Research Article / Araştırma Makalesi

Features and Relapse/Refractory Disease Risk Factors of Patients with Acquired Thrombotic Thrombocytopenic Purpura in the Western Mediterranean Region of Turkey

Türkiye'de Batı Akdeniz Bölgesindeki Edinsel Trombotik Trombositopenik Purpura Hastalarının Klinik Özellikleri ve Relaps/Refrakter Hastalık Risk Faktörleri

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Özet: Güncel yaklaşımlarla yanıt ve genel sağkalım oranları %90'ın üzerine çıkan trombotik trombositopenik purpurada (TTP), relapsı öngördürücü ve engelleyici parametrelerin önemi artmıştır. Bu açıdan Batı Akdeniz bölgesindeki immun TTP (iTTP) hastalarının klinik prezentasyonlarını, laboratuvar bulgularını, tedavilerini, tedavi yanıtlarını, relaps/refrakter hastalık durumlarını ve genel sağkalım oranlarını inceledik. Son 10 yılda tanı almış, iTTP tanılı 35 erişkin hasta çalışmaya dahil edildi. Hastaların ortanca takip süresi 46 (2-118) ay olup, 32 hasta (%91.4) hayattaydı. Birinci basamak tedavide 20 (%57.1) hastada klinik remisyon sağlanırken, relaps/refrakter hastalık nedeniyle ikinci sıra tedavi verilen 21 hastanın 20 sinde klinik remisyon sağlanmıştı. Birinci basamakta sadece 4 hastada kullanılan rituksimab ikinci sıra tedavi alan 14 hastaya verilmişti. Relapslar nedeni ile 5 hasta üç basamak, 2 hasta ise dört basamak tedavi almıştı. Yaş, cinsiyet, klinik prezentasyon, laboratuvar bulguları ve plazmaferez sayısı ile hem ADAMTS13 inhibitör düzeyleri hem de relaps/refrakter hastalık arasında bir ilişki yoktu. Geçmişte yaş, ADAMTS13 aktivasyonunun düşüklüğü, yüksek laktat dehidrogenaz gibi bazı parametreler prognostik olarak bildirilse de, %90'ın üzerinde yanıt ve genel sağkalım sağlayan güncel tedavi yaklaşımları ile bu değerlendirmelerin yeniden ele alınması gerektiğini düşünüyoruz. Çalışmamızda hem relaps/refrakter hastalık öngördürücü bir faktör hem de ADAMTS13 inhibitör düzeyinin etkilediği bir klinik yansıma saptamadık.
Anahtar Kelimeler: Trombotik mikroanjiyopati; Trombotik trombositopenik purpura, edinilmiş; ADAMTS13 proteini, insan

Abstract: The importance of parameters that predict and prevent relapse has increased in thrombotic thrombocytopenic purpura (TTP), where response and overall survival rates exceed 90% with current approaches. In this respect, we examined the clinical presentations, laboratory findings, treatments, treatment responses, states of relapsed/refractory disease and overall survival rates of immune-mediated TTP (iTTP) patients in the western Mediterranean region. 35 adult patients who were diagnosed with iTTP in the last 10 years were included in the study. The median follow-up period of the patients was 46 (2-118) months, and 32 patients (91.4%) survived. While clinical remission was achieved in 20 (57.1%) patients in the first-line treatment group, clinical remission was achieved in 20 of 21 patients who received second-line treatment due to relapsed/refractory disease. Rituximab, which was used as the first-line treatment in only 4 patients, was given to 14 patients as the second-line treatment. Due to relapse, 5 patients received third-line treatment, and 2 patients received fourth-line treatment. There was no relationship between age, sex, clinical presentation, laboratory findings, the number of plasmapheresis treatments, and either ADAMTS13 inhibitor levels or relapsed/refractory disease. Although several parameters, such as age, low ADAMTS13 activation, and high lactate dehydrogenase, have been reported to be prognostic in the past, we believe that these findings should be reconsidered with current treatment approaches that provide a greater than 90% response and overall survival. In our study, we did not detect either a predictive factor for relapsed/refractory disease or a clinical indicator influenced by ADAMTS13 inhibitor levels.
Keywords: Thrombotic microangiopathies; Thrombotic thrombocytopenic purpura, acquired; ADAMTS13 protein, human

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1. Introduction

Thrombotic thrombocytopenic purpura (TTP), which is among heterogenous group of diseases called thrombotic microangiopathies, is a multisystem disease that may be accompanied by neurological dysfunction, renal dysfunction and fever, as well as thrombocytopenia and hemolytic anemia. Due to the decrease/absence of the von Willebrand factor (vWf)-cleaving protease ADAMTS13 (A Disintegrin and Metalloproteinase with Thrombospondin-1 motifs; 13th member of the family), tissue ischemia and damage are caused by microthrombi in the microcirculation caused by vWf multimers that remain in the circulation (1). After TTP was first described in a fatal 16-year-old female patient in 1924, it was revealed in 1982 that vWf multimers were involved in its etiopathogenesis, and in 1998, this condition was shown to be caused by a protease deficiency that breaks down vWf multimers (2,3,4). While immune-mediated (acquired) TTP (iTTP) caused by an autoantibody against ADAMTS13 is mostly observed, congenital TTP (Upshaw–Schulman syndrome) caused by the absence of ADAMTS13 rarely occurs (5,6).

TTP is a rare hematological disease with a mean annual incidence of ~0.1 in children and ~3 new cases/million persons in adults (7,8). iTTP, which occurs in adults around the age of 40 on average, has been reported to be approximately twice as common in women (5,9). Although clinical symptoms and laboratory findings can suggest TTP, its definitive diagnosis is made by revealing the severe deficiency (activity <10%) of ADAMTS13, its only unique biological marker (10,11). On-time diagnosis is crucial because TTP is a medical emergency with a mortality rate of approximately 90% if left untreated (12). Due to increased awareness and on-time initiation of treatment, response rates to first-line treatment have increased to approximately 80-90% (13). In clinically suspected patients with evidence of thrombotic microangiopathy detected using PLASMIC and/or French scores, first-line treatment with therapeutic plasma exchange is recommended to remove autoantibodies and ultra-large vWf multimers and restore ADAMTS13 levels (14,15). In 2015, it was reported that despite plasma exchange and immunosuppressive treatment, mortality was still approximately 10-20% (10). However, with the use of rituximab as the first-line treatment in addition to steroids and plasma exchange, clinical responses and overall survival rates have increased to over 90%, and the relapse incidence rates have decreased significantly (16,17). With immunosuppression based on glucocorticoids and rituximab, the aim is to eliminate autoantibodies. In 2019, caplacizumab, which has a different mechanism of effect, targeting the A1 domain of vWf and providing rapid clinical improvement and thrombocyte normalization, was approved for use (18,19).

We thought that it was more important to reveal the predictive parameters of relapse in TTP, where overall survival rates have increased to over 90% with current treatment methods. For this reason, we wanted to present the relationships between demographic data, clinical findings, intensive care needs, laboratory results on arrival, PLASMIC scores and treatments received and the occurrence of relapsed/refractory disease in iTTP patients diagnosed after 2015 and to evaluate their response to treatments (mean response time, number of plasmapheresis procedures, relapsed/refractory disease) and mortality status. In addition to the literature, we planned to examine the relationship between patients' ADAMTS13 antibody levels and their laboratory findings on arrival, intensive care needs, response to treatment and relapse status.

2. Materials and Methods

Patients over the age of 18 who were diagnosed with TTP in the last 10 years at Akdeniz University Medical Faculty Hospital and the University of Health Sciences Antalya Training and Research Hospital Department of Hematology were included in the study. The study was conducted with the approval of the Clinical Research Ethics Committee of the University of Health Sciences Antalya Training and Research Hospital with decision number 16/6 dated 08/25/2022. The data were

collected from patient files, electronic hospital databases, hospital central laboratory records and apheresis unit data records.

The following information of iTTP patients was recorded: sex, age, date of diagnosis, fever findings, neurological involvement status, renal dysfunction status, hemoglobin levels, thrombocyte counts, lactate dehydrogenase (LDH) levels, ADAMTS13 activities and antibody levels, PLASMIC scores, intensive care needs, treatments received during the first attack (plasmapheresis volume, number of sessions, and immunosuppressive treatments), response to treatment, relapse status and treatments used for relapse, last follow-up time, and survival status. Clinical response was considered if the thrombocyte count was above 150000/mm^3 for 2 consecutive days with treatment and the LDH level returned to normal; refractory disease was considered if the patient never achieved clinical response status; remission was achieved if the patient's clinical response persisted for at least 30 days after stopping plasmapheresis; exacerbation was indicated if the disease recurred within 30 days after clinical response to treatment; and relapse was noted if the disease recurred after 30 days (20). The mean follow-up period was defined as the period from the date of the first diagnosis to the date of the last visit.

Statistical Analysis

IBM SPSS Statistics 23 program was used to analyze the data. For the descriptive data, continuous variables are depicted as the median (minimum-maximum) or mean (±standard deviation). Categorical variables are depicted as numerical values and percentages. The comparison of independent categorical data was made using the chi-square test. A t test was used to compare continuous variables with a normal distribution, and the Mann–Whitney U test was used to compare continuous variables without a normal distribution. For all tests, $p<0,05$ was accepted as the limit of statistical significance.

3. Results

Of the 38 patients diagnosed with TTP in both centers, 3 patients with congenital TTP were excluded from the study. The median age of the 35 patients diagnosed with iTTP was 41 (19-66), and 19 (54.3%) of the patients were female and 16 (45.7%) were male. A total of 28 (80%) patients had primary iTTP and 7 (20%) patients had secondary iTTP; of the secondary iTTP patients, 3 had secondary iTTP due to systemic lupus erythromatosis (SLE), 2 due to medication, 1 due to pregnancy and 1 due to trauma. Neurological findings, along with hemolytic anemia and thrombocytopenia, were present in 20 (57.1%) patients, renal dysfunction in 13 (37.1%) patients, fever in 5 (14.3%) patients and pentad in only 3 (8.6%) patients. Eleven (31.4%) patients needed intensive care support at their first admission. According to the PLASMIC score, 3 (8.5%) patients were in the medium-risk group (5 points), while 32 (91.5%) patients were in the high-risk group (6-7 points). The clinical, laboratory and demographic data of the patients are presented in Table 1.

Table 1. Demographic characteristics, clinical findings and laboratory results of the patients

Sex and clinical findings	**Number (n:35) (%)**	**Age and laboratory findings**	**(Mean ±sd)**
Sex (Female)	19 (54.3)	**Age**	40,2 ±11,1
iTTP (Primary)	28 (80)	**Hemoglobin** (g/dL)	8,5 ±2,0
Neurological findings (Yes)	20 (57.1)	**Leukocyte** (/mm^3)	9232 ±2790
Renal dysfunction (Yes)	13 (37.1)	**Neutrophile** (/mm^3)	6825 ±2515
Fever (Yes)	5 (14.3)	**Lymphocyte** (/mm^3)	1649 ±606

Intensive care (Yes)	11 (31.4)	**Thrombocyte** (/mm^3)	14000 ±7530
PLASMIC score		**LDH** (U/L)	1254 ±527
Medium (5 points)	3 (8.5)	**Total bilirubin** (mg/dL)	2,8 ±1,6
High (6-7 points)	32 (91.5)	**Creatinine** (mg/dL)	1,1 ±0,45

iTTP: *immune-mediated (acquired) thrombotic thrombocytopenic purpura,* ***LDH:*** *lactate dehydrogenase*

The median follow-up period of 35 patients was 46 (min: 2, max: 118) months, and 32 patients (91.4%) were alive during their last follow-up. Among the 3 patients who passed away, only one patient (with iTTP secondary to SLE in their third attack) passed away due to an iTTP attack.

In the first-line treatment, 27 (77.1%) patients received one plasma volume, and 8 (22.9%) patients received more than one plasma volume (1,5 or 2 volumes) of plasma exchange. The mean number of patients who underwent plasmapheresis as the first-line treatment was 15,9 (min: 3, max: 50). As an immunosuppressive treatment along with plasmapheresis, steroids alone were administered to 30 patients, and a combination of steroids and rituximab was administered to 4 patients. While the immunosuppressive treatment information of 2 patients could not be obtained, 3 patients did not receive immunosuppressive treatment (except for prophylactic low-dose steroids before plasmapheresis). In 2 patients, additional immunosuppressive drugs (azathioprine and cyclophosphamide) were used due to the diagnosis of SLE. After the first-line treatment, clinical remission was achieved in 20 (57.1%) patients, while 8 (22.9%) patients experienced disease exacerbation, and 7 (20%) patients experienced refractory disease. The number of days until response was 8,75 (min: 3, max: 30) in 28 (80%) patients who achieved clinical remission. Three patients who used rituximab achieved clinical remission, while one experienced refractory disease.

A total of 21 (60%) patients received second-line treatment, 15 of them due to refractory disease and disease exacerbation, and 6 due to relapse (30% of patients who achieved remission). The median number of days until second-line treatment was 23 (min: 8, max: 1812), while the median number of days until second-line treatment was 782 (min: 476, max: 1812) for those patients who experienced relapse. Rituximab was used in 14 patients, vincristine in 5 patients, cyclophosphamide in 4 patients, and steroids in all patients except refractory patients. The mean number of days that plasmapheresis was performed as a second-line treatment was 17,3 (min: 4, max: 58), and 5 patients were treated with more than 1 plasma volume (1,5 or 2 volumes). After the second-line treatment, clinical remission was achieved in all patients (95.2%), except for one refractory patient, and the mean number of days until response was 11,3 (min: 3, max: 35). In all 5 of the patients who developed relapse, steroid and rituximab were used in combination with plasmapheresis as a third-line treatment, and only one patient was additionally given cyclophosphamide and vincristine. Only one of the two patients (14 and 26 months later) who experienced a disease attack after the third-line treatment responded to the last treatment; the other patient passed away due to an iTTP attack.

The relationships between the clinical and laboratory characteristics of the patients and the need for second-line treatment were evaluated (Table 2). There were no statistically significant differences between fever, neurological findings, renal dysfunction, intensive care need, whether iTTP was primary or secondary, and sex, and the need for second-line treatment. Although small in number, two of the four patients who used rituximab as the first-line treatment had a history of relapse, and there was no relationship between the need for second-line treatment and the use of rituximab. The age and hemoglobin, leukocyte, thrombocyte, LDH, thrombocyte, creatinine and total bilirubin levels of 14 patients who needed treatment only once and 21 patients who

needed two or more lines of treatment were similar. In addition, the number of plasmapheresis procedures as the first-line treatment and the number of days until response were similar in both groups.

Table 2. The relationships between the demographic, clinical, laboratory characteristics and some findings in the first-line treatment of the patients and relapsed/refractory disease

	R/R disease (n:21) (%)	**P value**		**R/R disease (mean)**	**P value**
Sex (Female)	9 (42.8%)	0,09	**Age**	37,7	0,10
iTTP (Primary)	18 (85.7%)	0,30	**Hemoglobin** (g/dL)	8,4	0,68
Neurological findings (Yes)	12 (57.1%)	1,0	**Leukocyte** (/mm^3)	8881	0,37
Renal dysfunction (Yes)	8 (38.1%)	0,88	**Thrombocyte** (/mm^3)	14000	1,0
Fever (Yes)	3 (14.3%)	1,0	**LDH** (U/L)	1329	0,31
Intensive care (Yes)	8 (38.1%)	0,29	**Total bilirubin** (mg/dL)	3,15	0,09
Rituximab in the first-line treatment (Yes)	2 (9.5%)	0,64	**Creatinine** (mg/dL)	1,13	0,57
ADAMTS13 inhibitor (≥ 50) (U/ml)	11 (52.4%)	0,23	**ADAMTS13 inhibitor** (U/ml)	54,0	0,57
In first-line treatment	**Time to first-line response** (day)			9,8	0,31
	Number of plasmapheresis at the first-line treatment			14,9	0,58

ADAMTS13: *A Disintegrin and Metalloproteinase with Thrombospondin-1 motifs; 13th member of the family,* ***iTTP:*** *immune-mediated (acquired) thrombotic thrombocytopenic purpura,* ***LDH:*** *lactate dehydrogenase,* ***R/R:*** *relapsed/refractory*

ADAMTS13 activity was less than 2% in all patients, and varying concentrations (15,6-90 U/ml) of the ADAMTS13 inhibitor were observed. We did not detect a correlation between age and microangiopathic hemolytic anemia findings, such as hemoglobin, thrombocyte, LDH, and ADAMTS13 inhibitor levels. There was also no correlation between ADAMTS13 inhibitor levels and plasmapheresis as the first-line treatment, days until response, or days until second-line treatment. Although the mean ADAMTS13 inhibitor levels in 14 patients who received one line of treatment were lower than those in the relaps/refractory patients, the differences were not statistically significant (48.4 U/ml and 54.0 U/ml, respectively, p>0,05). In addition to the mean ADAMTS13 inhibitor levels of both groups, the mean antibody level of all patients was 52 (±5,09) U/ml. Therefore, a similar analysis was performed between patients with ADAMTS13 inhibitor levels of 50 U/ml and above and patients with levels below 50 U/ml. Patients in both groups had fever, neurological findings, renal dysfunction, and the need for intensive care, and the numbers of primary/secondary iTTP patients were similar (p>0,05). Additionally, in both groups, there was no significant difference in the number of patients with or without a complete response to first-line treatment (refractory disease and disease exacerbation) or the number of patients with and without the need for second-line treatment (p>0,05).

4. Discussion

In our study, the real-life data, including demographic, clinical, laboratory, treatment and response status data, of 35 iTTP patients were evaluated. In addition to comparing our results with the literature, we investigated the relationships between age, sex, clinical presentation, laboratory findings and number of plasmapheresis procedures and either ADAMTS13 inhibitor levels or relapsed/refractory disease.

The average age in our study was similar to that in the literature, and although the percentage of females was high (54.3%), it was slightly lower than that in the literature (approximately 70%) (5,9). In our study, secondary iTTP was detected in 20% of patients, and different rates have been reported in different studies, with the lowest being 23% and the highest being 67% (21-24). In our study, neurological findings were the most common (57.1%), followed by renal dysfunction (37.1%), and fever (14.3%) was the least common, while pentad was present in only 3 patients (8.6%). Although different rates have been reported in the literature, as in our study, neurological findings are most common (50-80%), followed by renal dysfunction, with fever and pentad being the lowest, reported in less than 10% of patients (7,11,21-27). Unlike in the literature, the intensive care needs of the patients at the time of admission were evaluated, and approximately one-third of the patients needed intensive care. While all patients had microangiopathic hemolytic anemia findings, the mean hemoglobin level (8,5 g/dl) and thrombocyte count (14000/mm^3) were consistent with the literature (hemoglobin: 7-8,2 g/dl, thrombocyte<30/mm^3) (7,11,21-27). It has been reported that a PLASMIC score of ≥5 (medium and high) provides very high sensitivity and specificity (0,99 (95% confidence range [CI], 0,91-1,00) and 0,57 (95% CI, 0,41-0,72), respectively), while a score of ≥6 (only high) slightly increases specificity (0,89; 95% CI, 0,81-0,94) and slightly reduces sensitivity (0,85; 95% CI, 0,67-0,94) (28). In our study, all patients had a PLASMIC score of ≥5, 3 (8.5%) patients were in the medium-risk (5 points) group, and 32 (91.5%) patients were in the high-risk (6-7 points) group.

Severe ADAMTS13 deficiency (activity <10%) supports the clinical diagnosis of TTP and validates the diagnosis in a patient with microangiopathic hemolytic anemia and thrombocytopenia. However, although rare, severe ADAMTS13 deficiency has also been reported to be associated with sepsis and some malignancies. In addition, in terms of clinical characteristics, ADAMTS13 activity ≥10% in possible TTP patients cannot exclude TTP diagnosis (11,29). In our study, the ADAMTS13 activity of all patients was less than 2%, and the presence of ADAMTS13 inhibitors was detected in all patients. Although inhibitors are expected in all patients with iTTP, they may not be detected in approximately 30% of patients, especially in the first acute attack. In this case, an enzyme-linked immunosorbent test or antibody screening test using the Western blot method may be required in addition to ordinary screening methods (10).

In TTP patients, whose mortality rate without treatment is >90%, mortality rates decrease to 10-15% with plasma exchange and corticosteroid treatment. However, the reported incidence of patients who are unresponsive to plasma exchange and corticosteroids and require additional treatment ranges from 10% to 42%. This prognosis improves drastically with the B-cell-targeting treatment rituximab, and clinical remission is achieved in 87-100% of patients following rituximab treatment (30). In our study, 91.4% (32 patients) of the patients with a median follow-up period of 46 months were alive, and only one patient passed away due to TTP. The rate of refractory disease and disease exacerbation after first-line treatment was present in 42.9% (15 patients) of patients, which is similar to the prevalence reported the literature. Although the use of rituximab in first-line treatment was quite low, the rate of rituximab use was higher in 21 patients requiring second-line treatment (14 patients, 66.6%). The clinical remission rate (95.2%) was higher after second-line treatment, in which steroids were used in all patients, cyclophosphamide and vincristine in a small

number of patients in addition to rituximab. In studies conducted after its effectiveness in relapsed/refractory patients, a clinical remission rate of >90% and, more importantly, a very low rate of relapse of approximately 10% were reported with the addition of rituximab to first-line treatment (16,17). It has been reported that rituximab, which is used as a first-line treatment because it reduces the rate of relapse from 50% to 10%, reduces relapse by being administered preemptively (31). In addition to these developments, the survival rate may increase with the rapid response provided by caplacizumab, which has recently entered into the treatment space and is an anti-vWf (32). However, this agent is recommended for use in selected/at-risk patients because of its increased bleeding risk and cost (33).

We believe that revealing the predictive factors for relapsed/refractory disease in TTP patients, whose mortality rate has decreased significantly, is an important goal in terms of subsequent treatment approaches and follow-up, and we performed several evaluations in our study from this point of view. However, age, sex, the presence of clinical findings (fever, neurological findings, renal dysfunction, and intensive care need), whether the patient had primary or secondary iTTP, laboratory findings (hemoglobin, leukocytes, thrombocyte, LDH, thrombocyte, creatinine, and total bilirubin levels), the number of plasmapheresis procedures as first-line treatment and the number of days until response were not predictive of the need for second-line treatment. Similar to our study, Hovinga et al. compared the demographic, clinical and laboratory characteristics of 16 patients with ADAMTS13 activity <10% who relapsed and 31 patients who did not relapse. They reported that only male sex had a significant relationship with relapse; there were no relationships between age, neurological findings, laboratory findings (hematocrit, thrombocyte, LDH, and creatinine levels) and plasma exchange numbers and relapse, as in our study (34). In various previous studies, advanced age, severe neurological findings, severe renal dysfunction, very high LDH levels (10 times the normal upper value), which mostly reflects organ damage, and increased cardiac troponin levels at the time of diagnosis have been associated with death and/or resistance to treatment (5,35). However, due to current first-line treatment approaches, where treatment responses are quite high and mortality is quite low, these indicators are considered controversial (5,6). Although there are not enough first-line treatments, the use of rituximab, which has been reported to have a low relapse rate after its use both in the treatment of relapsed/refractory patients and as a first-line treatment in the literature, is considered the most decisive factor in terms of relapse, as shown in our study.

Although previous studies have shown that severely low ADAMTS13 activity (<10%) predicts an increased need for plasma exchange and an increased risk of relapse, the predictive ability of this finding also seems to be limited, especially with the current treatment approach using rituximab as a first-line treatment (34). However, patients with severely low ADAMTS13 activity have been reported to have a lower mean thrombocyte count, less renal dysfunction, and more autoimmune symptoms (36). In our study, a comparison could not be made in this respect because all patients had an ADAMTS13 activity lower than 10% or a similar percentage. Although it is generally assumed that the titration of the inhibitor is associated with clinical results and that the disease may be more resistant to standard treatment in patients with high inhibitor titrations, it has been reported that it is not associated with the clinical picture and does not predict survival (11). Similar to the literature, in our study, we did not find a correlation between ADAMTS13 inhibitor levels and age, microangiopathic hemolytic anemia findings, such as hemoglobin, thrombocyte, and LDH levels, plasma exchange numbers, the number of days until response and the number of days until second-line treatment. In addition, the ADAMTS13 inhibitor levels at diagnosis were similar between patients who received only first-line treatment and patients who experienced refractory disease relapse. Unlike the literature, based on the mean inhibitor levels of the patients, we performed a similar analysis between patients with ADAMTS13

inhibitor levels of 50 U/ml and above and patients with levels below 50 U/ml. However, clinical findings such as fever, neurological findings, renal dysfunction, and need for intensive care were similar in both groups. Additionally, there was no difference in the number of patients who responded to first-line treatment or who required second-line treatment between the two groups.

5. Conclusion

In our study, where the mortality rate was quite low, we did not find a relationship between demographic characteristics, clinical or laboratory findings, ADAMTS13 inhibitor levels, or plasma exchange during first-line treatment and relapsed/refractory disease. In light of the available literature, we believe that factors that predict relapse rather than mortality are now required for TTP patients, whose overall survival rate has increased to more than 90% with new treatment approaches. Conducting analyses in this direction with studies that include more patients may help us identify patients at high risk of relapse and plan first-line treatments and follow-ups specifically for these patients.

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Ethics

Ethics Committee Approval: The study was approved by Clinical Research Ethics Committee of the University of Health Sciences Antalya Training and Research Hospital (Decision no: 16/6, Date: 08/25/2022).

Informed Consent: The authors declared that it was not considered necessary to get consent from the patients because the study was a retrospective data analysis.

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