRI, SII, and PIV. The results are presented in Table 4.

Table 4. Comparison of Inflammatory Markers Between Groups.

	Control (n=25)		Patient (n=25)		* <i>p.</i>
	Mean	Std. Dev.	Mean	Std. Dev.	
NLR	2,032	1,765	2,005	2,285	,963
PLR	117,609	52,916	102,636	46,921	,307
MLR	,248	,176	,213	,150	,473
SIRI	0,129	0,164	0,139	0,188	,842
SII	588,672	560,940	592,798	659,167	,981
PIV	394,378	586,885	502,8482	103,667	,654

* Significance levels based on independent samples *t*-test results.

3.5. Correlation Analysis

Correlation analysis was performed among the measured parameters within the patient group. A statistically significant positive correlation was identified between Pro-BNP levels and PLR values, with a correlation coefficient of 0.86 ($p < 0.05$). This indicates that as Pro-BNP levels increase, PLR values also tend to increase. In contrast, no statistically significant correlations were found among other paired variables outside of those mentioned ($p > 0.05$) (Table 5).

Table 5. Results of Correlation Analysis Between Measurements in the Patient Group.

		Pro BNP	Troponin T	CKMB	Troponin I
PLT	r	-,152	,453	,237	-,487
	p.	,773	,547	,763	,268
NLR	r	,599	,142	,445	-,246
	p.	,209	,858	,555	,595
PLR	r	,860*	-,523	,872	-,510
	p.	,028	,477	,128	,243
MLR	r	,473	-,589	,350	-,319
	p.	,343	,411	,650	,486
SIRI	r	,349	,361	,084	-,229
	p.	,498	,639	,916	,621
SII	r	,688	,392	,594	-,330
	p.	,131	,608	,406	,470
PIV	r	,475	,521	,266	-,261
	p.	,341	,479	,734	,572
	p.	,188	,254	,129	,545

r: Pearson correlation coefficients; *: $p < 0,05$.

3.6. ROC Analysis of Inflammatory Markers

Receiver Operating Characteristic (ROC) analysis revealed that the neutrophil-to-lymphocyte ratio (NLR) had a cut-off value of 1.21, with an area under the curve (AUC) of 56.5%, indicating its discriminative ability between patient and control groups. However, based on this calculation, the sensitivity (56.5%) and specificity (60.0%) values demonstrate that the NLR measurement does not provide statistically adequate discrimination between the patient and control groups ($p < 0.05$). Similarly, the platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR), systemic inflammatory response index (SIRI), systemic immune-inflammation index (SII), and pan-immune inflammation value (PIV) also showed insufficient discriminative power between the patient and control groups ($p < 0.05$) (Figure 3, Table 6).

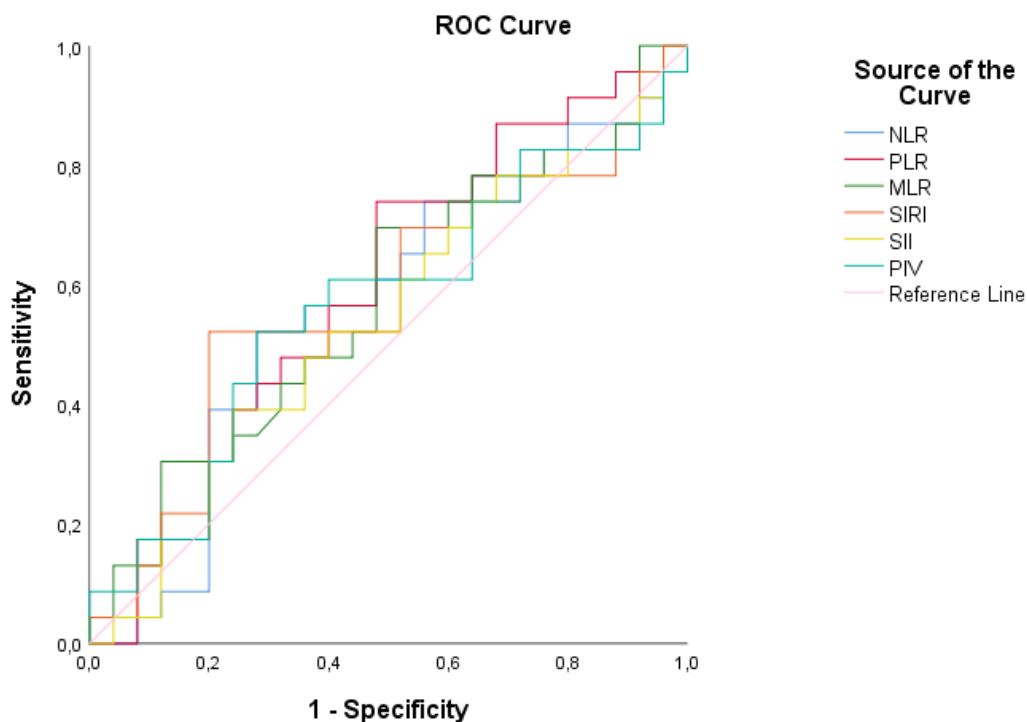


Figure 3. ROC Curve for IMA Measurement Across Groups.

Table 6. ROC Analysis of Measurements Across Groups.

Test Variables	Area (AUC)	Std. Error	<i>p.</i>	Cut-Off	Sensitivity	Specificity
NLR	,565	,085	,439	1,21	,568	,600
PLR	,591	,083	,279	98,15	,565	,560
MLR	,575	,084	,375	0,17	,522	,520
SIRI	,572	,085	,392	0,611	,527	,522
SII	,534	,085	,687	386,284	,525	,526
PIV	,565	,085	,439	191,807	,609	,605

AUC: Area Under Curve. Categorical variable: Group Cut-Off: Cut-off value.

3.7. Comparison by ECG/ECHO Abnormalities

Comparisons between patients with and without ECG/ECHO abnormalities revealed no statistically significant differences in any of the measured parameters ($p > 0.05$) (Table 7).

Table 7. Comparison of Measurements According to EKG/ECHO Abnormalities.

	EKG/ECHO Abnormality				<i>*p.</i>
	No (n=15)		Yes (n=10)		
	Mean	Std. Dev.	Mean	Std. Dev.	
Age	10,733	4,334	12,100	4,483	,454
Age at Diagnosis	4,667	2,498	5,100	2,998	,698
Hemoglobin	13,146	1,182	13,870	,918	,125
WBC	8419,231	2758,380	10118,000	4526,342	,278
Lymphocyte	3352,308	1145,136	3002,000	956,960	,444

Neutrophil	4181,538	2754,499	6142,000	4101,598	,185
Monocyte	598,462	391,490	555,000	306,095	,775
PLT	291538,46	74891,72	304900,00	74446,77	,675
NLR	1,705	2,415	2,395	2,166	,485
PLR	97,195	51,153	109,709	42,360	,539
MLR	,212	,144	,215	,167	,965
SIRI	0,114	0,158	0,174	0,227	,461
SII	502,861	717,859	709,717	590,039	,468
PIV	519,283	131,074	481,482	579,162	,933
Glucose	94,167	11,846	99,100	16,381	,422
Creatinine	,277	,113	,250	,164	,658
Aspartate Aminotransferase (AST)	166,083	151,280	148,500	115,591	,766
Alanine Aminotransferase (ALT)	191,417	184,558	129,500	117,995	,371
Alkaline Phosphatase (ALP)	145,000	21,714	118,200	66,744	,418
Gamma-Glutamyl Transferase (GGT)	16,250	18,661	6,000	.	,657
Bilirubin	,574	,351	,572	,235	,987
Creatie Kinaz (CK)	7608,889	5705,158	3734,833	2767,020	,149
ProBNP	16,900	.	295,240	405,682	,565
TroponinT	101,000	.	127,167	33,773	,571
Troponin I	,215	,163	,106	,009	,135

* Significance levels based on independent samples t-test results.

4. Discussion

This study examined the clinical, biochemical, and cardiological data of 25 patients diagnosed with Duchenne Muscular Dystrophy (DMD). The findings provide valuable insights into the clinical course, treatment strategies, and cardiac complications associated with DMD.

All patients included in the study were male, which is consistent with the expected inheritance pattern of DMD as an X-linked genetic disorder [8]. The median age of patients was 12 years (range: 5–18), and the mean age at diagnosis was 4.8 ± 2.6 years. This finding emphasizes that DMD is typically diagnosed during childhood, highlighting the importance of early diagnosis in monitoring disease progression [9]. The diagnosis of DMD is commonly established between ages 3 and 5, and early diagnosis can shorten the time to treatment initiation, aiding in the preservation of motor functions [10].

Regarding physical status and needs, the rate of wheelchair use was found to be 16%. Pane et al. reported that loss of ambulation in DMD patients generally begins around 12 years of age, coinciding with the initiation of wheelchair dependency [11] This indicates significant motor function decline with advancing age, with wheelchair use typically required in later stages. None of the patients required home mechanical ventilation or tracheostomy, suggesting that early treatment may mitigate

the impact of DMD on respiratory functions. Birnkrant et al. also stated that respiratory dysfunction in DMD patients usually becomes more prominent after loss of ambulation [12].

Cardiological assessments revealed important findings. The most frequently observed ECG abnormality was pathological Q waves (24%), consistent with literature reports indicating a 30–40% prevalence in DMD patients. This finding is considered an early marker of silent myocardial fibrosis and is associated with cardiomyopathy [13]. Another study linked frequent pathological Q waves in DMD patients with sudden cardiac death (SCD) [14].

Cardiac complications in DMD are known to commence early and become more pronounced with age [15]. In our study, there was no significant age difference between patients with or without cardiac pathology. Severe cardiac conditions such as left ventricular dysfunction and dilated cardiomyopathy were also observed. These results suggest that cardiac involvement in DMD may develop not only in advanced stages but also from early disease phases [16]. Furthermore, the detection of severe cardiac pathologies such as dilated cardiomyopathy in echocardiography underscores the importance of ongoing cardiological monitoring. According to our echocardiographic data, 16% (4/25) of patients had left ventricular dysfunction or structural anomalies, consistent with the approximately 22% prevalence reported in a large cohort study by Ramaciotti et al. [17]. The correlation between echocardiographic abnormalities and ECG findings was weak, further emphasizing the limited diagnostic value of ECG alone in DMD [18].

Cardiac treatments employed included ACE inhibitors, beta blockers, and digoxin. These therapies are vital for managing cardiomyopathy and other cardiac complications, highlighting the critical role of cardiac monitoring and treatment in DMD patients [19]. The need for cardiac therapy was confined to patients with ECG or echocardiographic abnormalities, and no significant relationship was found between clinical or biochemical parameters and cardiac treatment. This finding indicates that cardiac complications should be closely monitored through ECG and echocardiography, and that a multidisciplinary approach is necessary in managing these patients [15].

Biochemically, hemoglobin, white blood cell, lymphocyte, and neutrophil counts varied widely among patients, generally remaining within normal ranges, possibly reflecting the effectiveness of current treatment regimens. Notably, hemoglobin levels were significantly higher in the patient group ($p = 0.006$). Although elevated hemoglobin is uncommon in DMD, some studies report increases secondary to corticosteroid therapy [12].

The absence of significant differences in inflammatory markers between patient and control groups suggests a limited role for systemic inflammation biomarkers in routine monitoring of DMD [20]. Conversely, Yükcü and Arslan demonstrated that MLR, SIRI, and PIV have acceptable diagnostic value for detecting ascending aortic dilation in children with bicuspid aortic valve [7]. This association suggests inflammation may be an important factor in that patient group, whereas the lack of significant differences in inflammatory indices in DMD may indicate that inflammation is not directly related to cardiac complications in this population.

A notable finding in our study is the positive correlation between Pro-BNP and PLR, which may indicate a potential link between increased cardiovascular burden and inflammatory response. Pro-BNP is recognized as a useful biomarker for predicting left ventricular dysfunction and heart failure in DMD [21]. Although several studies have examined the prognostic value of PLR in cardiovascular diseases, it is not considered an independent predictor of mortality. A 2019 cohort study reported that higher PLR levels in patients with acute heart failure (AHF) were associated with increased mortality rates [22]. Studies directly evaluating the relationship between Pro-BNP and PLR are limited; however, both biomarkers have been shown to be important in assessing heart failure and acute coronary syndromes. For example, a study on chronic heart failure patients found a positive correlation between NT-proBNP levels and PLR [23]. To our knowledge, no previous studies have investigated this correlation specifically in the DMD population.

The ROC analysis revealed that none of the inflammatory parameters achieved sufficient diagnostic accuracy, limiting their utility for routine screening in DMD. Furthermore, the impact of

routine steroid use on inflammatory indices remains unclear and warrants further investigation. Prospective studies are needed to clarify these findings.

5. Conclusions

Our study comprehensively evaluated the clinical, cardiological, and biochemical characteristics of patients with Duchenne Muscular Dystrophy, notably highlighting the positive correlation between Pro-BNP and PLR. The findings suggest that DMD affects not only the muscular system but also the cardiovascular system from early stages, underscoring the importance of regular cardiac follow-up. However, larger prospective studies are necessary to elucidate the role of inflammatory markers in DMD.

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Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and approved by the Non-Interventional Research Ethics Committee of Ordu University (protocol code 2025/68; date of approval: 7 March 2025).

Informed Consent Statement: The data presented in this study are available on request from the corresponding author. The data are not publicly available due to ethical restrictions and patient confidentiality.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

DMD	Duchenne Muscular Dystrophy
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
PIV	Pan-Immune Inflammation Value
ECG	Electrocardiography
Pro-BNP	Pro-Brain Natriuretic Peptide
ROC	Receiver Operating Characteristic
QRS	QRS Complex
PR	PR Interval
ECHO	Echocardiography
SPSS	Statistical Package for the Social Sciences
AUC	Area Under the Curve
ACE	Angiotensin-Converting Enzyme
TTE	Transthoracic Echocardiography
RBB	Right Bundle Branch
SVT	Supraventricular Tachycardia
WBC	White Blood Cell

PLT	Platelet
CK-MB	Creatine Kinase-MB Isoenzyme
AST	Aspartate Aminotransferase
ALT	Alanine Aminotransferase
ALP	Alkaline Phosphatase
GGT	Gamma-Glutamyl Transferase (Gama-Glutamil Transferaz)
CK	Creatine Kinase
SCD	Sudden Cardiac Death

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