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Efficacy of therapeutic plasma exchange in HELLP syndrome: A single-center experience

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MAIN POINTS

- A statistically significant reduction in hemolysis findings was achieved with therapeutic plasma exchange.
- In patients with renal failure, a poor prognostic factor in HELLP syndrome, improvement in renal function was observed with therapeutic plasma exchange.
- Therapeutic plasma exchange is an effective treatment modality for both clinical improvement and reduce mortality in patients with persistent postpartum hemolysis.

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ABSTRACT

Aim: The objective of this study is to investigate the clinical efficacy of therapeutic plasma exchange in HELLP (Hemolysis, Elevated Liver Enzyme, Low Platelet) syndrome and its contribution to renal failure, which is an independent risk factor for maternal mortality.

Materials and Methods: From 2019 to 2024, 20 patients diagnosed with HELLP syndrome who underwent therapeutic plasma exchange (TPE) were included. We evaluated the patients' pre- and post-procedure values to determine the efficacy of the procedure.

Results: The median age of patients was 30 (19-38) years, and the median number of days of TPE was 6 days (3-14). There was a statistically significant increase in hemoglobin and platelet values and a statistically significant decrease in lactate dehydrogenase, total bilirubin, direct bilirubin, aspartate aminotransferase, alanine aminotransferase, urea, and creatinine values. The number of TPE sessions, length of stay in hospital, and the length of intensive care unit stay were significantly higher in hemodialysis patients.

Conclusion: TPE is an effective treatment modality for both clinical improvement and prevention of permanent renal failure in patients with persistent postpartum hemolysis who are followed for HELLP syndrome.

Keywords: HELLP syndrome, Therapeutic plasma exchange, Renal failure

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INTRODUCTION

HELLP (Hemolysis, Elevated Liver Enzymes, Low Platelet count) syndrome is a serious pregnancy complication with a high risk of fetal and maternal morbidity. Although HELLP syndrome occurs in about 0.5% to 0.9% of all pregnancies, its incidence is higher in women with severe preeclampsia [1]. While it typically develops between 28 and 37 weeks of gestation, it can also occur in the postpartum period, accounting for approximately 30% of cases [2].

Clinical findings of HELLP syndrome vary. Patients may present with nonspecific symptoms such as weakness, fatigue, headache, nausea, vomiting, and pain in the epigastric and right upper quadrant [3]. The exact cause and development process are not fully understood. Vasospasm, endothelial dysfunction, and impaired microcirculation caused by fibrin deposition may lead to clinical signs in affected organs. Complications include disseminated intravascular coagulopathy (DIC), hepatic rupture or hematoma, fulminant liver failure, pulmonary and brain edema, ascites, pleural effusion, retinal detachment, and acute kidney injury (AKI) [4]. Studies have shown that renal failure, one of the complications of HELLP syndrome, is an independent risk factor for maternal mortality [5].

Two classification systems, Tennessee and Mississippi, are used in the diagnosis of HELLP syndrome. Patients are divided into complete or partial according to the Tennessee classification. Patients who meet all the specified criteria are considered complete, while those meeting one or two are considered partial. The criteria are as follows:

1. Having at least two findings related to hemolysis (presence of schistocytes in peripheral smear, serum bilirubin $\geq$1.2 mg/dl, lactate dehydrogenase (LDH) $\geq$2 times the upper limit of normal, or serum haptoglobin $\leq$25 mg/dl, hemoglobin (Hb) value <8-10 g/dl not associated with bleeding)

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2. Elevated liver enzymes (aspartate aminotransferase (AST) or alanine aminotransferase (ALT) ≥2 times the upper limit of normal)

3. Presence of thrombocytopenia [platelet (PLT) <100.000 /μL] [3].

In the Mississippi classification, the severity of thrombocytopenia is assessed. In the presence of LDH > 600 IU/L and AST or ALT > 70 IU/L, PLT≤50.000/μL is considered class-1, PLT 50.000 to 100.000/μL is considered class-2, and PLT 100.000 to 150.000/μL is considered class-3 [6].

The only effective treatment for HELLP syndrome is delivery. In cases < 34 weeks of gestation without serious complications, delivery can be delayed up to 48 hours after corticosteroid treatment to induce fetal lung development. Patients older than 34 weeks or with serious complications such as hepatic bleeding, DIC, AKI, or pulmonary edema should be delivered immediately [7]. Although therapeutic plasma exchange (TPE) is generally not considered a primary treatment for the disease, studies indicate it can be applied effectively and safely in clinically selected patients [8,9].

Thrombotic microangiopathy is preventable with therapeutic plasma exchange (TPE). TPE can be indicated for patients exhibiting progressive increases in serum bilirubin and creatinine levels and severe thrombocytopenia, even after obstetric management and supportive care. The objective of this study is to share the clinical characteristics and treatment outcomes of patients with HELLP syndrome who received TPE after demonstrating unresponsiveness to labor, corticosteroids, and supportive care, and to contextualize these findings within the current literature.

MATERIALS AND METHODS

This retrospective study included 20 patients who were diagnosed with HELLP syndrome and underwent TPE between September 2019 and April 2024. The institutional review board approved the study (approval number: 2025/04-16) regarding ethical and scientific conduct. This study was conducted by the principles of the Helsinki Declaration.

Patients and data

All patient data were retrospectively collected from hospital registries and individual clinical notes. For each patient, the following information was recorded: age, gestational age, gestational week at delivery, survival status, presence of renal failure, hemodialysis status, number of therapeutic plasma exchange (TPE) sessions, total hospitalization days, intensive care unit (ICU) stay, and laboratory values before and after the TPE procedure. These laboratory values included hemoglobin (Hb), platelet count (PLT), lactate dehydrogenase (LDH), total bilirubin (TB), direct bilirubin (DB), aspartate aminotransferase (AST), alanine aminotransferase (ALT), urea, creatinine (Cr), prothrombin time (PT), international normalized ratio (INR), activated partial thromboplastin time (aPTT), and fibrinogen. Patients were classified according to both the Mississippi and Tennessee criteria for HELLP syndrome.

Patients with HELLP syndrome who did not respond to initial management including labor induction/delivery, corticosteroids, and supportive treatment (blood products, antibiotics, and antihypertensives) were identified. For these patients, central venous catheters were inserted, and TPE treatment was initiated within 24 hours postpartum. TPE was performed daily using a Braun device (Melsungen, Germany) with a 1.5 plasma volume exchange per session. TPE continued until the patient's LDH level normalized and platelet count remained above 100,000/μL for two consecutive days.

Statistical analysis

We didn't determine the sample size beforehand. Instead, we calculated the post-hoc power based on our results; if the power was above 80%, we proceeded with the relevant analysis. G*Power version 3.1 was used for all power calculations. For our statistical analyses, we used IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics are presented as n (%) for categorical variables and median (min-max) for continuous variables. We assessed the normality of continuous data using the Shapiro-Wilk test, with a p-value of less than 0.05 indicating non-normal distribution. Consequently, we used the nonparametric Wilcoxon test for pre- and post-procedure comparisons, and the Mann-Whitney U test for independent group comparisons. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The median age of the patients was 30 years (range: 19-38). Renal failure occurred in 12 (60%) patients, with 6 (30%) requiring hemodialysis. Of those requiring hemodialysis, three died, while the remaining three (15%) showed no permanent renal failure during follow-up. HELLP syndrome developed after miscarriage in 1 (5%) patient, after delivery in 10 (50%) patients, and during the third trimester in 9 (45%) patients.

The median number of TPE sessions was 6 (range: 3-14). Fresh frozen plasma (FFP) served as the replacement fluid for 19 patients, with albumin used for only 1 patient. According to the Mississippi classification, 50% of patients were Class 1 and 50% were Class 2. Based on the Tennessee classification, 65% were classified as complete and 35% as partial.

Baseline coagulation parameters showed a median aPTT of 24 seconds (range: 21-44), PT of 12 seconds (range: 10-24), INR of 0.9 (range: 0.8-2.1), and a fibrinogen level of 244 mg/dL (range: 100-597). Fifteen patients required intensive care unit (ICU) admission, while five did not. The median length of hospitalization was 12 days (range: 7-45), and the

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Table 1. Demographic and clinical characteristics of patients.

Variables	N:20	%
Age		
Median (min-max)	30 (19-38)	
Surival		
Alive	17	85.0
Exitus	3	15.0
Renal Failure		
Yes	12	60.0
No	8	40.0
Hemodialysis		
Yes	6	30.0
No	14	70.0
Pregnancy week		
After miscarriage	1	5.0
Postpartum	10	50.0
3th trimester	9	45.0
Number of TPE sessions		
Median (min-max)	6.0 (3-14)	
Replacement		
FFP	19	95.0
Albumin	1	5.0
Mississippi		
Class-1	10	50.0
Class-2	10	50.0
Tennessee		
Complete	13	65.0
Partial	7	35.0
aPTT		
Median (min-max)	24 (21-44)	
PT		
Median (min-max)	12 (10-24)	
INR		
Median (min-max)	0.9 (0.8-2.1)	
Fibrinogen		
Median (min-max)	244 (100-597)	
Duration of hospitilization (days)		
Median (min-max)	12 (7-45)	
Duration of intensive care unit (days)		
Median (min-max)	3 (0-33)	
Intensive care		
Yes	15	60
No	5	40

aPTT; activated partial thromboplastin time, FFP; fresh frozen plasma, INR; international normalized ratio, PT; prothrombin time, TPE; therapeutic plasma exchange.

median ICU stay was 3 days (range: 0-33). During the follow-up period, 85% of patients survived, while 15% died.

Treatment response and outcomes

Following TPE, hemoglobin (Hb) and platelet (PLT) values significantly increased (p<0.001 for both). Conversely, LDH (p<0.001), total bilirubin (Tb, p=0.001), direct bilirubin (Db, p=0.003), AST (p<0.001), ALT (p<0.001), urea (p=0.002), and creatinine (Cr, p<0.001) values significantly decreased (Table 2).

Table 2. Comparison of laboratory parameters before and after TPE.

Variables	Before Process N=20 Median (min-max)	After Process N=20 Median (min-max)	p
Hb (g/dl)	7.4 (6.3-11.4)	10.4 (7.5-12.3)	**<0.001**
PLT (µL)	50000 (10000-75000)	155000 (71000-395000)	**<0.001**
LDH (U/L)	1412.5 (438-5897)	306.5 (134-864)	**<0.001**
Tb (mg/dl)	2.2 (0.6-9.4)	0.7 (0.3-14.8)	**0.001**
Db (mg/dl)	0.7 (0.1-7.3)	0.2 (0.1-9.5)	**0.003**
AST (U/L)	158 (16-2496)	28.5 (14-624)	**<0.001**
ALT (U/L)	122.5 (6-1046)	23.5 (9-140)	**<0.001**
Urea (mg/dl)	58 (19-174)	40 (19-101)	**0.002**
Cr (mg/dl)	1.67 (0.5-47)	0.9 (0.4-2.7)	**<0.001**

Hb: Hemoglobin PLT: Platelet LDH: Lactate dehydrogenase Tb: Total bilirubin Db: Direct bilirubin AST: Aspartate aminotransferase ALT: Alanine aminotransferase Cr: Creatinine.

Subgroup comparisons

Patients who required hemodialysis had a significantly higher number of TPE sessions (p=0.015), longer hospitalization days (p=0.046), and longer ICU stays (p=0.024) compared to those who did not (Table 3). There were no significant differences in the number of TPE sessions, length of hospitalization, or ICU stay when comparing patients by Mississippi classes (p>0.05) (Table 4) or Tennessee types (p>0.05) (Table 5).

DISCUSSION

Ongoing debates regarding the diagnosis, treatment, and prognosis of HELLP syndrome stem from several challenges: the lack of standardized diagnostic criteria, the failure of clinical and laboratory improvement post-delivery in some cases (despite it being the main treatment), and no consensus on which multi-system organ involvement carries a worse prognosis. Our study aims to contribute to the literature by demonstrating that renal failure may be a poor prognostic indicator and that therapeutic plasma exchange (TPE) is an effective treatment option for patients who do not clinically improve after delivery.

HELLP Syndrome is a clinical condition associated with microangiopathic hemolytic anemia, thrombocytopenia, and elevated liver enzymes. Two definitions are used in the diagnosis of the disease: the Tennessee and Mississippi classifications. In our study, we used both classification systems and classified all patients according to both classification systems. According to the Mississippi classification, there were equal numbers of patients in class 1 and class 2, and we did not observe a significant difference among the groups in terms of the number of days of procedure, length of hospitalization, and intensive care unit length of stay. According to the Tennessee classification, although our patients did not show a homogeneous distribution, we again did not observe a significant difference in terms of the number of days of procedure, length of hospitalization, and intensive care unit length of stay. Although

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Table 3. Comparison of the number of TPE session, length of hospitalization and intensive care unit stay according to hemodialysis groups.

Variables	HD		p
	Yes N=6 Median (min-max)	No N=14 Median (min-max)	
TPE session	9.5 (5-14)	6 (3-9)	0.015
Length of hospitalization (days)	15.5 (9-34)	11 (7-45)	0.046
Length of intensive care stay (days)	9.5 (3-33)	2.5 (0-30)	0.024

Table 4. Comparison of the number of TPE session, length of hospitalization and intensive care unit stay according to Mississippi classes.

Variables	Mississippi		p
	Class-1 N=10 Median (min-max)	Class-2 N=10 Median (min-max)	
TPE session	7 (4-11)	5.5 (3-14)	0.436
Length of hospitalization (days)	11 (7-20)	14 (8-45)	0.631
Length of intensive care stay (days)	4 (0-11)	3 (0-33)	0.990

Table 5. Comparison of the number of TPE session, length of hospitalization and intensive care unit stay according to hemodialysis groups according to Tennessee types.

Variables	Tennessee		p
	Complete N=13 Median (min-max)	Partial N=7 Median (min-max)	
TPE session	6 (4-14)	5 (3-9)	0.376
Length of hospitalization (days)	11 (7-34)	15 (8-45)	0.551
Length of intensive care stay (days)	3 (0-33)	6 (0-30)	0.992

these classification systems aid in diagnosis, we found no statistically significant differences regarding patient follow-up or prognosis. This lack of difference is likely attributable to the limited number of patients in our study.

HELLP syndrome, a severe pregnancy complication, carries a significant risk of maternal mortality, with reported rates in the literature ranging from 1% to 60%. For instance, Martin et al. reported a mortality rate of 3.2%, Sibia et al. found 1.1%, and Isler et al. observed 60%. In our study, the mortality rate was 15%, aligning with this broad range [10-12]. This variability likely stems from differences in patient clinical characteristics, the timing of TPE initiation, and variations in study sample sizes.

Studies consistently highlight renal failure as an independent risk factor for increased mortality in HELLP syndrome [5], often presenting as the most severe form of acute renal failure in pregnancy [13]. While appropriate management of Acute Kidney Injury (AKI) can prevent irreversible renal damage in HELLP syndrome, delays in diagnosis and treatment can lead to permanent renal failure [14]. In our cohort, 12 patients (60%) experienced renal failure, with 6 (30%) requiring hemodialysis. Of those on hemodialysis, three (15%) died, but importantly, the remaining three (15%) showed no permanent renal failure during follow-up. Comparing patients who underwent hemodialysis to those who did not, we found a statistically significant increase in TPE sessions, length of hospitalization, and intensive care unit stay in the hemodialysis group. This underscores that renal insufficiency is indeed a poor prognostic factor in HELLP syndrome, consistent with existing literature.

Childbirth remains the primary treatment for HELLP syndrome, with spontaneous resolution of thrombotic microangiopathy expected in most cases postpartum. However, in some instances, clinical and laboratory parameters may not improve despite delivery, corticosteroid administration, and supportive treatment. In these refractory cases, therapeutic plasma exchange (TPE) is performed to reduce pathogenic antibodies, minimize organ damage, and improve clinical and laboratory outcomes. Our study demonstrated that in patients unresponsive to initial management, TPE led to a statistically significant increase in platelet counts and a decrease in LDH levels.

Limitations

Our study has several limitations, including the inability to evaluate ADAMTS-13 levels due to technical inadequacy, the absence of a control group, and a small sample size.

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CONCLUSION

Given the high mortality rate associated with HELLP syndrome, timely diagnosis and early intervention are of vital importance. For patients who do not adequately respond to delivery and corticosteroid treatment, and who continue to exhibit signs of hemolysis, low platelet counts, and elevated LDH, TPE can be initiated within 24 hours postpartum. This intervention can potentially prevent persistent renal failure with its poor prognosis and reduce mortality by improving overall clinical outcomes.

Ethics Committee Approval: This study received approval from the Institutional Review Board of Fırat University (Date: 27.02.2025, Approval Number: 2025/04-16).

Informed Consent: Informed consent was not obtained due to the retrospective design of the study.

Peer-review: Externally peer-reviewed.

Conflict of Interest: The authors declare that they have no competing interests.

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