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# Serum Lactate Dehydrogenase Elevates and Inversely Correlates with Platelet Count in Immune Thrombocytopenia: A Case-control Study in Adults

## İmmün Trombositopenide Serum Laktat Dehidrojenaz Yükselir ve Trombosit Sayısıyla Ters Korelasyon Gösterir: Yetişkinlerde Olgu Kontrol Çalışması

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ABSTRACT

**Background:** Platelets have high lactate dehydrogenase (LDH) activity. Although widely used as a marker of hemolysis, the rise of LDH in high platelet turnover without concomitant hemolysis -such as in immune thrombocytopenia (ITP)- is not well established. This study aimed to evaluate pre and post-treatment serum LDH levels in patients diagnosed with ITP and compare this with a healthy control group (CG).

**Materials and Methods:** Two hundred twenty-six patients who were newly diagnosed with ITP [123 patients with treatment indication (ITP-T) and 103 patients without treatment indication (ITP-WT)] and 131 patients as CG were enrolled. Serum LDH level were measured at diagnosis and during early response evaluation. Pre-and post-treatment LDH levels of ITP-T patients were compared and the differences in LDH according to the response in the first two weeks were examined.

**Results:** LDH was higher in newly diagnosed ITP patients than in the CG (218 IU/L, and 159 IU/L, respectively p<0.001). LDH levels of ITP-T, ITP-WT, and CG were 241.8 IU/L, 191.5 IU/L, and 159.3 IU/L, respectively (p<0.001). An inverse correlation was found between LDH levels and platelet counts in the entirety of the newly diagnosed ITP patient group (p<0.001). However, when the subgroups of ITP patients were examined, a correlation was found only in the ITP-T group (p=0.009); no correlation was found in the ITP-WT group. The alteration of the LDH in the ITP-T group according to the response was -6.7 IU/L, -15.3 IU/L, and -21.6 IU/L in patients without response, response, and complete response, respectively (p>0.05).

**Conclusion:** The LDH level was found to be moderately high in patients with ITP at the time of diagnosis, and slightly improved after the treatment. Oncoming LDH isoenzyme studies may be determined to find out which isoenzyme is responsible for its rise and if can it be used as a marker in the diagnosis or follow-up of ITP.

**Keywords:** Immune thrombocytopenia, lactate dehydrogenase, treatment

ÖZ

**Amaç:** Laktat dehidrojenaz (LDH) farklı dokularda bulunmaktadır. Trombositlerin yüksek LDH aktivitesine sahip olduğu bilinmektedir. Hemolizin bir belirteci olarak LDH'nin yükselmesi yaygın olarak kullanılmasına rağmen, hemoliz olmaksızın yüksek trombosit döngüsü olan immün trombositopenide (ITP) LDH'nin yükselmesi yeteri kadar irdelenmemiştir. Çalışmamızda ITP tanısı konulan hastalarda tedavi öncesi ve sonrası serum LDH düzeylerini değerlendirmeyi ve kontrol grubu (KG) ile karşılaştırmayı amaçladık.

**Gereç ve Yöntemler:** Çalışmamıza ITP tanısı konan iki yüz yirmi altı hasta [tedavi endikasyonu olan (ITP-T) 123 hasta ve tedavi endikasyonu olmayan (ITP-WT) 103 hasta] ve 131 kişilik sağlıklı KG dahil edildi. Serum LDH düzeyi tanı anında ve erken yanıt değerlendirmesi sırasında ölçüldü. Ayrıca ITP-T hastalarının tedavi öncesi ve sonrası LDH düzeyleri karşılaştırıldı ve ilk 2 hafta içinde ITP'ye yönelik alınan cevaba göre LDH değişimindeki farklılıklar değerlendirildi.

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ÖZ

**Bulgular:** LDH yeni tanı ITP hastalarında KG'ye göre daha yüksek saptandı (sırasıyla 218 IU/L ve 159 IU/L, p<0.001). ITP-T, ITP-WT ve KG'nin LDH seviyeleri sırasıyla 241.8±72.2 IU/L,191.5±39.2 IU/L ve 159.3±23.6 IU/L saptandı (p<0.001). Tüm ITP grubunda LDH düzeyleri ile trombosit sayıları arasında ters korelasyon gözlendi (p<0.001). Tedavi alan ve almayan gruplar ayrı ayrı değerlendirildiğinde sadece ITP-T grubunda hastaların trombosit sayıları ile LDH düzeyleri arasında korelasyon saptanırken (p=0.009); ITP-WT grubunda korelasyon saptanmadı. Yanıta göre LDH düzeylerindeki değişim yanıtsız, yanıtlı ve tam yanıtlı hastalarda sırasıyla -6.7±20.2 IU/L, -15.3±7.9 IU/L ve -21.6±8.6 IU/L olarak saptandı (p>0.05).

**Sonuç:** ITP hastalarında LDH enzim düzeyi tanı anında orta derecede yüksek, tedavi sonrasında ise hafif derecede azalmış olarak bulundu. Gelecekte bu konu ile ilgili yapılacak LDH izoenzim çalışmaları ile yükselen LDH enziminin alt tipi belirlenebilir ve ITP tanı ve takibinde belirteç olarak kullanılabilir.

**Anahtar Kelimeler:** İmmün trombositopeni, laktat dehidrojenaz, tedavi

## Introduction

Immune thrombocytopenia (ITP) is an acquired hematologic disease induced by autoantibodies produced by B lymphocytes -mostly of the IgG type- against platelet membrane glycoproteins such as GPIIb/IIIa (1). The major destruction site of antibody-coated (opsonized) platelets is the spleen. The incidence of ITP is 2.9:100,000/year, peaking over the age of 60 and reaching 9:100,000/year over the age of 75 (2). Treatment is recommended for patients who have symptoms of bleeding and/or have a platelet count of less than 20,000-30,000/microL (3). The first-line treatment is composed of corticosteroids (CS) and/or intravenous immune globulin (IVIG) (4).

Lactate dehydrogenase (LDH) is a cytoplasmic enzyme present in many organs and tissues in the body. There are many pathological conditions (tissue damage, hemolytic anemia, infections, drugs, endocrine diseases, malignancies, rheumatic diseases, idiosyncratic, etc.) that can elevate serum LDH levels. Platelets are also known to have high LDH activity (5). While broadly used as a marker of hemolysis, LDH elevation in high platelet turnover without concurrent hemolysis, as in ITP is not well established. To our knowledge, there is only one report presenting an increase in LDH in newly diagnosed ITP patients compared with the healthy control group (CG) (6).

We hypothesized that the destruction of platelets in ITP gives rise to intracytoplasmic LDH entering the bloodstream, and increases serum LDH levels. With successful treatment, the enzyme level decreases as a result of the reduction of platelet destruction. In line with this hypothesis, we aimed to show the changes in the LDH level in newly diagnosed ITP patients and compare this with healthy individuals, as well as pre-and post-treatment LDH levels in ITP patients in terms of treatment type and efficacy.

## Material and Methods

### Patients selection

Between October 2016-December 2020, two hundred twenty-six patients diagnosed with ITP and 131 controls in University of Health Sciences Türkiye, Sultan 2. Abdulhamid Han Hospital and Gülhane Faculty of Medicine Hematology Clinics, were enrolled in this study. The data was obtained from the hospitals' electronic registration system and patient files retrospectively.

Since ITP is a diagnosis of exclusion, patients with a thrombocytopenia duration of fewer than three months were examined with a detailed history and laboratory tests before being recruited to the study (complete blood count, liver and kidney function tests, peripheral blood smear, direct antiglobulin test, tests for HIV, hepatitis C, and B viruses, coagulation, rheumatological tests, and thyroid function tests, etc.). Bone marrow biopsy was performed on all patients over 60 years of age to exclude myelodysplastic syndromes. In patients under 60 years of age, and only if a suspicion of any other hematologic disease, a bone marrow biopsy was also performed. Diseases that could cause secondary ITP were firmly excluded. By strict exclusion of all other possible causes of thrombocytopenia, a diagnosis of primary ITP was recorded. Pregnant women, patients with malignancy, patients under the age of 18, and those with another pathology accompanying high LDH were excluded from the study. The CG was selected randomly from healthy, non-thrombocytopenic individuals who did not have any disease or medication that could affect the LDH level.

For ITP patients, treatment decisions were given by the treating physician according to the depth of thrombocytopenia and/or any clinically significant bleeding. Preferred first-line treatment included the use of CS or CS plus IVIG.

Age, gender, platelet counts, serum LDH, bleeding location, and severity at the time of diagnosis were recorded. The response to first-line treatment was defined as follows: Complete response if platelet count ⩾100,000/microL measured on two occasions, and response if platelet count ⩾30000/microL and a greater than twofold increase in platelet count from baseline measured on two occasions, according to International Working Group Descriptive Terminology for ITP (7). An increase of less than 30,000/microL in the platelet count or less than twofold above baseline in the first two weeks after treatment was considered unresponsive to treatment.

All procedures involving human participants and performed in the study were per the ethical standards of the institutional and/or national research committee as well as per the 2013 Declaration of Helsinki and its later amendments or comparable ethical standards. Approval letters were obtained from the participating hospitals before the application to the ethics committee. Ethics committee approval was obtained for this retrospective multicenter study [Local Ethics Committee of İstanbul Medeniyet University (date: 24/03/2021, decision no: 2021/0216)]. Due to the retrospective nature of data collection, we could not obtain informed consent from the participants.

### Material and Methods

Serum LDH level was measured at the time of diagnosis and during early response evaluation by Beckman Coulter AU5800 using the International Federation of Clinical Chemistry-recommended procedure (8). Blood collection for evaluation of LDH was completed with all patients in less than one minute while using a tourniquet. The reference ranges for LDH were 0-248 U/L.

The patients were divided into two groups, ITP patients with treatment indication (ITP-T) and ITP patients without treatment indication (ITP-WT). CG, ITP-T, and ITP-WT groups were compared in terms of variables. The ITP-T group was also divided into 2 subgroups according to the first-line treatment strategies (CS vs CS plus IVIG). To evaluate the effect of bleeding status on LDH, all ITP patients were divided into groups according to either the presence or absence of bleeding. In addition, the ITP-T group was divided into three groups according to treatment response (as described above).

The primary objective was to determine the differences in LDH levels between newly diagnosed ITP patients and healthy controls. The secondary objective was to determine the difference in LDH levels between ITP-T and ITP-WT groups. Furthermore, we compared pre-and post-treatment LDH levels of ITP-T patients and examined the differences in LDH change according to the response obtained within the first two weeks. The effects of IVIG use and bleeding status on LDH levels were also investigated as the tertiary objective.

### Statistical Analysis

The study population was described by using frequencies with associated percentages for qualitative data and descriptive statistics. The assumption of normality for all parameters was satisfied, as assessed by the Kolmogorov-Smirnov test. Z score was measured on Kurtosis and Skewness in cases where normality could not be achieved by the Kolmogorov-Smirnov test; the range of [-3, +3] was accepted as a normal distribution. If the assumption of homogeneity of variances was satisfied, an independent sample t-test was used; but if the assumption of homogeneity was breached, a Welch t-test was used to compare two independent groups. A Pearson's correlation test was performed to assess the relationship between continuous variables, then supplemented by a linear regression test. A One-Way Multivariate Analysis of Variance was performed to determine the difference in multiple variables in the three groups.

## Results

The median age for ITP and CG was 42 years (18-91) and 43 years (20-79) respectively, with a predominance of females (66.8% vs 66.1%) in both groups. One-hundred and twenty-three patients (54.4%) were in the ITP-T group and 103 patients (45.6%) were in the ITP-WT group. Petechiae was observed in 86 ITP-T patients (69.9%), and 30% had accompanying mucosal bleeding. Three of these patients only have isolated mucosal bleeding. Only one patient presented with genitourinary bleeding and 33 patients (26.8%) did not have any bleeding symptoms. The first-line treatment strategy in the ITP-T group was as follows: 82 patients (66.7%) were treated with CS alone, and 41 patients (33.3%) were treated with CS plus IVIG.

Laboratory parameters of ITP groups (with and without treatment) and CG were summarized in Table 1. LDH levels of patients with ITP and CG were 218 (64) IU/L, and 159 (23) IU/L, respectively [p<0.001, 95% confidence interval (CI), 0.10-0.14]. Platelet counts of ITP-T, ITP-WT, and CG were 11,777 (9.141)/microL, 63,511 (19,348)/microL, and 244,000 (56,553) /microL, respectively (p<0.001, for each pair, $\eta^2$=0.9). LDH levels of ITP-T, ITP-WT, and CG were as follows; 241.8 (72.2) IU/L, 191.5 (39.2) IU/L, and 159.3 (23.6) IU/L, respectively (p<0.001, for each pair, $\eta^2$=0.328).

There was no correlation between LDH levels and platelet counts in CG (p=0.406), but there was a moderate inverse correlation between LDH level and platelet count in patients with ITP (p<0.001, r=-0.410) with whom the platelet

count explaining 17% of the variation in LDH level (Table 2). ITP patients were grouped according to the treatment requirement, and only in the ITP-T group, a correlation was found between the patient's platelet counts and LDH levels (p=0.009, r=0.23). No correlation was found in the ITP-WT group.

LDH levels were 246 (71) IU/L and 199 (51) IU/L in ITP patients with and without any bleeding symptoms respectively (p<0.001, 95% CI, between -0.11 and -0.06) (Table 3). Multivariate linear regression was run to execute the effect of platelet counts and bleeding on LDH levels. There were homoscedasticity and normality of the residuals. Platelet counts statistically significantly predicted LDH levels, F(2.223) =24.29 (p<0.001), accounting for 17.9% of the variation in LDH levels with adjusted $R^2$=17.1%, a medium-size effect. There was no effect of bleeding on LDH levels (p=0.092).

An independent sample t-test and Welch t-test were run for comparison of patients with ITP who were treated with only CS or CS&IVIG, which are summarized in Table 4. Before treatment, platelet counts of patients who were treated with CS or CS plus IVIG was 14,821 (9184)/μL and 5.688 (5.201)/μL, respectively (p<0.001); LDH levels of patients before treatment were 230 (67) IU/L and 264 (76) IU/L (p=0.041). After treatment, LDH levels of patients who were treated with CS or CS plus IVIG were 219 (68) IU/L and 237 (51) IU/L, respectively (p=0.085). Comparing the response of patients in each group, 67 patients (87.1%) had a response [with a complete response in 35 patients (45.5%)] in the CS group, and 31 patients (75.6%) response [with a complete response in 21 patients (51.2%)] in the CS plus IVIG group (p=0.108). Ten patients in both groups did not respond to the treatments.

We compared pre-treatment and post-treatment LDH levels and platelet counts of the ITP-T group. The mean pre-treatment LDH levels of patients who were treated were 241.8 (72.2) IU/L, and post-treatment LDH levels were 225.7 (63.6) IU/L (p=0.006). Mean pre-treatment and post-treatment platelet counts were 11,770 (9.140)/microL and 135,160 (123,848) /microL, respectively (p<0.001).

Changes in the LDH levels according to the response (pre-and post-treatment) in the ITP-T group were -6.7 (20.2) IU/L, -15.3 (7.9) IU/L, and -21.6 (8.6) IU/L in patients with no response, response, and complete response, respectively. There was no statistically significant difference due to response to the treatment (p>0.05).

## Discussion

The LDH activity of platelets in humans was first described in 1954 (5). Although it was shown in the 1960s that platelets have elevated LDH activity, little attention has been paid to this issue since then.

To our knowledge, only one study on this subject was published; this study compared the LDH levels of 182 ITP

**Table 1. Laboratory parameters of ITP groups (with and without treatment) and control group**

| | ITP - T | ITP - WT | ITP - all | CG | p-value |
|---|---|---|---|---|---|
| WBC (/microL) | 7750 (2420) | 6490 (2050) | 7177 (2345) | 7181 (1554) | **<0.001** |
| Hgb (g/dL) | 13.4 (1.6) | 13.4 (1.4) | 13.4 (1.5) | 13.8 (1.6) | 0.959 |
| PLT (/microL) | 11777 (9141) | 63629 (19424) | 35500 (29900) | 244400 (56600) | **<0.001** |
| MPV (fl) | 12 (2.1) | 10.8 (2.2) | 11.4 (2.6) | 9.4 (1.4) | **<0.001** |
| LDH (IU/L) | 241 (72) | 191 (39) | 218 (64) | 159 (23) | **<0.001** |

ITP-T: ITP patients with treatment indication, ITP-WT: ITP patients without treatment indication, CG: Control group, WBC: White blood cell, Hgb: Hemoglobin, PLT: Platelet, MPV: Mean platelet volume, IU: International unit, g: Gram, microL: Microliter, dL: deciliter, L: Liter, fl: Femtoliter, p-value ⩽0.05: Statistically significant. All significant p-values are in bold

**Table 2. Correlation between LDH, platelet count, and MPV in patients diagnosed with ITP**

| | LDH | PLT | MPV |
|---|---|---|---|
| **LDH** | | **p<0.001** | **p=0.013** |
| | | r=-0.410 | r=0.166 |
| **PLT** | **p<0.001** | | **p<0.001** |
| | r=-0.410 | | r=-0.282 |
| **MPV** | **p=0.013** | **p<0.001** | |
| | r=0.166 | r=-0.282 | |

LDH: Lactate dehydrogenase, PLT: Platelet, MPV: Mean platelet volume, p-value ⩽0.05: Statistically significant. All significant p-values are in bold

patients and 241 healthy blood donors, and mean LDH levels were determined as 215 U/L and 155 U/L, respectively (p<0.001). The authors found an inverse correlation between LDH level and platelet count and also demonstrated that the correlation got stronger when they lowered the platelet count threshold (6). In our study, we found that LDH levels of patients with ITP and CG were 218 (64) IU/L, and 159 (23) IU/L, respectively (p<0.001). There was no correlation between LDH levels and platelet counts in CG (p=0.406); but there was a moderate correlation between LDH levels and platelet count (p<0.001, r=-0.410) in patients with ITP similar to the aforementioned study.

Our study demonstrated that there is an inverse relationship between LDH level and platelet count. As expected, we observed the highest LDH value in the group with the lowest platelets. There was an inverse correlation between the platelet count and LDH levels only in the ITP-T group (p=0.009); no correlation was found in the ITP-WT and CG. While there was no correlation between LDH and platelet count in the ITP-WT group, a statistically significant increase in LDH level was observed compared to the CG. The reason for the lack of correlation between LDH level and platelet counts in the ITP-WT group may be less platelet destruction.

We found it worthy of investigation that, in patients with bleeding symptoms, LDH levels may increase due to hemolysis of extravascular erythrocytes, and therefore we compared laboratory parameters of ITP patients with or without bleeding symptoms. As a result of multivariate linear regression analysis, we found that bleeding did not affect LDH levels, possibly due to the difference in platelet count in the two groups (p=0.092). There may be an increase in LDH levels due to massive bleeding and hematomas, but since none of the patients have such bleeding, existing differences developed only concerning the platelet count.

Although a slight difference was observed between pre-treatment and post-treatment LDH levels, that difference was considered statistically significant. The changes in the LDH levels according to response were as: -6.7 (20.2) IU/L, -15.3 (7.9) IU/L, and -21.6 (8.6) IU/L in patients with no response, response, and complete response, respectively; this decrease was not statistically significant (p>0.05). We also showed that the highest amount of LDH reduction occurred in patients with the best response, but it was

**Table 3. Comparison of ITP patients' laboratory parameters according to bleeding symptoms**

| | | | | Confidence interval | |
|---|---|---|---|---|---|
| | **Bleeding (n=94)** | **Non bleeding (n=132)** | **p-value** | **Lower** | **Upper** |
| WBC (/microL) | 7560 (2240) | 6905 (2390) | **0.026** | -7.61 | -0.49 |
| Hgb (g/dL) | 13.4 (1.6) | 13.4 (1.4) | 0.992 | -0.40 | 0.40 |
| PLT (/microL) | 12126 (14841) | 52220 (26556) | **<0.001** | 106 338 | 137 376 |
| MPV (fl) | 12.2 (2.1) | 11 (2.2) | **<0.001** | -0.25 | -0.08 |
| LDH (IU/L) | 246 (71) | 199 (50) | **<0.001** | -0.11 | -0.06 |

WBC: White blood cell, Hgb: Hemoglobin, PLT: Platelet, MPV: Mean platelet volume, LDH: Lactate dehydrogenase, microL: Microliter, fl: Femtoliter, IU: International unit, L: Liter, g: Gram, dL: Deciliter, p-value ≤0.05: Statistically significant. All significant p-values are in bold

**Table 4. Comparison of first-line treatment strategies in ITP patients**

| | | | | Confidence interval | |
|---|---|---|---|---|---|
| | **Steroid (n=82)** | **Steroid & IVIG (n=41)** | **p-value** | **Lower** | **Upper** |
| PLT before treatment (/microL) | 14821 (9184) | 5688 (5201) | **<0.001** | 0.32 | 0.58 |
| PLT after treatment (/microL) | 136410 (124966) | 132837 (123256) | 0.190 | -0.72 | 0.35 |
| Change in PLT (/microL) | 121852 (125295) | 127149 (123305) | 0.975 | -0.20 | 0.19 |
| LDH before treatment (IU/L) | 230 (67) | 264 (76) | **0.012** | -0.108 | -0.013 |
| LDH after treatment (IU/L) | 219 (68) | 237 (51) | 0.085 | -1.47 | 0.09 |
| Change in LDH (IU/L) | -11 (58) | -26 (75) | 0.264 | -9.59 | 39.9 |
| Hgb before treatment (g/dL) | 13.4 (1.5) | 13.5 (1.9) | 0.666 | -0.74 | 0.47 |
| Hgb after treatment (g/dL) | 13.4 (1.6) | 13.1 (1.7) | 0.325 | -0.31 | 0.93 |
| Change in Hgb (g/dL) | 0.04 (1.1) | -0.4 (1.7) | 0.131 | -0.14 | 1.05 |

IVIG: Intravenous immune globulin, PLT: Platelet, LDH: Lactate dehydrogenase, Hgb: Hemoglobin, microL: Microliter, L: Liter, IU: International unit, dL: Deciliter, g: Gram, p-value ≤0.05: Statistically significant. All significant p-values are in bold

not statistically significant. LDH levels were found to be higher after treatment compared to the CG, and this may be due to the continual underlying platelet destruction despite platelet values reaching safe levels. According to this study's primary and secondary objectives, we assessed LDH levels in the early response period. Different results could be obtained if the LDH value is evaluated in a later period of the disease.

As a result, we observed that the LDH levels in ITP patients were higher than in the CG and slightly decreased after treatment, but they could not reach the LDH levels of the CG. The main reason for the low platelet count in ITP is the accelerated platelet clearance due to macrophages in the spleen causing autoantibody-mediated platelet destruction. However, this is not the only pathophysiological mechanism of the disease. Some patients have moderately impaired platelet production due to antibody and/or cytotoxic T cell-mediated megakaryocytic damage without platelet destruction (9). During the maturation process of megakaryocytes, GP Ib/IX and GPIIb/IIIa expression increase on their surface. Anti-platelet autoantibodies against GP Ib/IX and/or GP IIb/IIIa are expected to attack megakaryocytes such as platelets. *In vitro* studies have shown that autoantibodies against anti-GP Ib/IX and GP IIb/IIIa reduce megakaryocyte production and maturation in ITP patients (10,11). Yang et al. (12) showed that the number of megakaryocytes increased in ITP, but that megakaryocyte maturation was impaired and thrombocyte release decreased. They also showed inhibition of cell apoptosis in immature megakaryocytes (12). Based on the complex pathophysiological mechanism of ITP, we can postulate as to why the LDH level does not increase at the time of diagnosis in some of our patients: Presumably, the pathophysiology that caused ITP in some patients differs in the way of platelet destruction.

Hemolysis is a complication that may develop after high-dose IVIG therapy (13). This situation may cause an increase in LDH levels post-treatment. We did not observe an increase in the mean LDH level of our patients who received IVIG; we found a decrease of 24 IU/L in the mean LDH level after IVIG treatment. We could not detect a significant difference between the mean hemoglobin values before and after treatment in the group of patients who received IVIG; 13.5 g/dL and 13.1 g/dL, respectively (p=0.130). Based on these findings, we can estimate that our patients did not have any clinically significant hemolysis after IVIG treatment. This finding is also consistent with Wilson et al. (14) showing that hemolysis developing after IVIG treatment is usually not clinically significant.

There are five known isoenzymes of LDH, and these isoenzymes have a tissue-specific distribution (15). Schneider et al. (16) showed that isoenzymes 2 and 3 were more dominant than other LDH isoenzymes in platelets. Although we saw an increase in LDH levels in ITP patients, we couldn't pinpoint which LDH isoenzyme was the source of this alteration due to the retrospective nature of our study. If we had analyzed the LDH isoenzyme test, we could perhaps have discovered more future guiding results.

**Study Limitations**

Several limitations of our study deserve to be mentioned. The study was retrospective, and due to the lack of information on this subject in the literature, we could not compare all our results to previous studies. It was not possible to evaluate LDH levels in a later stage of the disease after treatment in our patient group.

**Conclusion**

Although it was within the range of normal laboratory reference values, the LDH level of ITP patients was observed to be significantly higher than the CG. There was an inverse correlation between platelet counts and LDH levels in the ITP-T group. It was observed that the presence of bleeding did not affect the LDH levels. A small difference was observed between pre-treatment and post-treatment LDH levels and was found to be statistically significant. We observed that there was no clinically significant hemolysis in our patients after IVIG treatment. With future LDH isoenzyme studies, the isoenzyme of the rising LDH enzyme may be determined and used as a marker in the diagnosis and follow-up of ITP.

**Ethics**

**Ethics Committee Approval:** Ethics committee approval was obtained for this retrospective multicenter study [Local Ethics Committee of İstanbul Medeniyet University (date: 24/03/2021, decision no: 2021/0216)].

**Informed Consent:** Due to the retrospective nature of data collection, we could not obtain informed consent from the participants.

**Peer-review:** Externally peer-reviewed.

**Authorship Contributions**

Surgical and Medical Practices: E.K., S.S., M.Y., H.E.G., M.A., M.K.K., Concept: E.K., S.S., M.Y., T.E., H.E.G., I.E.Ö., E.Ö., M.A., M.K.K., Design: E.K., S.S., M.Y., H.E.G., I.E.Ö., E.Ö., M.A., M.K.K., Data Collection or Processing: E.K., S.S., M.Y., Analysis or Interpretation: E.K., S.S., M.Y., T.E., I.E.Ö., E.Ö., Literature Search: E.K., T.E., I.E.Ö., Writing: E.K., T.E., I.E.Ö., E.Ö.

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