AHOT | Acta Haematologica Oncologica Turcica

Acta Haematol Oncol Turc 2025;58(2):136-142

Original Article

DOI: 10.4274/ahot.galenos.2025.2025-4-4

The Retrospective Analysis of Patients with Primary Immune Thrombocytopenia: The Associated Factors with Bleeding and The Factors with Treatment Response

Turhan Köksal, Mustafa Yılmaz

Karadeniz Technical University Faculty of Medicine, Department of Hematology, Trabzon, Türkiye

ABSTRACT

Aim: Immune thrombocytopenic purpura (ITP) is an acquired autoimmune disorder characterized by isolated thrombocytopenia and is twice as common in women as in men. Although severe bleeding is rare, identifying risk factors for bleeding can guide treatment decisions. This study aimed to evaluate the relationships between age, platelet count, hemoglobin level, mean platelet volume (MPV), and bleeding in ITP patients. Additionally, the impact of variables such as age, gender, platelet count, bone marrow megakaryocyte count, MPV, intravenous immunoglobulin (IVIG) response (in splenectomized patients), and remission duration on treatment response was investigated.

Methods: We retrospectively analyzed the medical records of 101 patients (81 females, 20 males) diagnosed with ITP and followed at the Hematology Outpatient Clinic of Karadeniz Technical University Farabi Hospital between 2008 and 2011. Statistical analysis was performed to assess the relationship between clinical/laboratory variables and bleeding, first-line treatment response, and splenectomy outcomes.

Results: Low platelet count and elevated MPV were significantly associated with bleeding ($p<0.05$). MPV elevation was also a favorable factor in predicting first-line treatment response. Among splenectomized patients, a positive response to IVIG was associated with better splenectomy outcomes ($p<0.05$). Furthermore, longer remission durations were significantly correlated with favorable splenectomy responses ($p<0.01$).

Conclusion: MPV may serve as a useful marker for both bleeding risk and treatment response in ITP. A favorable IVIG response may predict splenectomy success. The association between remission duration and splenectomy response adds valuable insight to individualized management strategies in ITP.

Keywords: Immune thrombocytopenia, mean platelet volume, splenectomy

Introduction

Immune (idiopathic) thrombocytopenic purpura (ITP) is an acquired autoimmune disease characterized by isolated thrombocytopenia due to accelerated platelet destruction and impaired platelet production. It has an incidence of 40-160/1,000,000 and is twice as common in women as in men. Although rare, severe bleeding may occur in patients with platelet counts below 20-30x10^9/L. Despite low platelet counts in patients with ITP, the low rate of severe bleeding may be explained because the available platelets are more functional despite their low number. It has been found that advanced age and a history of previous bleeding are risk factors for severe bleeding in patients with ITP [1,2]. Mean platelet volume (MPV) is higher when accompanied by young, larger than normal platelets. High MPV indicates the appearance of platelets which are thought to be more active in terms of hemostasis-providing effect compared to young-large volume and normal platelets. In this study, we aimed to investigate the relationship between age, hemoglobin level, platelet count, and MPV and severe bleeding in patients with ITP.

In this study, we aimed to retrospectively analyze the factors affecting treatment response in patients treated with steroid, intravenous immunoglobulin (IVIG), splenectomy, and rituximab. For this purpose, it was planned to investigate the effects of age, sex, peripheral blood platelet count, bone

Address for Correspondence: Turhan Köksal MD, Karadeniz Technical University Faculty of Medicine, Department of Hematology, Trabzon, Türkiye
E-mail: dr.turhankoksal@hotmail.com **ORCID ID:** orcid.org/0009-0002-7955-2838

Received: 13.04.2025 **Accepted:** 19.07.2025 **Publication Date:** 13.08.2025

Cite this article as: Köksal T, Yılmaz M. The retrospective analysis of patients with primary immune thrombocytopenia: the associated factors with bleeding and the factors with treatment response. Acta Haematol Oncol Turc. 2025;58(2):136-142

marrow megakaryocyte count, MPV, response to IVIG (in splenectomized patients), and disease duration on treatment response.

Methods

The study included 101 patients, of whom 81 were female and 20 were male. Our study was conducted by retrospectively analyzing the files of patients who were examined and treated, with the diagnosis of ITP, in the Hematology Outpatient Clinic of Karadeniz Technical University Faculty of Medicine Farabi Hospital between 2008 and 2011. The study was conducted according to the principles of the Declaration of Helsinki, and approval was obtained from the Ethics Committee of Karadeniz Technical University Faculty of Medicine (decision no: 2012/95, date: 23.07.2012).

Exclusion criteria for ITP patients:

- Physical examination is characterized by features other than bleeding findings,

- Abnormalities in peripheral smear and complete blood count other than thrombocytopenia,

- Hepatitis B surface antigen, hepatitis C virus (HCV), human immunodeficiency virus (HIV), antinuclear antibody (ANA), anti-double stranded DNA be positive,

- Abnormalities in chest radiography,

- Impairment in thyroid function tests and complete urine analysis,

- The emergence of findings in bone marrow aspiration and biopsy that exclude ITP.

In this study, we planned to investigate the relationship between age, platelet count, hemoglobin level, MPV, and bleeding in patients with ITP. We planned to investigate the effects of age, gender, peripheral blood platelet count, bone marrow megakaryocyte count, MPV, response to IVIG (in splenectomized patients), and duration of remission on the next treatment response in relapsed patients.

Treatment Response Criteria

In accordance with the American Society of Hematology (ASH) 2019 guidelines, treatment response was categorized as follows: complete response (CR): platelet count ≥100×10^9/L and no bleeding. Response: platelet count ≥30×10^9/L and at least a twofold increase from baseline without bleeding. No response: platelet count <30×10^9/L or less than a twofold increase from baseline, or manifestation of bleeding. These criteria were adopted to evaluate the first-line and second-line treatment efficacy in our study cohort.

Statistical Analysis

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) version 17.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean ± standard deviation, and categorical variables as number and percentage. Group comparisons were conducted using the independent samples t-test for continuous variables. A p value of less than 0.05 was considered statistically significant.

Results

Eighty-one female and 20 male patients were included in our study. The mean age of patients with no or mild bleeding (n=82) was 43±16 years. The mean age of patients with moderate or severe bleeding (n=19) was 49±21 years (p=0.29). The platelet count was 40469±32160 in patients with no or mild bleeding and 16900±12485 in patients with moderate or severe bleeding (p=0.001) ; a significant difference was found (Figure 1). MPV mean value was 10.1±1.4 in patients with no or mild bleeding and 8.7±1.3 in patients with moderate or severe bleeding (p=0.001). A significant difference was found (Figure 2). The mean hemoglobin value was 13.2±1.6 in patients with no or mild bleeding and 12.8±1.6 in patients with moderate or severe bleeding (p=0.34) (Table 1).

Treatment was indicated in 65 of 101 patients. Among the 65 patients with treatment indication, 31 patients received

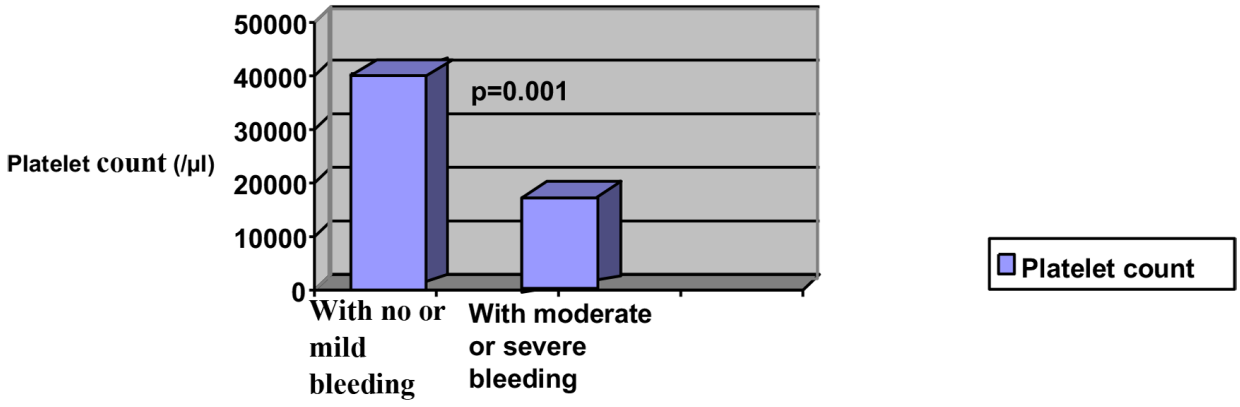

Figure 1. Relationship between platelet count and bleeding in ITP patients
ITP: Immune thrombocytopenic purpura, MPV: Mean platelet volume

only steroid treatment (1 mg/kg methylprednisolone), and 16 patients received only IVIG treatment (1 g/kg/day for 2 days). Eighteen patients received IVIG treatment together with steroids. Treatment responses of the patients were analyzed. Of the 49 patients who received steroids (steroid only and steroid + IVIG), 29 responded, while 20 did not respond. Of 34 patients who received IVIG (IVIG only and steroid + IVIG), 21 responded and 13 were non-responders. Overall, 41 patients responded to first-line treatment, while 24 patients were non-responders. The mean age of patients who did not respond to first-line treatment was 45±20 years, while the mean age of patients who responded was 45±17 years (p=0.9). The mean platelet count of first-line treatment non-responders was 16,583±1360, while the mean platelet count of responders was 16,820±1600 (p=0.9). The mean number of bone marrow megakaryocytes in first-line treatment-naive patients was 6±2.6, while the mean number of bone marrow megakaryocytes in responders was 6.3±2.1 (p=0.5). The MPV was found to be 10±1.4/fL in first-line treatment responders and 8.8±1.4/fL in non-responders (p=0.002) (Table 2, Figure 3).

Splenectomy was performed as second-line treatment. Of the 28 patients who underwent splenectomy by laparotomy, 21 had a complete response (CR) (71%), while 8 (29%) were non-responders. There was no significant difference between responders and non-responders in terms of platelet count, age, and MPV (Table 3). Since the existence of an IVIG response before splenectomy may indicate a good response to the procedure, we examined the response status to IVIG treatment

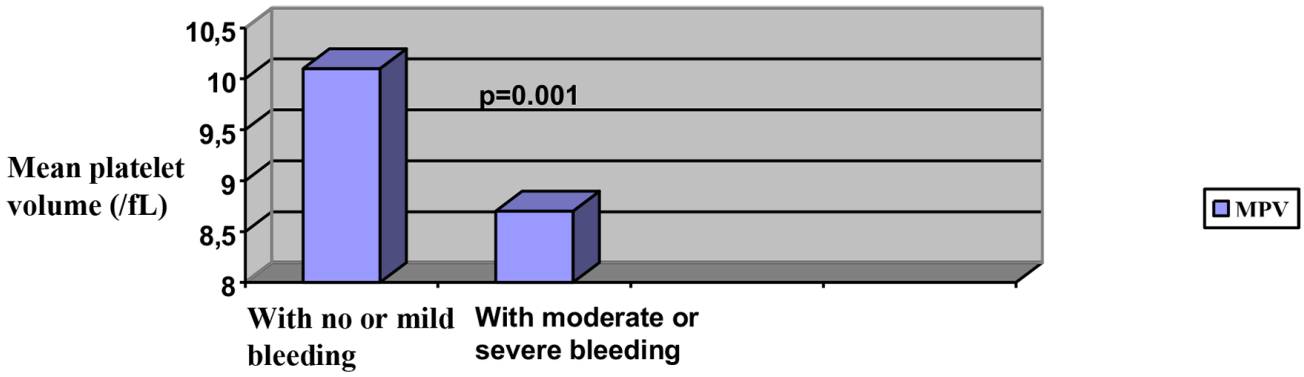

Figure 2. Relationship between MPV and bleeding in ITP patients
ITP: Immune thrombocytopenic purpura, MPV: Mean platelet volume

Table 1. The associated factors with bleeding in ITP patients

	With no or mild bleeding (n=82)	With moderate or severe bleeding (n=19)	p
Age	43±16	49±21	0.29
Platelet count	40469±32160	16900±12485	0.001
MPV	10.1±1.4	8.7±1.3	0.001
Hemoglobin	13.2±1.6	12.8±1.6	0.34

ITP: Immune thrombocytopenic purpura, MPV: Mean platelet volume

Table 2. The associated factors with first line treatment response in ITP patients

	Non-responders (n=24)	Responders (n=41)	p
Age	45±20	45±17	0.9
Platelet count	16583±1360	16820±16000	0.9
Megakaryocytes	6±2.6	6.3±2.1	0.5
MPV	8.8±1.4	10±1.4	0.002

ITP: Immune thrombocytopenic purpura, MPV: Mean platelet volume

Table 3. Factors associated with splenectomy treatment response in ITP

	Non-responder (n=8)	Responder (n=21)	p
Age	46±21	44±17	NS
Platelet count	22222±19227	14250±7949	NS
MPV	9.7±0.97	9.5±1.85	NS
Duration of remission	200±126	113±101	0.04

ITP: Immune thrombocytopenic purpura, MPV: Mean platelet volume, NS: Not significant

of patients who underwent splenectomy. It was found that 11 of 13 patients who received IVIG as first-line treatment before splenectomy and were found to be non-responders underwent splenectomy as second-line treatment. Of these 11 patients, 5 (45.5%) responded while 6 were non-responders. Splenectomy was performed as second-line treatment in 5 of 21 patients, who received IVIG as first-line treatment before splenectomy and responded to this treatment. All of these 5 (100%) patients responded to splenectomy (p=0.93).

The mean duration of remission was 176±124 (25-500) days in patients who received first-line treatment, and had a treatment response, but who were then indicated for second-line treatment due to relapse. The mean duration of remission after first-line treatment was 200±126 days in patients who received second-line treatment and had a treatment response, and 113±101 days in those patients who had no treatment response (p=0.04) (Figure 4).

Discussion

Our results are in agreement with recent findings in the literature. Ahmad et al. [3] emphasized the bleeding risks associated with ITP, while Ghanima et al. [4] reviewed the clinical efficacy and safety of thrombopoietin receptor agonists. Provan et al. [5] discussed predictors of bleeding severity, and Cooper and Ghanima [6] proposed updated therapeutic frameworks. Consistent with the ASH 2019 guidelines and these contemporary studies, MPV has emerged as a clinically relevant biomarker not only for platelet activity, but also as a predictor of bleeding tendency and treatment response in patients with ITP. Our data showing an inverse correlation between MPV and bleeding severity, and a positive correlation with treatment response, support this position.

In this study, we analyzed the factors affecting bleeding and treatment response in patients with ITP. Of the 101 patients included in our study, 81 (80.2%) were female; 20 (19.8%) were male and the P/E ratio was found to be 4.05. Adult ITP is

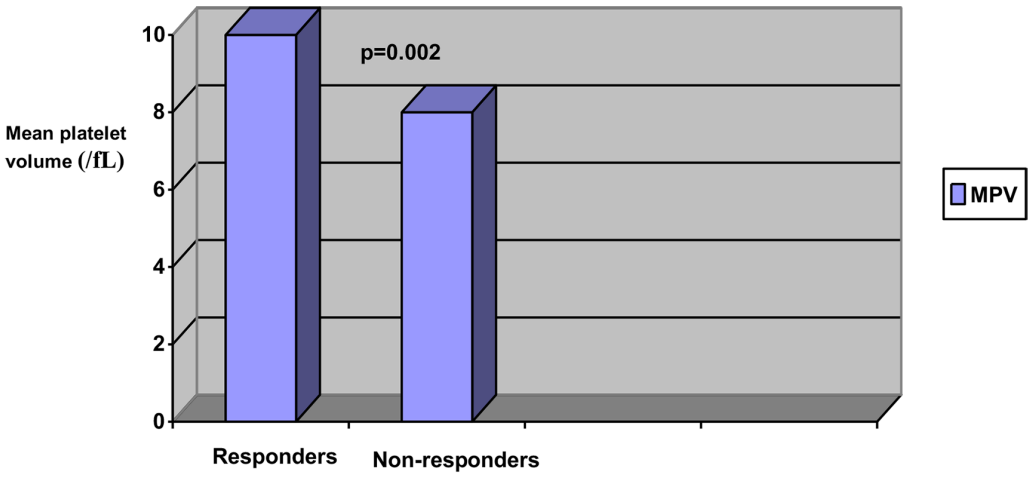

Figure 3. Relationship between MPV and treatment response in ITP patients
ITP: Immune thrombocytopenic purpura, MPV: Mean platelet volume

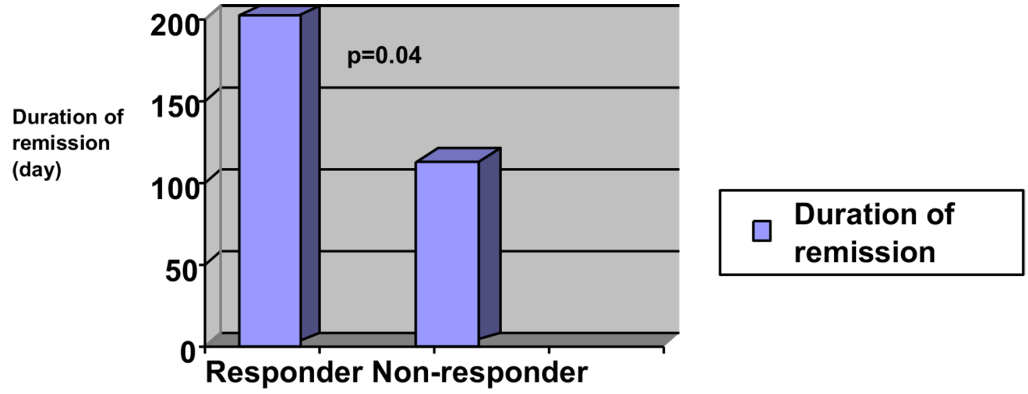

Figure 4. Relationship between splenectomy response and remission duration in ITP patients
ITP: Immune thrombocytopenic purpura

reported more common in women in studies and guidelines,. In a series of 162 cases (122 females, 40 males) conducted by Yenerel et al. [7] from İstanbul University, the F/M ratio was found to be 3/1. In a study conducted by Reid [8] in the United States of America between 1995 and 2001, the F/M ratio was found to be 4/1. In a retrospective study conducted by Kaya et al. [9] in 2011 and covering the years 1993-2009, the F/M ratio was found to be 3.1 in 110 patients, 83 of whom were female and 27 of whom were male. In a retrospective study conducted at Dicle University in 2012, in which 109 patients with splenectomy were examined, 88 (80.7%) of the patients were female and 21 (19.3%) were male. The M/F ratio was found to be 4.19 [10]. ITP was reported to be observed more frequently in females, ranging from two to four times, according to the literature, and our study was found to be compatible with the literature in this respect.

Of the patients included in our study, 82 (81.2%) had no/light bleeding and 19 (18.8%) had moderate/severe bleeding. In a series of 162 cases by Yenerel et al. [7] from İstanbul University, the rate of patients with moderate/severe bleeding was 17.3% and the rate of patients with no/light bleeding was 82.7%, which was similar to those in our study. In our study, age was examined among the factors affecting bleeding, and the median age was found to be 43±16 years in patients with no/mild bleeding and 49±21 years in patients with moderate/severe bleeding. Although the median age of patients with mild/no bleeding was lower, there was no significant statistical difference in terms of age between patients with mild/no bleeding and those with moderate/severe bleeding. There are publications showing that the risk of bleeding increases with increasing age. In one study, the 5-year fatal bleeding risk predicted for patients over the age of 60 years with a platelet count below $30x10^9$/L was 48%, while this rate was 2.2% in patients younger than 40 years, [11]. In our study, a statistically significant difference was found between the two groups in terms of platelet count among the factors affecting bleeding. The platelet count was found to be 40,469±32,160 in patients with no/mild bleeding and 16,900±12,485 in patients with moderate/severe bleeding (p=0.001). Accordingly, platelet count is significantly lower in patients with moderate/severe bleeding. In the ASH 2011 ITP guideline, it was stated that the increase in bleeding risk became evident below 20 or $30x10^9$/L in different studies, and the treatment limit was $30x10^9$/L, although there was no definite limit [12]. The statistical difference identified in our study was found to be compatible with the literature.

When we analyzed MPV, one of the factors affecting bleeding, we found a significant difference between the two groups as MPV: 10.1±1.4/fL in patients with no/light bleeding and MPV: 8.7±1.3/fL in patients with moderate/severe bleeding (p=0.001). High MPV indicates platelets are thought to be more active in terms of their hemostasis effect compared to young, large-volume, and normal platelets. This may indicate that high MPV is a protective factor in terms of bleeding risk. When we looked at hemoglobin levels among the possible factors that may increase the risk of bleeding, we found that they were not associated with the risk of bleeding in patients with ITP.

One hundred and eleven patients (81.2%) received steroids, IVIG, or both as first-line treatment. Twenty patients (19.8%) were followed up without treatment. In our study, 29 (59%) of 49 patients who received steroid treatment responded. In a study by Kaya et al. [9], 11 of 110 patients (10%) were followed up without treatment. The results of the study were similar to those of previous studies in terms of treatment-free follow-up. In the study by Kaya et al. [9], 71.7% of the patients who were started on steroids responded, while 28.2% were found to be unresponsive. Aydoğdu et al. [13], obtained a CR in 34 (58%) of 62 chronic ITP patients, with standard 1 mg/kg corticosteroid treatment. In a study conducted on 125 adult patients with ITP, approximately 40% achieved a permanent response lasting 2.5 years with steroid treatment [14]. Mazzucconi et al. [15] summarized 2 cohort studies and reported high response rates with dexamethasone. Our study is compatible with the literature in this respect.

When we analyzed the factors affecting first-line treatment, no significant difference was found between responders and non-responders in terms of age, platelet count, and megakaryocyte count. A statistically significant difference was found with a mean MPV of 10±1.4 fL in responders and 8.8±1.4 fL in non-responders (p=0.002). No study analyzing the effect of MPV elevation on treatment response was found in the available literature. Elevated MPV indicates the increase in the volume of platelets in the peripheral blood and may be an indicator of the high compensatory capacity of the bone marrow. Therefore, elevated MPV may be a positive marker for first-line treatment response.

We examined the second-line treatment responses of the patients. We found that 21 (71%) of 28 patients who underwent splenectomy through the laparotomy method had a CR and 8 were non-responders. We could not detect a significant difference in terms of platelet count, age, and MPV between patients who had a CR to secondary treatment and non-responders. Numerous studies have shown that two-thirds of the patients usually responded within days to splenectomy [12]. Parameters to predict splenectomy success have been studied, and it was observed that young age may serve as a preliminary indicator. In our study, although the age of patients who responded to splenectomy was slightly lower, no statistically significant difference was found. In a study by Önder et al. [10], splenectomy was performed in 109 patients and 82.6% of these patients had CR, and 12.8% had partial response. One patient (0.9%) died. In this study, a very high response rate was achieved when the literature was considered. In a study by McMillan [16], the CR rate to splenectomy was found to be 70%. In a study by Kaya et al. [9], the response rate to splenectomy was found to be 75%. Our study was consistent with the literature in terms of response rate to splenectomy. We investigated whether demonstrating a response to IVIG treatment before splenectomy is an indicator of a good response to splenectomy. Some studies in the literature indicate that IVIG response is a positive indicator

for splenectomy response [17,18]. However, other studies indicate that a response after IVIG is not an indicator that remission will be achieved with splenectomy [19-21]. In our study, all 5 patients (100%) with an IVIG response achieved a CR to splenectomy, whereas only 5 of 11 patients (45.5%) without an IVIG response did so . However, this difference was not statistically significant in our study, probably due to the insufficient number of patients (p=0.93). There are no data in the literature on the effect of time to relapse on splenectomy response. In our study, although response rates to splenectomy were higher in patients with late relapse after first-line treatment, age still seems to be the most objective criterion for response to splenectomy.

Study Limitations

This study has some limitations. Its retrospective and single-center design may limit the generalizability of the results and introduce selection bias. Due to the nature of retrospective data, not all confounding variables could be controlled. The relatively small sample size, especially in subgroups such as splenectomized patients, may have reduced the statistical power. Also, the absence of long-term follow-up data prevents assessment of sustained treatment outcomes.

Conclusion

This retrospective analysis suggests that low platelet count and decreased MPV are significantly associated with increased bleeding risk in patients with ITP. Furthermore, elevated MPV may serve as a predictive marker for favorable response to first-line therapy. Although no statistically significant association was found between pre-splenectomy IVIG response and splenectomy outcomes, a trend toward improved response in IVIG responders was observed. The observed correlation between longer remission duration and splenectomy success warrants further investigation. These findings highlight the potential clinical utility of MPV as a prognostic parameter in both bleeding risk stratification and therapeutic response prediction in ITP.

Ethics

Ethics Committee Approval: The study was conducted according to the principles of the Declaration of Helsinki, and approval was obtained from the Ethics Committee of Karadeniz Technical University Faculty of Medicine (decision no: 2012/95, date: 23.07.2012)

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: T.K., Concept: T.K., Design: T.K., M.Y., Data Collection or Processing: T.K., Analysis or Interpretation: T.K., M.Y., Literature Search: T.K., M.Y., Writing: T.K., M.Y.

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

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Rodeghiero F, Stasi R, Gernsheimer T, et al. Standardization of terminology, definitions and outcome criteria in immune thrombocytopenic purpura of adults and children: report from an international working group. Blood. 2009;113:2386-2393.
2. Toltl LJ, Arnold DM. Pathophysiology and management of chronic immune thrombocytopenia: focusing on what matters. Br J Haematol. 2011;152:52-60.
3. Ahmad SA, Liu O, Feng A, et al. Prevalence and characteristics of acute ischemic stroke and intracranial hemorrhage in patients with immune thrombocytopenic purpura and immune thrombotic thrombocytopenic purpura: a systematic review and meta-analysis. Neurol Res Pract. 2025;7:19.
4. Ghanima W, Cooper N, Rodeghiero F, Godeau B, Bussel JB. Thrombopoietin receptor agonists: ten years later. Haematologica. 2019;104:1112-1123.
5. Provan D, Arnold DM, Bussel JB, et al. Updated international consensus report on the investigation and management of primary immune thrombocytopenia. Blood Adv. 2019;3:3780-3817.
6. Cooper N, Ghanima W. Immune thrombocytopenia. N Engl J Med. 2019;381:945-955.
7. Yenerel MN, Atamer T, Ayer M, et al. Clinical follow-up and treatment response of the 162 patients with chronic ıdiopathic thrombocytopenic purpura. J Ist Faculty Med. 2007;70:6-10.
8. Reid MM. Chronic idiopathic thrombocytopenic purpura: incidence, treatment, and outcome. Arch Dis Child. 1995;72:125-128.
9. Kaya M, Demir C, Esen R, Atay A. Kronik idiopatik trombositopenik purpuralı olgularımız. Van Tıp Dergisi. 2011;18:141-146.
10. Önder A, Kapan M, Gül M, et al. Splenectomy in patients with idiopathic thrombocytopenic purpura: Analysis of 109 cases. Dicle Med J. 2012;39:49-53.
11. Cohen YC, Djulbegovic B, Shamai-Lubovitz O, Mozes B. The bleeding risk and natural history of idiopathic thrombocytopenic purpura in patients with persistent low platelet counts. Arch Intern Med. 2010;160:1630-1638.
12. Neunert C, Lim W, Crowther MA, et al. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. Blood. 2011;117:4190-4207.
13. Aydoğdu İ, Tayfun E, Akan H, et al. Clinic Course of idiopathic thrombocytopenic purpura: results of 62 patients. Türkiye Tıp Dergisi. 1997;2:73-76.
14. Cheng Y, Wong RS, Soo YO, et al. Initial treatment of ımmune thrombocytopenic purpura with high-dose dexamethasone. N Engl J Med. 2003;349:831-836.
15. Mazzucconi MG, Fazi P, Bernasconi S, et al. Therapy with high-dose dexamethasone (HD-DXM) in previously untreated patients affected by idiopathic thrombocytopenic purpura: a GIMEMA experience. Blood. 2007;109:1401-1407.
16. McMillan R. The pathogenesis of chronic immune (idiopathic) thrombocytopenic purpura. Semin Hematol. 2007;44 (1 Suppl 1):5-9.
17. Law C, Marcaccio M, Tam P, Heddle N, Kelton JG. High-dose intravenous immune globulin and the response to splenectomy in patients with idiopathic thrombocytopenic purpura. N Engl J Med. 1997;336:1494-1498.
18. Holt D, Brown J, Terrill K, et al. Response to intravenous immunoglobulin predicts splenectomy response in children with immune thrombocytopenic purpura. Pediatrics. 2003;111:87-90.

19. Bussel JB, Kaufmann CP, Ware RE, Woloski BM. Do the acute platelet responses of patients with immune thrombocytopenic purpura (ITP) to IV anti-D and to IV gammaglobulin predict response to subsequent splenectomy? Am J Hematol. 2001;67:27-33.
20. Ruivard M, Caulier MT, Vantelon JM, et al. The response to high-dose intravenous immunoglobulin or steroids is not predictive of outcome after splenectomy in adults with autoimmune thrombocytopenic purpura. Br J Haematol. 1999;105:1130-1132.
21. Radaelli F, Faccini P, Goldaniga M, et al. Factors predicting response to splenectomy in adult patients with idiopathic thrombocytopenic purpura. Haematologica. 2000;85:1040-1044.