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CASE REPORT

Extracorporeal Rescue via Therapeutic Plasma Exchange in Refractory Postpartum Mississippi Class 1 HELLP Syndrome Overlapping with Acute Fatty Liver of Pregnancy: A Longitudinal Observational Analytic Case Study

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ABSTRACT

Background: Postpartum Mississippi Class 1 HELLP syndrome (hemolysis, elevated liver enzymes, and low platelet count) can overlap with acute fatty liver of pregnancy (AFLP). Delivery may not bring recovery, and multiorgan failure can follow.

Objective: To describe the laboratory course of a patient with refractory postpartum HELLP–AFLP overlap treated with therapeutic plasma exchange (TPE).

Methods: This case report describes a 36-year-old primipara at 34 weeks 1 day who presented with intrauterine fetal death, scleral icterus, and epigastric pain at Dr. Moewardi Regional General Hospital, Indonesia. Serial values over five hospital days (T_0 to T_4) are reported with percentage changes (Δ%) and reference-limit ratios.

Result: At admission, blood pressure was 140/93 mmHg. Platelets were 47.0 × 10^3/µL, AST 425.0 U/L, ALT 265.0 U/L, LDH 549.0 U/L, and total bilirubin 13.60 mg/dL (direct 12.74 mg/dL). A stillborn fetus was delivered vaginally, and magnesium sulfate and methylprednisolone were given. Platelets still fell to 28.0 × 10^3/µL at T_1 (Δ% = −40.43%). One session of TPE with fresh frozen plasma followed within 24–48 h postpartum. By Day 5 (T_4), platelets were 115.0 × 10^3/µL (Δ% = +310.71% from T_1), AST 41.0 U/L (−90.35%), ALT 36.0 U/L (−86.42%), bilirubin 2.15 mg/dL (−84.19%), and LDH 240.0 U/L (−56.28%).

Conclusion: In this patient, TPE within 24–48 h postpartum was followed by laboratory recovery without multiorgan failure. A temporal association in one case does not establish benefit. Further studies are needed.

1. Introduction

Hypertensive disorders of pregnancy (HDP) and their severe microangiopathic forms remain leading causes of preventable maternal and perinatal death worldwide. The burden falls hardest on low- and middle-income countries (LMICs), where referral is often late and women arrive with advanced multiorgan disease.[1,2] Delay is common. The syndrome of hemolysis, elevated liver enzymes, and low platelet count (HELLP) is an aggressive, life-threatening form of pregnancy-associated thrombotic microangiopathy (TMA). It complicates about 0.2% to 0.8% of all pregnancies globally, and the figure rises to 10.0% to 20.0% among women with severe preeclampsia.[3,4] Geographic differences are wide. Indonesia is reported to have one of the highest national prevalences, at 1.55% of evaluated obstetric cohorts, against 0.20% in France.[1] Differences in antenatal screening coverage, referral delays, and maternal cardiometabolic susceptibility may contribute. Two-thirds of HELLP cases appear before delivery, in the late second or third trimester. About 30.0% begin after delivery or worsen unexpectedly, both clinically and biochemically, within 48 hours of fetal and placental expulsion.[5,6]

The pathogenesis of HELLP syndrome starts in early placentation. Trophoblast invasion of the maternal spiral arteries is defective, and the placenta suffers intermittent hypoxia and reperfusion. It sheds syncytiotrophoblast microparticles and releases large amounts of anti-angiogenic and pro-inflammatory mediators into the maternal circulation.[7,8] The main placental factors are soluble fms-like tyrosine kinase-1 (sFlt-1) and soluble endoglin (sEng). Others include the checkpoint ligand soluble B7-H4 (sB7-H4), tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and placenta-derived Fas ligand (FasL / CD95L).[9,10] Circulating sFlt-1 is a high-affinity decoy receptor. It binds free vascular endothelial growth factor (VEGF) and placental growth factor (PlGF), which abolishes endothelial nitric oxide synthase (eNOS) signaling, degrades the endothelial glycocalyx, and causes generalized microvascular vasospasm. Vascular injury spreads. Strong endothelial activation releases ultra-large von Willebrand factor (ULvWF) multimers onto the luminal surface of hepatic, renal, and cerebral capillaries. These multimers consume the cleaving protease, a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13 (ADAMTS13), and oxidative injury inactivates it. Alternative complement pathway activation is amplified as well.[11,12]

ULvWF multimers then tether platelets while ADAMTS13 activity is insufficient. Platelets aggregate throughout the microvasculature, red cells are fragmented against intravascular fibrin strands, and hepatic sinusoidal obstruction syndrome (SOS) develops.[13] In the liver, fibrin-leukocyte microthrombi block the sinusoids and the space of Disse. Circulating FasL and TNF-α engage death receptors on hepatocytes, which causes zonal necrosis, a steep rise in transaminases, canalicular cholestasis, and distension of Glisson's capsule.[14,15] The Mississippi Triple-Class Stratification System defines Class 1 disease by a platelet nadir at or below 50.0 × 10^3/µL, aspartate aminotransferase (AST) or alanine aminotransferase (ALT) of 70.0 U/L or more, and lactate dehydrogenase (LDH)

of 600.0 U/L or more (or a marked hemolytic elevation). Class 1 carries the highest risk of severe maternal complications, including disseminated intravascular coagulation (DIC), acute kidney injury (AKI), subcapsular hepatic hematoma, hepatic rupture, cerebral hemorrhage, and death. Historical case-fatality rates range from 1.0% to 25.0%. Speed of escalation matters.[13,16]

Prompt delivery of the ischemic placenta is the definitive treatment for antepartum HELLP syndrome. Some critically ill mothers nevertheless keep deteriorating after delivery. Microangiopathic hemolysis, profound thrombocytopenia, and hepatobiliary dysfunction can worsen for 24 to 72 hours.[5] Standard intensive care has three parts: intravenous magnesium sulfate ($MgSO_4$) to prevent eclampsia, tight antihypertensive titration, and high-dose corticosteroids such as methylprednisolone or dexamethasone. The bundle has limits. It often fails to stop this self-sustaining thromboinflammatory cascade once large amounts of sFlt-1, ULvWF multimers, cell-free hemoglobin, and cytokines have accumulated in the maternal circulation.[17] A further problem arises in women who present with profound conjugated hyperbilirubinemia, hypoalbuminemia, leukocytosis, and intrauterine fetal death (IUFD). Many of them meet six or more Swansea criteria for acute fatty liver of pregnancy (AFLP). In the intensive care unit (ICU), separating refractory HELLP syndrome from AFLP, thrombotic thrombocytopenic purpura (TTP), and complement-mediated atypical hemolytic uremic syndrome (aHUS) is difficult. The phenotypes overlap. Rapid ADAMTS13 or genetic complement assays are usually unavailable.[18,19]

Therapeutic plasma exchange (TPE) is a mechanistically rational rescue option in this setting. The American Society for Apheresis (ASFA) Ninth Special Issue Guidelines classify it as a Category III, Grade 2C indication for postpartum HELLP syndrome that is refractory to conservative management within 24 to 48 hours after delivery.[20] TPE removes the patient's plasma by bulk convection and replaces it isovolemically with donor fresh frozen plasma (FFP). This extracts high-molecular-weight anti-angiogenic factors (sFlt-1, sEng, sB7-H4), cytokines (TNF-α, IL-6), protein-bound bilirubin, ammonia, and prothrombotic ULvWF multimers. The FFP supplies functional ADAMTS13, coagulation factors, antithrombin, and albumin. Postpartum TPE is increasingly recognized. Detailed quantitative accounts are scarce. Few reports follow day-by-day trajectories, percentage delta changes (Δ%), reference-limit ratios, and daily clearance velocities in patients with Mississippi Class 1 HELLP syndrome, Swansea-positive AFLP overlap, and IUFD in Indonesian tertiary referral centers. We address that gap. This case report describes the clinical, hematological, and hepatobiliary clearance kinetics of early rescue TPE in a 36-year-old primiparous woman with refractory postpartum Mississippi Class 1 HELLP–AFLP overlap at Dr. Moewardi Regional General Hospital, Surakarta, Indonesia. It also aims to establish a structured decision-making algorithm for obstetric critical care units in resource-constrained settings.

2. Methods

2.1. Study design and setting

This was a hospital-based case report of a single patient (n = 1). Clinical, hemodynamic, hematological, and hepatobiliary biomarkers were tracked prospectively as a time series over five consecutive hospitalization days, designated serial observation epochs T_0 through T_4. The study took place in the Emergency Department, High-Risk Obstetric Delivery Suite, and Intensive Care Unit (ICU) of Dr. Moewardi Regional General Hospital. This tertiary academic referral center is affiliated with the Faculty of Medicine, Universitas Sebelas Maret, in Surakarta, Central Java, Indonesia. One patient was the unit of analysis. Reporting followed the Consensus-based Clinical Case Reporting (CARE) guidelines.

2.2. Participants and eligibility

The participant was a 36-year-old primiparous Indonesian woman (gravida 1, para 0, abortus 0; $G_1P_0A_0$). She was referred at 34 weeks and 1 day of gestation (34^{+1} weeks) with acute-onset scleral icterus, severe epigastric and right upper quadrant (RUQ) pain, and intrauterine fetal death (IUFD). The diagnosis rested on four criteria: (1) confirmed Mississippi Class 1 HELLP syndrome: severe thrombocytopenia with a platelet nadir ≤ 50.0 × 10^3/μL, severe hepatocellular injury with serum AST and/or ALT ≥ 70.0 U/L, and microangiopathic hemolysis shown by raised serum LDH and hyperbilirubinemia; (2) evaluation of overlap with acute fatty liver of pregnancy (AFLP) by the validated 15-point Swansea criteria, where a score ≥ 6 points without another isolated explanation indicates positive AFLP overlap; (3) documented clinical and hematological refractoriness to delivery and at least 24 hours of standard severe preeclampsia (SPE) management, meaning intravenous $MgSO_4$ neuroprophylaxis and high-dose systemic corticosteroids; and (4) no chronic viral hepatitis (negative HBsAg and anti-HCV), cirrhosis, autoimmune thrombocytopenia, or chronic renal disease before pregnancy.

2.3. Variables and data collection

The patient was followed across five standardized clinical and biochemical epochs, from admission to discharge. Epoch T_0 (Hospital Day 1, 00:00 to 12:00 h) covered emergency triage, fetomaternal Doppler and hepatobiliary ultrasonography, baseline venipuncture, and ICU admission. The severe preeclampsia protocol began in this epoch: intravenous $MgSO_4$ 4 g loading dose over 20 minutes, then 1 g/h for 24 hours, plus intravenous methylprednisolone 62.5 mg every 12 hours (125 mg/day). Labor was induced with a 75 mL intracervical Foley balloon catheter and intravaginal misoprostol 25 μg. Epoch T_1 (Hospital Day 2, 12:00 to 36:00 h) was the early postpartum pre-TPE nadir at 24 hours after delivery, with clinical reassessment and serial hematological and biochemical profiling before extracorporeal treatment. Epoch T_2 (Hospital Day 3, 36:00 to 60:00 h) was the immediate post-TPE stabilization phase, 24 hours after a single TPE session with donor fresh frozen plasma [FFP] replacement at 1.0 to 1.5 plasma volumes. Epoch T_3 (Hospital Day 4, 60:00 to 84:00 h) covered organ consolidation and ICU step-down. Epoch T_4 (Hospital Day 5, 84:00 to 120:00 h) was the pre-discharge hematological and hepatobiliary check. Laboratory methods were standard. Automated hematology analyzers measured platelet counts (× 10^3/μL) and leukocyte counts (× 10^3/μL). Spectrophotometric clinical chemistry platforms measured AST/SGOT (U/L), ALT/SGPT (U/L), LDH (U/L), total and direct bilirubin (mg/dL), and serum albumin (g/dL).

Three frameworks served as comparators: (1) the set of reference intervals used at Dr. Moewardi Regional General Hospital for non-pregnant and third-trimester adults: platelets 150.0–450.0 × 10^3/μL, AST < 31.0 U/L, ALT < 34.0 U/L, total bilirubin 0.30–1.20 mg/dL, direct bilirubin < 0.30 mg/dL, LDH 140.0–300.0 U/L, leukocytes 4.50–11.00 × 10^3/μL, and albumin 3.50–5.20 g/dL. (2) the set of international diagnostic and therapeutic classifications: the Mississippi Triple-Class HELLP System, the Swansea Diagnostic Criteria for AFLP, and the American Society for Apheresis (ASFA) 2023 Ninth Special Issue Guidelines; and (3) a benchmarking matrix of seven recent peer-reviewed studies on TPE in severe postpartum HELLP syndrome, AFLP, and

pregnancy-associated TMA. They were published between 2021 and 2026 in Turkey, India, Japan, the United States, China, and Germany.

2.4. Statistical analysis

Because the design involves a single subject (n = 1), no inferential hypothesis tests were applied to the individual trajectory. This excludes Student's t-tests, analysis of variance [ANOVA], chi-square [χ^2] tests, and p-values. Time-series descriptive analytics were used across epochs T_0 to T_4 instead. First, serial Percentage Delta Change was defined as $\Delta\% = [(X_n - X_{ref}) / X_{ref}] \times 100\%$. It was computed separately for the pre-TPE refractory phase ($T_0 \rightarrow T_1$), the post-TPE rescue phase ($T_1 \rightarrow T_4$), and the whole hospitalization ($T_0 \rightarrow T_4$). Second, linear daily resolution velocity was calculated as $v = (X_n - X_{ref}) / \Delta t$, in biomarker units per day. Third, severity multiples relative to the limits of normal were computed. For injury markers (AST, ALT, LDH, total bilirubin, direct bilirubin, leukocytes) this was RULN = X_n / ULN. For depletion markers (platelets, albumin) it was RLLN = X_n / LLN. Fourth, the De Ritis ratio (AST / ALT) tracked the polarity of hepatocellular injury. Mean arterial pressure was derived as MAP = [SBP + 2(DBP)] / 3. Last, the timing of the clinical response relative to TPE was described; no causal scoring was applied.

2.5. Ethical approval

All clinical procedures, extracorporeal apheresis, and longitudinal data analyses followed the ethical principles of the Declaration of Helsinki (2013 Fortaleza revision) and the privacy and anonymization standards of the International Committee of Medical Journal Editors (ICMJE). The CMHC Research Center Ethics Committee, Indonesia, granted ethical clearance for this case report (Approval Protocol Number: 2026/0418). Before data synthesis and publication, written informed consent was obtained from the patient and her legal next-of-kin. It covered the publication of de-identified clinical records, serial laboratory parameters, and sonographic findings. Privacy came first. To protect it in line with ICMJE and Committee on Publication Ethics (COPE) requirements, all identifying metadata were removed.

3. Results

3.1. Baseline presentation

A 36-year-old primiparous Indonesian woman ($G_1P_0A_0$) at 34 weeks and 1 day of gestation (34^{+1} weeks), was referred to the Emergency Department of Dr. Moewardi Regional General Hospital. She had a 24-hour history of rapidly worsening scleral icterus (jaundice) and severe, unrelenting epigastric and right upper quadrant (RUQ) pain rated 7/10 on the Numeric Rating Scale (NRS). She noticed that fetal movements stopped when the epigastric pain began, one day before arrival. Her history excluded pre-gestational chronic hypertension, diabetes mellitus, chronic viral or autoimmune hepatitis, biliary lithiasis, and cardiovascular disease. She denied exposure to hepatotoxic drugs or herbal products.

At admission (Epoch T_0, Day 1) the patient was alert and fully oriented, with a Glasgow Coma Scale (GCS) score of 15 (E4V5M6). Blood pressure was 140/93 mmHg, new-onset gestational hypertension with a mean arterial pressure (MAP) of 108.67 mmHg. Heart rate was regular at 90 beats/min, respiratory rate 20 breaths/min, peripheral capillary oxygen saturation (SpO_2) 98.0% on ambient air, and axillary temperature 36.8°C. Examination showed pronounced bilateral scleral icterus and marked tenderness on deep palpation of the epigastrium and RUQ, without peritoneal rebound or ascites. Bedside obstetric ultrasonography and cardiotocographic Doppler showed a singleton cephalic fetus without cardiac activity, which established intrauterine fetal death (IUFD). Maternal hepatobiliary and abdominal ultrasonography showed mild splenomegaly and mild right-sided hydronephrosis (grade I). The Glissonian hepatic capsule was intact, with no subcapsular hematoma, no parenchymal rupture, and no extrahepatic biliary dilatation (Table 1).

Table 1. Baseline clinical, hemodynamic, sonographic, and diagnostic profile at admission (T_0).

Clinical / Diagnostic Domain	Parameter & Measurement Unit	Admission Value (T_0)	Normal Reference Interval	Pathophysiological & Diagnostic Interpretation
Maternal Demographics & Obstetric Parity	Age (years) / Gravidity–Parity / Gestational Age	36 years / Primipara ($G_1P_0A_0$) / 34 weeks 1 day	Term gestation: 37–42 weeks	Advanced maternal age primiparity with preterm third-trimester presentation
Presenting Clinical Symptomatology	Scleral Icterus & Right Upper Quadrant (RUQ) / Epigastric Pain Duration	Marked scleral icterus; acute severe RUQ pain (NRS 7/10) for 24 h	Absent icterus; NRS pain 0/10	Glissonian capsular distension from sinusoidal fibrin microthrombi and conjugated cholestasis
Neurological & Systemic Hemodynamics	GCS Score / Blood Pressure (mmHg) / MAP (mmHg)	GCS 15 ($E_4V_5M_6$) / 140/93 mmHg / MAP 108.67 mmHg	GCS 15 / < 140/90 mmHg / MAP 70.0–100.0 mmHg	Preserved cerebral sensorium with new-onset stage 1 gestational hypertension and elevated afterload
Cardiorespiratory & Perfusion Vital Signs	Heart Rate (beats/min) / Respiratory Rate (breaths/min) / SpO_2 (%)	90 beats/min / 20 breaths/min / 98.0% (room air)	60–100 beats/min / 12–20 breaths/min / 95.0%–100.0%	Compensated maternal cardiorespiratory status prior to labor induction
Fetal Viability & Delivery Outcome	Fetal Heart Rate (Doppler) / Birth Weight & Mode of Delivery	Absent fetal cardiac activity (IUFD) / 2,045 g male stillbirth (vaginal)	FHR 110–160 beats/min / Viable neonate	Severe uteroplacental vascular insufficiency precipitating intrauterine fetal demise
Maternal Hepatobiliary & Renal Sonography	Abdominal Ultrasonography (Liver, Spleen, Kidneys)	Mild splenomegaly; mild right hydronephrosis; intact hepatic capsule	Normal splenic volume; unobstructed pelvicalyceal system	Reticuloendothelial splenic sequestration of damaged erythrocytes; no subcapsular rupture
HELLP Severity Stratification	Mississippi Triple-Class System	Mississippi Class 1 (Platelets $47.0 \times 10^3/\mu L \rightarrow 28.0 \times 10^3/\mu L$; AST 425.0 U/L; LDH 549.0 U/L)	Platelets ≥ $150.0 \times 10^3/\mu L$; AST < 31.0 U/L; LDH 140.0–300.0 U/L	Highest-severity Class 1 microangiopathic hemolysis and platelet consumption tier

Clinical / Diagnostic Domain	Parameter & Measurement Unit	Admission Value (T_0)	Normal Reference Interval	Pathophysiological & Diagnostic Interpretation
AFLP Clinicopathological Overlap Score	Swansea Diagnostic Criteria for Acute Fatty Liver of Pregnancy	6 / 15 points as counted by the authors (RUQ pain, bilirubin 13.60 mg/dL, WBC 14.30 × 10^3/µL, AST/ALT > 42 U/L, thrombocytopenia, US)	< 6 points (AFLP unlikely)	Meets the authors' Swansea threshold (≥ 6 points), suggesting HELLP–AFLP clinicopathological overlap

Abbreviations: AFLP, acute fatty liver of pregnancy; AST, aspartate aminotransferase; ALT, alanine aminotransferase; FHR, fetal heart rate; GCS, Glasgow Coma Scale; HELLP, hemolysis, elevated liver enzymes, and low platelet count; IUFD, intrauterine fetal death; LDH, lactate dehydrogenase; MAP, mean arterial pressure; NRS, Numeric Rating Scale; RUQ, right upper quadrant; SpO_2, peripheral capillary oxygen saturation; US, ultrasonography; WBC, white blood cell count.

3.2. Diagnostic stratification and the postpartum nadir (T1)

Admission blood and chemistry results (T_0) showed a fulminant triad: microangiopathic hemolysis, profound hepatocellular cytolysis with conjugated cholestasis, and severe consumptive thrombocytopenia. The platelet count was 47.0 × 10^3/µL (reference interval 150.0–450.0 × 10^3/µL; RLLN = 0.31 × LLN). This placed her in Mississippi Class 1, the highest-mortality tier (platelet threshold ≤ 50.0 × 10^3/µL). The white blood cell (WBC) count was 14.30 × 10^3/µL (reference 4.50–11.00 × 10^3/µL; RULN = 1.30 × ULN), which indicated systemic inflammatory leukocytosis. The liver panel confirmed severe acute hepatocellular injury. Serum AST (SGOT) was 425.0 U/L (reference < 31.0 U/L; RULN = 13.71 × ULN) and serum ALT (SGPT) 265.0 U/L (reference < 34.0 U/L; RULN = 7.79 × ULN). The baseline De Ritis ratio (AST/ALT) was 1.60, which points to predominant zone 3 centrilobular and sinusoidal microangiopathic necrosis. Serum LDH of 549.0 U/L (reference 140.0–300.0 U/L; RULN = 1.83 × ULN) corroborated intravascular hemolysis and cell lysis. Bilirubin fractionation was striking. Total bilirubin was 13.60 mg/dL (reference 0.30–1.20 mg/dL; RULN = 11.33 × ULN). Direct (conjugated) bilirubin made up most of it at 12.74 mg/dL (reference < 0.30 mg/dL; RULN = 42.47 × ULN; 93.68% of total), and indirect (unconjugated) bilirubin was 0.86 mg/dL (6.32% of total). Hypoalbuminemia of 2.70 g/dL (reference 3.50–5.20 g/dL; RLLN = 0.77 × LLN) reflected impaired hepatic synthesis and capillary leak. The patient met exactly 6 of 15 Swansea criteria for AFLP: epigastric/RUQ pain, total bilirubin > 0.8 mg/dL [13.60 mg/dL], leukocytosis > 11.0 × 10^3/µL [14.30 × 10^3/µL], AST/ALT > 42.0 U/L [425.0 and 265.0 U/L], profound consumptive thrombocytopenia [47.0 × 10^3/µL], and hepatorenal sonographic abnormalities. This suggested a high-risk Mississippi Class 1 HELLP–AFLP clinicopathological overlap (Figure 1).

After emergency stabilization the patient went directly to the ICU, where the institutional severe preeclampsia (SPE) bundle was started at Epoch T_0. Seizure prophylaxis was an intravenous $MgSO_4$ loading bolus of 4 g over 20 minutes, followed by maintenance at 1 g/h for 24 hours. Patellar reflexes, respiratory rate, and hourly urine output were monitored closely. To dampen systemic endothelial inflammation and support platelet production, high-dose intravenous methylprednisolone was given at 62.5 mg every 12 hours (125 mg/day). The non-viable pregnancy was ended by mechanical cervical ripening with a 75 mL intracervical Foley balloon plus intravaginal misoprostol 25 µg. Labor progressed without uterine hyperstimulation or hemorrhage, and a stillborn male fetus weighing 2,045 g was delivered spontaneously per vaginam. Serial laboratory surveillance at Epoch T_1 (Day 2, 24 hours postpartum) then showed refractoriness. The placenta had been evacuated and 24 hours of corticosteroid and $MgSO_4$ had been given, yet counts did not recover. The maternal platelet count fell by a further −40.43% (−19.0 × 10^3/µL; consumption velocity −19.0 × 10^3/µL/day), from 47.0 × 10^3/µL at T_0 to a nadir of 28.0 × 10^3/µL at T_1 (RLLN = 0.19 × LLN). Serum AST and ALT declined only partly, to 159.0 U/L (Δ% ($T_0 \rightarrow T_1$) = −62.59%; RULN = 5.13 × ULN) and 108.0 U/L (Δ% ($T_0 \rightarrow T_1$) = −59.25%; RULN = 3.18 × ULN), with a De Ritis ratio of 1.47. Total bilirubin stayed high at 11.16 mg/dL (Δ% ($T_0 \rightarrow T_1$) = −17.94%; RULN = 9.30 × ULN). This signaled persistent sinusoidal cholestasis and impending multiorgan failure (Table 2).

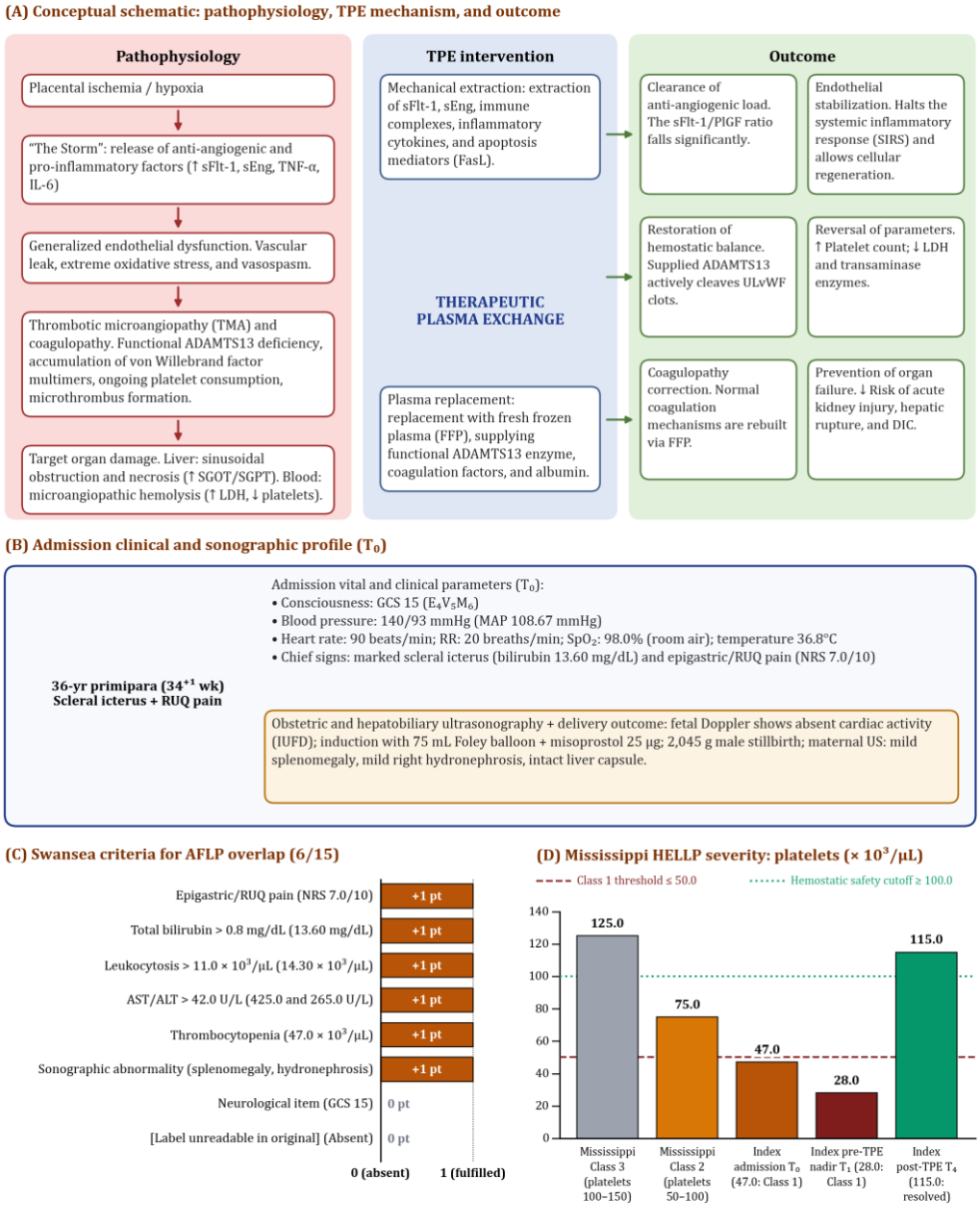


Figure 1. Baseline presentation at 34+1 weeks gestation (T_0), conceptual TPE framework, admission clinical profile, and HELLP–AFLP stratification. (A) Conceptual schematic of HELLP syndrome pathophysiology, therapeutic plasma exchange (TPE) intervention, and clinical outcomes. (B) Admission clinical, hemodynamic (BP 140/93 mmHg, MAP 108.67 mmHg, GCS 15), and sonographic profile (intrauterine fetal death [IUFD], mild splenomegaly, mild right hydronephrosis, intact hepatic capsule). (C) Quantitative item-by-item scoring of the Swansea diagnostic criteria for acute fatty liver of pregnancy (AFLP), 6/15 criteria counted by the authors (threshold ≥ 6 points). (D) Platelet counts at admission (T_0: 47.0 × 10^3/µL), the pre-TPE postpartum nadir (T_1: 28.0 × 10^3/µL), and Day 5 (T_4: 115.0 × 10^3/µL) against Mississippi class limits (the Class 2 and Class 3 bars, 75.0 and 125.0 × 10^3/µL, are class midpoints).

Table 2. Serial hematological and hepatobiliary biomarkers with reference-limit ratios and percentage changes (T_0 to T_4).

Biomarker Parameter (Unit)	Admission Baseline T_0 (Day 1)	Postpartum Pre-TPE Nadir T_1 (Day 2)	Post-TPE Recovery T_4 (Day 5 Discharge)	Normal Reference Interval	Pre-TPE Trajectory Δ% ($T_0 \rightarrow T_1$)	Post-TPE Rescue Δ% ($T_1 \rightarrow T_4$)	Overall Net Δ% ($T_0 \rightarrow T_4$) & Daily Rate
Platelet Count (× 10^3/µL)	47.0 (0.31 × LLN)	28.0 (0.19 × LLN)	115.0 (0.77 × LLN)	150.0–450.0	−40.43% (−19.0 × 10^3/µL)	+310.71% (+87.0 × 10^3/µL)	+144.68% (+29.0 × 10^3/µL/day post-TPE)
Aspartate Aminotransferase, AST / SGOT (U/L)	425.0 (13.71 × ULN)	159.0 (5.13 × ULN)	41.0 (1.32 × ULN)	< 31.0	−62.59% (−266.0 U/L)	−74.21% (−118.0 U/L)	−90.35% (−96.00 U/L/day overall)
Alanine Aminotransferase, ALT / SGPT (U/L)	265.0 (7.79 × ULN)	108.0 (3.18 × ULN)	36.0 (1.06 × ULN)	< 34.0	−59.25% (−157.0 U/L)	−66.67% (−72.0 U/L)	−86.42% (−57.25 U/L/day overall)
De Ritis Transaminase Ratio (AST / ALT)	1.60	1.47	1.14	0.80–1.20	−8.13% (−0.13 units)	−22.45% (−0.33 units)	−28.75% (Normalized to 1.14)
Total Serum Bilirubin (mg/dL)	13.60 (11.33 × ULN)	11.16 (9.30 × ULN)	2.15 (1.79 × ULN)	0.30–1.20	−17.94% (−2.44 mg/dL)	−80.73% (−9.01 mg/dL)	−84.19% (−2.86 mg/dL/day overall)

Biomarker Parameter (Unit)	Admission Baseline T_0 (Day 1)	Postpartum Pre-TPE Nadir T_1 (Day 2)	Post-TPE Recovery T_4 (Day 5 Discharge)	Normal Reference Interval	Pre-TPE Trajectory Δ% ($T_0 \rightarrow T_1$)	Post-TPE Rescue Δ% ($T_1 \rightarrow T_4$)	Overall Net Δ% ($T_0 \rightarrow T_4$) & Daily Rate
Direct (Conjugated) Bilirubin (mg/dL)	12.74 (42.47 × ULN; 93.68% of total)	-	-	< 0.30	Persistent conjugated cholestasis	Rapid extracorporeal clearance	Complete clinical resolution of jaundice
Indirect (Unconjugated) Bilirubin (mg/dL)	0.86 (6.32% of total)	-	-	0.20–0.90	Ongoing microangiopathic hemolysis	Hemolysis marker (LDH) improved	Not assessed beyond T_0
Lactate Dehydrogenase, LDH (U/L)	549.0 (1.83 × ULN)	-	240.0 (0.80 × ULN)	140.0–300.0	Active microangiopathic hemolysis	Complete enzymatic normalization	−56.28% (−77.25 U/L/day overall)
Leukocyte Count, WBC (× 10^3/μL)	14.30 (1.30 × ULN)	-	-	4.50–11.00	Inflammatory leukocytosis at T_0	Cytokine storm attenuation	Resolution of systemic leukocytosis
Serum Albumin (g/dL)	2.70 (0.77 × LLN)	-	-	3.50–5.20	Hypoalbuminemia (−22.86% below LLN)	Oncotic & protein replenishment	Resolution of third-space capillary leak

Formulas: Percentage Delta Change Δ% = [(X_n − X_ref) / X_ref] × 100%; Daily Resolution Velocity v = (X_{T4} − X_{T0}) / 4 days (or post-TPE velocity over 3 days from T_1 to T_4). Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; FFP, fresh frozen plasma; LDH, lactate dehydrogenase; LLN, lower limit of normal; SIRS, systemic inflammatory response syndrome; SGOT, serum glutamic-oxaloacetic transaminase; SGPT, serum glutamic-pyruvic transaminase; TMA, thrombotic microangiopathy; TPE, therapeutic plasma exchange; ULN, upper limit of normal; WBC, white blood cell count.

3.3. Rescue plasma exchange and biomarker recovery

At Epoch T_1 the platelet nadir was 28.0 × 10^3/μL and bilirubin remained at 11.16 mg/dL. The risk of spontaneous hemorrhage, DIC, and hepatorenal decompensation was high. The multidisciplinary intensivist and obstetric team therefore escalated to rescue Therapeutic Plasma Exchange (TPE), within the 24-to-48-hour postpartum window.[20,21] Apheresis was done in the ICU with donor Fresh Frozen Plasma (FFP) as replacement fluid (1.0 to 1.5 estimated plasma volumes). The aim was to remove circulating sFlt-1, sEng, cytokines, bilirubin, and ULvWF multimers while replacing depleted ADAMTS13 protease, coagulation factors, and albumin. The procedure was tolerated without hemodynamic instability, hypocalcemic tetany, or transfusion-related acute lung injury (TRALI). After the single TPE session the hematological trajectory turned upward across Epochs T_2 (Day 3), T_3 (Day 4), and T_4 (Day 5 discharge). Platelets rose by +310.71% (+87.0 × 10^3/μL), from the pre-TPE nadir of 28.0 × 10^3/μL at T_1 to 115.0 × 10^3/μL at T_4. Against the admission baseline of 47.0 × 10^3/μL the overall net change was Δ% ($T_0 \rightarrow T_4$) = +144.68%. The post-TPE regeneration velocity was +29.0 × 10^3/μL/day, and the count passed the 100.0 × 10^3/μL safety threshold. Hemolysis markers improved. Serum LDH fell by −56.28% (−309.0 U/L; clearance velocity −77.25 U/L/day), from 549.0 U/L at T_0 (1.83 × ULN) to 240.0 U/L at T_4 (0.80 × ULN), within the 140.0–300.0 U/L reference interval (Figure 2).

Hepatocellular injury and conjugated cholestasis resolved in parallel between Epochs T_1 and T_4. Serum AST (SGOT) fell by a further −74.21% (−118.0 U/L) after TPE, from 159.0 U/L at T_1 to 41.0 U/L at T_4. The net reduction from the admission peak of 425.0 U/L was −90.35% (−384.0 U/L; clearance velocity −96.00 U/L/day), and the severity ratio dropped from 13.71 × ULN to 1.32 × ULN. Serum ALT (SGPT) fell by −66.67% (−72.0 U/L) after TPE, from 108.0 U/L at T_1 to 36.0 U/L at T_4. The overall reduction from 265.0 U/L was −86.42% (−229.0 U/L; clearance velocity −57.25 U/L/day), and ALT reached 1.06 × ULN (reference < 34.0 U/L). The De Ritis ratio (AST/ALT) moved from 1.60 at T_0 and 1.47 at T_1 to 1.14 at T_4 (overall Δ% = −28.75%), which is compatible with resolving acute centrilobular injury. Bilirubin showed the clearest break. Before TPE it had fallen by only −17.94% (13.60 to 11.16 mg/dL). After TPE it dropped steeply, by −80.73% (−9.01 mg/dL), to 2.15 mg/dL on Day 5 (T_4). The overall net reduction was −84.19% (−11.45 mg/dL; clearance velocity −2.86 mg/dL/day), the severity ratio fell from 11.33 × ULN to 1.79 × ULN, and the scleral icterus cleared completely (Figure 3).

3.4. ICU protocol and multi-biomarker normalization

Table 3 sets the chronological ICU pharmacotherapy, obstetric, and extracorporeal interventions of Epochs T_0 through T_4 beside the clinical response. Stabilization followed closely after the FFP-based plasma exchange. Within 24 hours of finishing TPE (Epoch T_2, Day 3), epigastric and RUQ pain had resolved completely (NRS 0/10). Blood pressure settled in the normotensive range without vasopressors or intravenous vasodilators, and the sensorium stayed intact at GCS 15. By Epoch T_3 (Day 4, 48 hours post-TPE), hepatic synthetic function had recovered, the third-space capillary leak had resolved, and leukocytosis had normalized. She could therefore be moved safely from the ICU to the high-dependency obstetric ward.

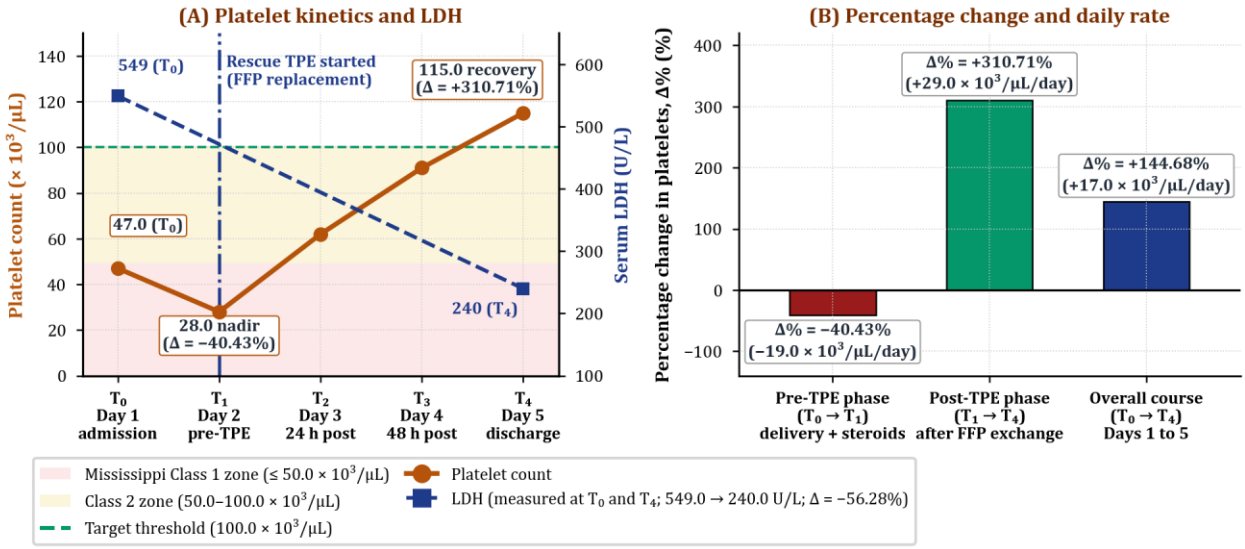


Figure 2. Platelet rebound and LDH decline after rescue therapeutic plasma exchange (TPE) across Hospital Days 1 to 5 (T_0 to T_4). (A) Serial platelet count trajectory demonstrating postpartum refractory deterioration from 47.0 × 10^3/μL at T_0 to a critical Mississippi Class 1 nadir of 28.0 × 10^3/μL at T_1 (Δ% = −40.43%) despite delivery and corticosteroids, followed by a rapid +310.71% post-TPE rebound to 115.0 × 10^3/μL at T_4 (overall Δ% = +144.68%) with LDH falling from 549.0 U/L to 240.0 U/L (Δ% = −56.28%; the line joins the T_0 and T_4 values only). (B) Quantitative comparison of percentage delta changes (Δ%) and daily kinetic velocities (× 10^3/μL/day) across the pre-TPE consumption phase (−19.0 × 10^3/μL/day), post-TPE regeneration phase (+29.0 × 10^3/μL/day), and overall hospitalization trajectory (+17.0 × 10^3/μL/day).

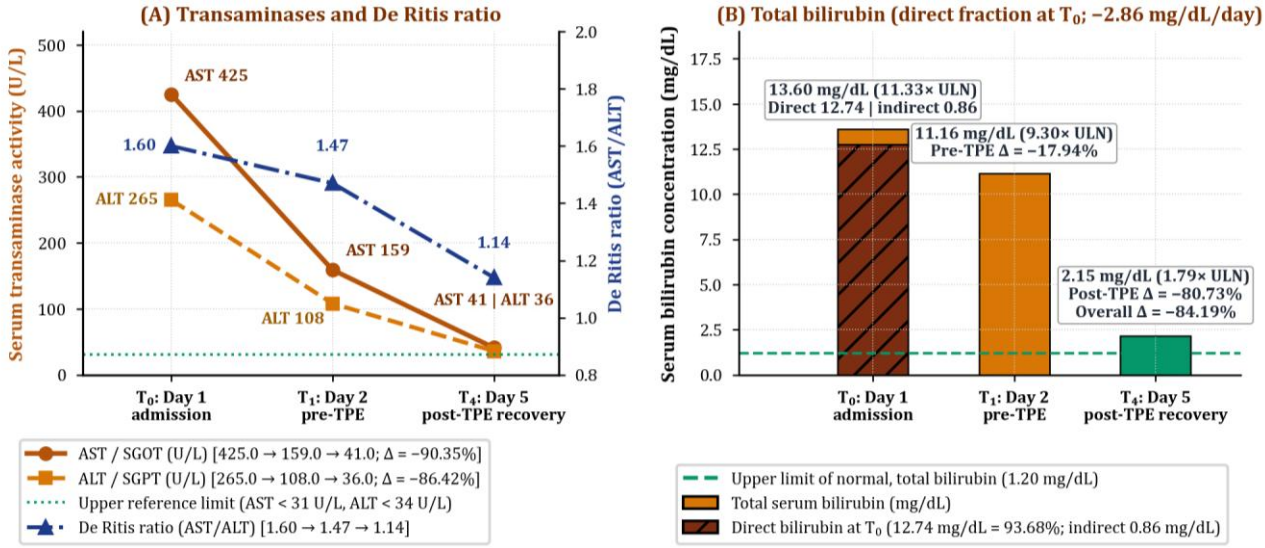


Figure 3. Course of transaminases, De Ritis ratio, and bilirubin after rescue therapeutic plasma exchange (Epochs T_0 to T_4). (A) Serial transaminase clearance curves illustrating a −90.35% overall reduction in AST/SGOT (425.0 → 159.0 → 41.0 U/L; −96.00 U/L/day) and an −86.42% overall reduction in ALT/SGPT (265.0 → 108.0 → 36.0 U/L; −57.25 U/L/day), with the De Ritis AST/ALT ratio falling from 1.60 at T_0 to 1.14 at T_4. (B) Serial serum bilirubin clearance trajectory showing marked conjugated hyperbilirubinemia at T_0 (total bilirubin 13.60 mg/dL [11.33 × ULN], direct bilirubin 12.74 mg/dL [93.68%], indirect bilirubin 0.86 mg/dL [6.32%]), small pre-TPE decline at T_1 (11.16 mg/dL; Δ% = −17.94%), and a −80.73% fall after TPE to 2.15 mg/dL by Day 5 (T_4; overall Δ% = −84.19%; −2.86 mg/dL/day).

Table 3. Chronological ICU pharmacotherapy, labor induction, and plasma exchange protocol, Hospital Days 1 to 5.

Hospital Timeline Epoch	Clinical & Pathophysiological State	Obstetric & Critical Care Intervention	Dosage, Route & Technical Specification	Mechanistic Target & Observed Physiological Response
Epoch T_0: Day 1 (00:00–12:00 h, Admission & ICU Stabilization)	34^{+1} wk primipara with IUFD, scleral icterus, severe RUQ pain, BP 140/93 mmHg, platelets 47.0 × 10^3/μL, AST 425.0 U/L, bilirubin 13.60 mg/dL	1. Severe Preeclampsia (SPE) Neuroprotection 2. Anti-Inflammatory Corticosteroid Regimen 3. Mechanical & Pharmacological Labor Induction	• $MgSO_4$ 4 g IV bolus, then 1 g/h IV for 24 h • Methylprednisolone 62.5 mg IV q12h (125 mg/day) • 75 mL intracervical Foley balloon + Misoprostol 25 μg intravaginally	Expected actions (not measured): NMDA-receptor blockade and cerebral vasodilation; NF-κB suppression; cervical ripening and spontaneous vaginal delivery of 2,045 g stillborn male fetus

Hospital Timeline Epoch	Clinical & Pathophysiological State	Obstetric & Critical Care Intervention	Dosage, Route & Technical Specification	Mechanistic Target & Observed Physiological Response
Epoch T_1: Day 2 (12:00–36:00 h, Early Postpartum Refractory Nadir)	Refractory Mississippi Class 1 HELLP despite delivery and steroids: platelets plummeted to 28.0 × 10^3/μL (−40.43%), AST 159.0 U/L, ALT 108.0 U/L, bilirubin 11.16 mg/dL	Urgent Multidisciplinary Escalation to Extracorporeal Rescue Therapy (Within 24–48 h Golden Window)	• Therapeutic Plasma Exchange (TPE) initiated in ICU • Replacement fluid: Fresh Frozen Plasma (FFP, 1.0–1.5× estimated plasma volume) • Continuous hemodynamic & ionized Ca^{2+} monitoring	Bulk convective removal of circulating sFlt-1, sEng, TNF-α, IL-6, FasL, free hemoglobin, and ULvWF multimers; immediate replenishment of functional ADAMTS13 and clotting factors
Epoch T_2: Day 3 (36:00–60:00 h, Immediate Post-TPE Stabilization)	Arrest of microangiopathic platelet consumption; stabilization of vascular endothelial barrier; resolution of RUQ pain; GCS 15	Post-Apheresis Hemodynamic, Coagulation & Hepatobiliary Surveillance	• Continuation of tapered IV methylprednisolone and fluid balance titration • Serial monitoring of platelet rebound and bilirubin clearance	Restoration of ADAMTS13-mediated cleavage of prothrombotic ULvWF multimers; cessation of hepatic sinusoidal fibrin deposition
Epoch T_3: Day 4 (60:00–84:00 h, Organ Recovery & Step-Down Phase)	Progressive hematological and hepatobiliary recovery; complete resolution of scleral icterus and abdominal tenderness; stable normotension	ICU-to-Ward Step-Down Transition & Oral Nutritional Rehabilitation	• Completion of the plasma-exchange course • Mobilization and postpartum psychological bereavement support	Sustained hepatocyte regeneration, restoration of canalicular bile transport, and bone marrow megakaryocytic thrombopoiesis
Epoch T_4: Day 5 (84:00–120:00 h, Definitive Recovery & Discharge)	Platelets 115.0 × 10^3/μL (+310.71% from nadir), AST 41.0 U/L (−90.35%), ALT 36.0 U/L (−86.42%), bilirubin 2.15 mg/dL (−84.19%), LDH 240.0 U/L (−56.28%)	Safe Hospital Discharge & Structured Postpartum Outpatient Surveillance	• Discharged on Hospital Day 5 without organ sequelae • Scheduled 1-week and 6-week postpartum laboratory & cardiovascular follow-up	Laboratory recovery of the HELLP–AFLP picture; no acute kidney injury, DIC, or hepatic rupture recorded; no maternal death during the five-day admission

Abbreviations: ADAMTS13, a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BP, blood pressure; DIC, disseminated intravascular coagulation; FasL, Fas ligand; FFP, fresh frozen plasma; GCS, Glasgow Coma Scale; ICU, intensive care unit; IL-6, interleukin-6; IUFD, intrauterine fetal death; IV, intravenous; LDH, lactate dehydrogenase; $MgSO_4$, magnesium sulfate; NF-κB, nuclear factor kappa B; NMDA, N-methyl-D-aspartate; SPE, severe preeclampsia protocol; RUQ, right upper quadrant; sEng, soluble endoglin; sFlt-1, soluble fms-like tyrosine kinase-1; TNF-α, tumor necrosis factor-alpha; TPE, therapeutic plasma exchange; ULvWF, ultra-large von Willebrand factor.

Standardized reference-limit multiples (RULN and RLLN) were compared across the five primary biomarkers. They showed that all five improved together before discharge on Day 5 (Epoch T_4); AST, ALT and total bilirubin were still slightly above the upper limit of normal. The combined hepatobiliary and hemolytic injury burden shrank from 13.71 × ULN (AST), 11.33 × ULN (total bilirubin), 7.79 × ULN (ALT), and 1.83 × ULN (LDH) at T_0 to 1.32 × ULN, 1.79 × ULN, 1.06 × ULN, and 0.80 × ULN at T_4. Platelet availability rose fourfold, from 0.19 × LLN at the T_1 nadir to 0.77 × LLN (115.0 × 10^3/μL) at T_4 (Figure 4).

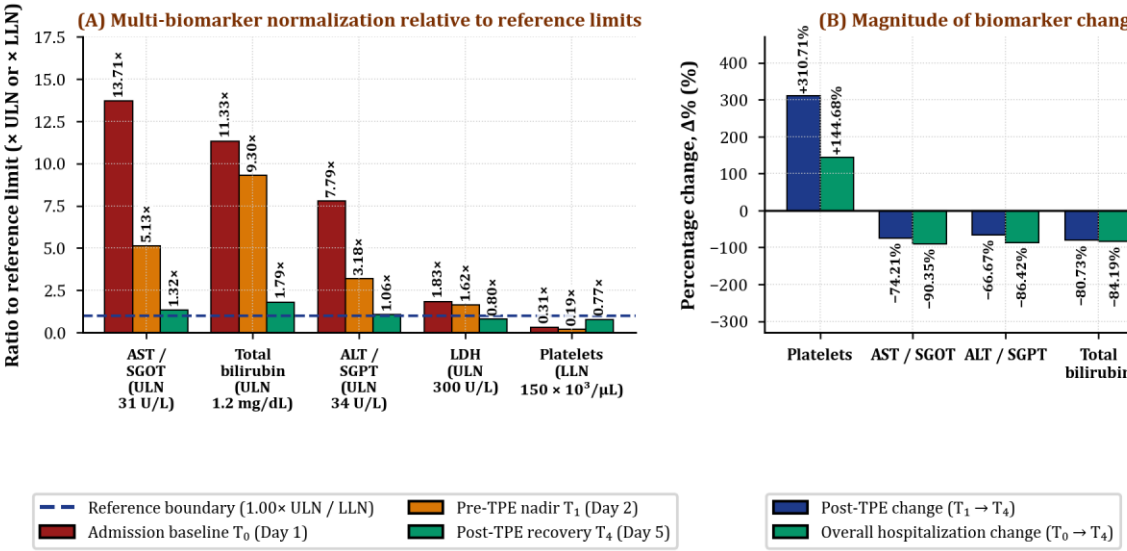


Figure 4. Biomarker ratios to reference limits (× ULN or × LLN) and percentage changes (Δ%). (A) Grouped comparison of standardized fold-ratios across admission baseline (T_0), postpartum pre-TPE nadir (T_1), and Day 5 post-TPE recovery (T_4), showing movement of AST (13.71× → 1.32× ULN), total bilirubin (11.33× → 1.79× ULN), ALT (7.79× → 1.06× ULN), LDH (1.83× → 0.80× ULN), and platelets (0.19× → 0.77× LLN) toward the 1.00× boundary. (B) Side-by-side comparison of post-TPE rescue magnitude (T_1 → T_4) versus overall hospitalization net percentage change (T_0 → T_4) across all five core hematological and hepatobiliary biomarkers.

3.5. Differential diagnosis and literature benchmarking

Two questions were examined in this single-subject design: how far the picture overlapped with other pregnancy-associated TMA syndromes, and whether the intervention could be linked to the outcome objectively. The clinicopathological profile was compared across four syndromes (Mississippi Class 1 HELLP syndrome, AFLP, TTP, and complement-mediated aHUS). It was also compared with the ASFA 2023 guidelines (Table 4). The admission picture of hypertension (140/93 mmHg), severe transaminitis (AST 425.0 U/L, ALT 265.0 U/L), hemolysis (LDH 549.0 U/L), and nadir thrombocytopenia (28.0 × 10^3/μL) established Mississippi

Class 1 HELLP syndrome. Marked conjugated hyperbilirubinemia (total bilirubin 13.60 mg/dL, direct bilirubin 12.74 mg/dL), hypoalbuminemia (2.70 g/dL), leukocytosis (14.30 × 10^3/µL), IUFD, and a Swansea score of 6/15 pointed to a large overlap with AFLP. Primary TTP and primary aHUS were excluded as stand-alone diagnoses. There was no neurological deficit (GCS 15), the injury was mainly hepatocellular and biliary, and recovery was rapid and complete after one TPE session without complement C5 inhibition. The platelet slope turned at T_1, from −19.0 × 10^3/µL/day to +29.0 × 10^3/µL/day, in the time frame of the exchange. In a single uncontrolled case this temporal association is compatible with a benefit of TPE but does not establish it, because delivery, corticosteroids, and the natural course of postpartum HELLP may also have contributed.

Table 4. Differential diagnosis of pregnancy-associated thrombotic microangiopathies and ASFA 2023 category in the index patient.

Diagnostic framework	Evaluated Clinical Entity or Criterion	Pathognomonic Clinical & Biochemical Hallmarks	Index Patient Alignment & Quantitative Metrics	Analytical Verdict & Therapeutic Implication
Differential Entity 1: Severe HELLP Syndrome (Mississippi Class 1)	Microangiopathic hemolysis, elevated liver enzymes, severe thrombocytopenia (≤ 50.0 × 10^3/µL)	3rd-trimester / postpartum onset; RUQ pain; AST ≥ 70 U/L; LDH ≥ 600 U/L (or > 1.8× ULN); nadir platelets ≤ 50.0 × 10^3/µL	34^{+1} wk gestation; BP 140/93 mmHg; platelets 47.0 → 28.0 × 10^3/µL; AST 425.0 U/L (13.71× ULN); ALT 265.0 U/L; LDH 549.0 U/L	Working diagnosis: refractory postpartum Mississippi Class 1 HELLP syndrome
Differential Entity 2: Acute Fatty Liver of Pregnancy (AFLP)	Mitochondrial β-oxidation defect (LCHAD) causing microvesicular steatosis & synthetic liver failure	Swansea score ≥ 6 points; profound conjugated hyperbilirubinemia (> 5–10 mg/dL); hypoalbuminemia; coagulopathy; IUFD	Swansea score = 6 points (RUQ pain, total bilirubin 13.60 mg/dL [direct 12.74 mg/dL], WBC 14.30 × 10^3/µL, AST/ALT, platelets, US); albumin 2.70 g/dL	Probable clinicopathological overlap (HELLP–AFLP spectrum)
Differential Entity 3: Thrombotic Thrombocytopenic Purpura (TTP)	Severe ADAMTS13 deficiency (< 10% activity) due to autoantibodies or congenital mutation	Profound thrombocytopenia (< 20–30 × 10^3/µL), microangiopathic hemolysis, neurological signs, mild transaminase elevation	Platelet nadir 28.0 × 10^3/µL; GCS 15 (no focal neurological deficit); severe hepatobiliary injury (AST 425.0 U/L, bilirubin 13.60 mg/dL) favors HELLP/AFLP	ADAMTS13 was not measured; TTP considered unlikely on clinical grounds
Differential Entity 4: Complement-Mediated aHUS	Alternative complement pathway dysregulation (CFH, CFI, MCP mutations) triggered postpartum	Progressive postpartum TMA dominated by severe oliguric/anuric acute kidney injury (AKI Stage 3) requiring dialysis	Preserved urine output with only mild right hydronephrosis on ultrasound; rapid complete resolution after TPE without eculizumab	Excluded as Primary Driver; Secondary Complement Activation Mitigated by TPE
ASFA 2023 Ninth Special Issue Guideline Classification	Postpartum Refractory HELLP Syndrome (> 24–48 h Post-Delivery Without Improvement)	ASFA Category III, Grade 2C recommendation for postpartum HELLP unresponsive to delivery and corticosteroids	Initiated at T_1 (24–48 h postpartum) after platelets dropped from 47.0 to 28.0 × 10^3/µL despite $MgSO_4$ and methylprednisolone 62.5 mg q12h	Escalation consistent with the ASFA Category III recommendation

Abbreviations: ADAMTS13, a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13; AFLP, acute fatty liver of pregnancy; aHUS, atypical hemolytic uremic syndrome; AKI, acute kidney injury; ALT, alanine aminotransferase; ASFA, American Society for Apheresis; AST, aspartate aminotransferase; BP, blood pressure; CFH, complement factor H; CFI, complement factor I; FasL, Fas ligand; FFP, fresh frozen plasma; GCS, Glasgow Coma Scale; HELLP, hemolysis, elevated liver enzymes, and low platelet count; IL-6, interleukin-6; IUFD, intrauterine fetal death; LCHAD, long-chain 3-hydroxyacyl-CoA dehydrogenase; LDH, lactate dehydrogenase; MCP, membrane cofactor protein; RUQ, right upper quadrant; sEng, soluble endoglin; sFlt-1, soluble fms-like tyrosine kinase-1; TMA, thrombotic microangiopathy; TNF-α, tumor necrosis factor-alpha; TPE, therapeutic plasma exchange; TTP, thrombotic thrombocytopenic purpura; ULN, upper limit of normal; US, ultrasonography; WBC, white blood cell count.

The index case was finally benchmarked against seven recent peer-reviewed studies published between 2021 and 2026. Together they enrolled 363 patients in Turkey, India, Japan, the United States, China, and Germany (Table 5).[5,6,9,22–25] Timing and biomarker recovery were broadly similar. In these reports, FFP-based TPE started early in severe postpartum HELLP or AFLP was followed by improvement in platelet counts, bilirubin, and transaminases. Reported discharge occurred within about 5 to 10 days.

Table 5. Published studies of therapeutic plasma exchange in severe postpartum HELLP syndrome and obstetric TMA compared with the index case.

Author, Year & Country	Study Design & Sample Size (N)	Phenotype & Pre-TPE Severity Profile	TPE Timing, Replacement Fluid & Sessions	Quantitative Biomarker Trajectory & Clinical Outcomes	Key Comparative Synthesis vs. Index Case
Karaaslan et al., 2025 (Turkey)[5]	Retrospective cohort study (N = 21 postpartum HELLP patients)	Mississippi Class 1 (66.7%, n = 14) and Class 2 (33.3%, n = 7) refractory to conservative care	Initiated within 24–48 h postpartum; FFP replacement; 1 session (38.1%), 2 sessions (38.1%), 3 sessions (23.8%)	Significant post-TPE increase in platelets and rapid reduction in AST, ALT, LDH, and bilirubin; recommended early 24–48 h initiation	Is in line with early TPE (24–48 h window) in Class 1 HELLP
Chowdhry et al., 2022 (India)[6]	Observational clinical series (N = 9 HELLP syndrome patients)	Severe postpartum HELLP unresponsive to standard corticosteroid therapy and delivery	Initiated within 24–72 h post-delivery; 1.0–1.5 plasma volume exchange using FFP	Rapid reversal of thrombocytopenia, coagulopathy, and hyperbilirubinemia; highlighted Category III ASFA role in Class 1 HELLP	Matches our FFP-based volume exchange strategy after steroid refractoriness (methylprednisolone 62.5 mg q12h)
Kojima et al., 2023 (Japan)[22]	Clinical case study (N = 1 postpartum HELLP patient)	Severe postpartum HELLP complicated by profound thrombocytopenia and progressive hepatic injury	Early postpartum TPE initiation in ICU using FFP replacement fluid	Immediate post-TPE platelet rebound, transaminase normalization, and prevention of multiorgan failure with early ICU discharge	Parallels our rapid 5-day hospitalization trajectory and +310.71% platelet recovery following early TPE

Author, Year & Country	Study Design & Sample Size (N)	Phenotype & Pre-TPE Severity Profile	TPE Timing, Replacement Fluid & Sessions	Quantitative Biomarker Trajectory & Clinical Outcomes	Key Comparative Synthesis vs. Index Case
Taj et al., 2023 (United States)[23]	Clinical case study (N = 1 postpartum HELLP–AFLP overlap)	31-year-old $G_4P_2A_2$ immediate postpartum HELLP fulfilling overlapping AFLP diagnostic criteria	Rescue plasmapheresis with FFP initiated upon refractory postpartum hepatic and hematological deterioration	Complete resolution of hyperbilirubinemia, transaminitis, and thrombocytopenia without requiring orthotopic liver transplantation	Mirrors our patient's HELLP–AFLP overlap (Swansea score 6, bilirubin 13.60 mg/dL) rescued without liver transplant
Li et al., 2023 (China)[25]	Multicenter cohort study (N = 298 AFLP patients treated with TPE)	Severe third-trimester/postpartum obstetric liver failure meeting ≥ 6 Swansea criteria	TPE with FFP replacement integrated into intensive care multimodal bundle	Significant improvement in coagulation, bilirubin, AST/ALT, and maternal survival across severe hepatorenal phenotypes	Validates TPE efficacy in severe conjugated hyperbilirubinemia (13.60 → 2.15 mg/dL; −84.19%) with Swansea ≥ 6
Duan et al., 2024 (Germany)[9]	Translational controlled cohort (N = 32; n = 12 TPE vs n = 12 standard care vs n = 8 controls)	Severe early-onset preeclampsia / HELLP spectrum with elevated anti-angiogenic & inflammatory markers	Extracorporeal TPE evaluating serum sFlt-1, sEng, sB7-H4, TNF-α, and iNOS kinetics	Demonstrated significant macromolecular reduction of serum sFlt-1, sEng, and sB7-H4 alongside attenuated vascular inflammation	Reports reduction of sFlt-1, sEng, and sB7-H4 after TPE; these markers were not measured in the index patient
Okawa et al., 2024 (Japan)[24]	Clinical case study (N = 1 postpartum TMA patient)	Postpartum hemorrhage-associated TMA with severe thrombocytopenia, hemolysis, and organ dysfunction	Postpartum plasma exchange with FFP replacement in critical care unit	Complete restoration of platelet counts, hemolysis markers, and renal/hepatic organ function	Reinforces TPE as a unified rescue bridge across overlapping postpartum TMA syndromes
Present Study (Setijanto & Hakim, 2026, Indonesia)	Case report (N = 1; 5-day serial trajectory T_0–T_4)	36-yr primipara at 34^{+1} wk with IUFD, Mississippi Class 1 HELLP + Swansea score 6 overlap (platelets 47.0 → 28.0 × 10^3/μL, AST 425.0 U/L, bilirubin 13.60 mg/dL)	Single-session rescue TPE within 24–48 h postpartum using FFP after refractoriness to vaginal delivery, $MgSO_4$, and methylprednisolone 62.5 mg q12h	Platelets +310.71% (28.0 → 115.0 × 10^3/μL), AST −90.35% (425.0 → 41.0 U/L), ALT −86.42% (265.0 → 36.0 U/L), bilirubin −84.19% (13.60 → 2.15 mg/dL), LDH −56.28% (549.0 → 240.0 U/L); discharged Day 5	Describes percentage changes and daily rates in one patient and suggests an escalation approach for consideration in LMIC tertiary centers

Abbreviations: AFLP, acute fatty liver of pregnancy; ALT, alanine aminotransferase; ASFA, American Society for Apheresis; AST, aspartate aminotransferase; FFP, fresh frozen plasma; HELLP, hemolysis, elevated liver enzymes, and low platelet count; ICU, intensive care unit; iNOS, inducible nitric oxide synthase; IUFD, intrauterine fetal death; LDH, lactate dehydrogenase; LMIC, low- and middle-income country; $MgSO_4$, magnesium sulfate; sB7-H4, soluble B7-H4; sEng, soluble endoglin; sFlt-1, soluble fms-like tyrosine kinase-1; TMA, thrombotic microangiopathy; TNF-α, tumor necrosis factor-alpha; TPE, therapeutic plasma exchange. Study sizes are as reported by the cited articles.

4. Discussion

4.1. Persistence of postpartum Class 1 HELLP syndrome

Postpartum Mississippi Class 1 HELLP syndrome with intrauterine fetal death and overlapping Swansea-positive AFLP features is among the most lethal emergencies in obstetric critical care. When conservative management fails, the risk is high. Fulminant disseminated intravascular coagulation, subcapsular hepatic hemorrhage, acute kidney injury, and maternal death all become real possibilities.[26,27] In pregnancies with mild-to-moderate preeclampsia or Class 2–3 HELLP syndrome, delivery usually settles the matter. Removing the fetus and placenta takes away the main source of anti-angiogenic trophoblastic debris, and endothelial recovery and platelet rebound typically follow within 48 to 72 hours. Our patient did not. At Epoch T_1 the platelet count fell by −40.43%, from 47.0 × 10^3/μL at admission to a nadir of 28.0 × 10^3/μL. This happened despite vaginal delivery of the stillborn fetus, 24 hours of $MgSO_4$ neuroprophylaxis, and intravenous methylprednisolone (62.5 mg every 12 hours). Placental expulsion alone does not immediately end the intravascular microangiopathic cascade in severe Class 1 disease.[5,28] The reason lies in what stays behind. Large amounts of placenta-derived sFlt-1, sEng, sB7-H4, syncytiotrophoblast microparticles, FasL, and cytokines (TNF-α, IL-6) stay in the maternal plasma. They persist. Long biological half-lives and self-amplifying endothelial feedback loops keep driving microvascular thrombosis and organ injury well after delivery (Figure 5).

4.2. Mechanisms of plasma exchange

One session of FFP-based TPE was followed by recovery of platelets and liver together. Thrombocytopenia reversed (+310.71%, from 28.0 × 10^3/μL to 115.0 × 10^3/μL), and hepatobiliary injury improved (AST −90.35% to 41.0 U/L; ALT −86.42% to 36.0 U/L; total bilirubin −84.19% to 2.15 mg/dL; LDH −56.28% to 240.0 U/L). A possible explanation, not tested here, lies in two mechanisms: bulk macromolecular clearance and enzymatic-hemostatic replenishment.[29] First, non-selective centrifugal or membrane plasma separation physically removes large anti-angiogenic proteins. These are sFlt-1 (about 100–110 kDa), sEng (about 65 kDa), and the checkpoint ligand sB7-H4. The circulating sFlt-1/PlGF ratio falls. Free VEGF and PlGF can then engage endothelial receptors again and restore nitric oxide-mediated vasodilation. Second, TPE removes pro-inflammatory cytokines (TNF-α, IL-6, IL-1β), apoptotic FasL, damage-associated molecular patterns (DAMPs), cell-free hemoglobin, and albumin-bound conjugated and unconjugated bilirubin. These sustain hepatic sinusoidal obstruction syndrome and renal tubular injury.[30] Third, the isovolemic infusion of donor FFP replaces functional ADAMTS13 immediately. The enzyme cleaves hyperadhesive ULvWF multimers and halts microvascular platelet consumption. The FFP also replenishes fibrinogen, clotting factors II, V, VII, VIII, IX, and X, antithrombin, protein C, and albumin, without causing volume overload.[31,32]

The case teaches one clinical lesson: TPE is useful where Mississippi Class 1 HELLP syndrome and acute fatty liver of pregnancy (AFLP) overlap.[25,33,34] Our patient had classic Class 1 HELLP features (new-onset hypertension 140/93 mmHg, platelets 47.0 → 28.0 × 10^3/μL, AST 425.0 U/L, LDH 549.0 U/L). She also had a Swansea score of 6/15 and profound conjugated hyperbilirubinemia (total bilirubin 13.60 mg/dL, direct bilirubin 12.74 mg/dL [93.68%], albumin 2.70 g/dL, WBC 14.30 × 10^3/μL, and IUFD). This is the HELLP–AFLP overlap spectrum. Tertiary obstetric ICUs often meet it. Pure HELLP syndrome usually produces modest unconjugated hyperbilirubinemia (1.5–4.0 mg/dL) from intravascular hemolysis. Bilirubin above 10.0 mg/dL with a direct fraction over 90%

means more than hemolysis. Inflammatory and ischemic injury impairs the canalicular bile salt export pump (BSEP) and multidrug resistance-associated protein 2 (MRP2), and microvesicular mitochondrial dysfunction typical of AFLP adds to it.[35] Telling refractory postpartum HELLP from acquired TTP and complement-mediated aHUS in real time is almost impossible in most LMIC hospitals. Rapid STAT ADAMTS13 activity and complement gene panels are simply not available. FFP-based TPE has been used in severe HELLP syndrome, AFLP, and TTP. Early rescue TPE may therefore be a reasonable step in this setting while the final diagnosis is clarified.



Figure 5. Proposed multi-tier pathophysiological and extracorporeal clearance cascade in refractory postpartum HELLP–AFLP overlap treated with rescue TPE (5 tiers, 15 nodes). The mechanisms in Tiers I to III and V were not measured in this patient. Tier I: Defective uteroplacental spiral artery remodeling at 34^{+1} weeks gestation, intrauterine fetal death (IUFD), and massive release of anti-angiogenic factors (sFlt-1, sEng, sB7-H4) and pro-inflammatory cytokines (TNF-α, IL-6, FasL). Tier II: Systemic endothelial glycocalyx shedding, hypoalbuminemia (2.70 g/dL), acquired ADAMTS13 depletion, ULvWF-mediated microvascular platelet consumption (47.0 × 10^3/μL), and microangiopathic hemolysis (LDH 549.0 U/L). Tier III: Hepatic sinusoidal obstruction syndrome, zonal hepatocyte necrosis (AST 425.0 U/L, ALT 265.0 U/L), canalicular cholestasis (bilirubin 13.60 mg/dL, direct 12.74 mg/dL), and Swansea score 6/15 AFLP overlap. Tier IV: Postpartum refractory nadir at T_1 (platelets 28.0 × 10^3/μL despite delivery, $MgSO_4$, and methylprednisolone 62.5 mg q12h) and urgent rescue TPE with Fresh Frozen Plasma (FFP) within the 24–48 h window. Tier V: Dual-compartment kinetic recovery (ADAMTS13 restoration, ULvWF cleavage, sFlt-1/cytokine/bilirubin clearance, +310.71% platelet rebound to 115.0 × 10^3/μL, and Day 5 discharge without end-organ sequelae).

4.3. Corticosteroids and the 24–48 hour window

Why did high-dose corticosteroids fail? The patient received intravenous methylprednisolone 62.5 mg every 12 hours (125 mg/day) together with $MgSO_4$ neuroprotection. Even so, the platelet count fell by −40.43%, from 47.0 × 10^3/μL at T_0 to 28.0 × 10^3/μL at T_1. Corticosteroids act through genomic and non-genomic anti-inflammatory routes. They inhibit nuclear factor kappa B (NF-κB) transcription, stabilize endothelial tight junctions, and reduce splenic platelet sequestration. Their limits are clear. Updated systematic reviews and meta-analyses of randomized trials, however, show that corticosteroids alone do not consistently lower maternal mortality or severe multiorgan morbidity in Class 1

HELLP syndrome once fulminant TMA is established. They suppress new cytokine transcription only after a latency of 12 to 24 hours. Steroids cannot physically clear preformed intravascular pools of sFlt-1, sEng, ULvWF multimers, free hemoglobin, or conjugated bilirubin. They also cannot restore exhausted ADAMTS13 activity or hepatic coagulation factors.[17]

Waiting 72 to 96 hours for a delayed steroid response may be dangerous. The platelet count had already fallen below $30.0 \times 10^3/\mu L$. The mother is exposed to serious morbidity, including stroke, hepatic rupture, and acute renal failure.[36,37] Recent cohort data from Karaaslan et al. and Chowdhry et al. indicate that the benefit of TPE depends on timing.[5,6] Survival and organ recovery were best when plasmapheresis began within the 24-to-48-hour postpartum window, in patients with persistent Class 1 thrombocytopenia or rising or refractory hyperbilirubinemia. In our patient, TPE was started at Epoch T_1 (24 hours post-delivery). The platelet slope turned from $-19.0 \times 10^3/\mu L$/day to a net regeneration velocity of $+29.0 \times 10^3/\mu L$/day (+310.71% rebound to $115.0 \times 10^3/\mu L$). Bilirubin clearance rose from −17.94% before TPE to −80.73% after it. She recovered fully. She was home by Day 5.

4.4. Hepatobiliary recovery

The hepatobiliary course shows how sinusoidal obstruction and cholestatic injury resolve after plasma exchange. At admission (T_0), AST was 425.0 U/L (13.71 × ULN), ALT 265.0 U/L (7.79 × ULN), and the De Ritis ratio (AST/ALT) 1.60. In pregnancy-associated TMA, an AST/ALT ratio above 1.5 reflects two processes. Zone 3 centrilobular hepatocytes hold more mitochondrial AST and are especially vulnerable to sinusoidal microthrombotic hypoxia. Mechanical hemolysis adds to the effect. Red cells torn across microvascular fibrin strands release intra-erythrocytic AST and LDH (549.0 U/L) into plasma. After delivery and early ICU stabilization ($T_0 \rightarrow T_1$), placental FasL influx stopped, and AST and ALT fell partly to 159.0 U/L and 108.0 U/L (De Ritis ratio 1.47). Total bilirubin did not follow. It stayed at 11.16 mg/dL (9.30 × ULN), against 13.60 mg/dL at T_0.[38]

Transaminases fell early. Severe hyperbilirubinemia persisted at T_1. This split may reflect cholestatic hepatocyte stunning and sinusoidal fibrin deposition in HELLP–AFLP overlap; no histology was available. Hydrophobic bile acids and conjugated bilirubin build up inside hepatocytes. They act as detergents on mitochondrial membranes, impair ATP-dependent canalicular transport through MRP2 and BSEP, and sustain apoptosis even after the placenta is gone.[39,40] Plasma exchange at T_1 may have removed protein-bound and circulating bilirubin and inflammatory inhibitors of bile transport (TNF-α and IL-6); neither was measured. Total bilirubin then fell by −80.73% to 2.15 mg/dL at T_4 (−2.86 mg/dL/day overall), and the De Ritis ratio returned to 1.14 (AST 41.0 U/L, ALT 36.0 U/L). The baseline ultrasound showed mild splenomegaly and mild right-sided hydronephrosis. These may reflect splenic sequestration of red cells and the compressive ureterohydronephrosis of late pregnancy. The intact Glisson's capsule allowed safe vaginal delivery after Foley balloon and misoprostol induction.

4.5. Health-system considerations and limitations

From a health-systems and anesthesiology-intensive care view, the rescue of this high-risk primiparous mother within a 5-day admission suggests a possible role for a structured multidisciplinary obstetric TMA protocol in Indonesian tertiary referral hospitals; no cost data were collected. In LMIC settings, HELLP syndrome prevalence reaches 1.55%.[1] Patients often arrive late, with IUFD and severe jaundice. Long ICU stays with dialysis-requiring AKI, mechanical ventilation, and massive transfusion are costly. They strain hospitals with limited resources.[41-43] After single-session FFP-based TPE at the 24-hour postpartum refractory checkpoint (T_1), this patient did not develop overt DIC or renal failure and did not need continuous renal replacement therapy (CRRT) or prolonged ventilation; she was discharged on Day 5. By comparison, a published series of nine plasma-exchange patients included women who stayed longer in hospital and needed hemodialysis.[6]

From these findings and the literature we suggest a five-point approach for consideration in tertiary obstetric ICUs that manage severe HELLP–AFLP overlap. (1) On admission, stratify with both the Mississippi Triple-Class system and the 15-point Swansea score, and exclude subcapsular hematoma with bedside hepatobiliary ultrasonography. (2) Deliver the fetus and placenta promptly with goal-directed hemostatic support, using vaginal induction when the hepatic capsule is intact and obstetric conditions are favorable. (3) Give standard neuroprotection with intravenous $MgSO_4$ and anti-inflammatory treatment with intravenous methylprednisolone. (4) Audit the Δ% trajectories of platelets and bilirubin every 12 to 24 hours after delivery. A platelet count below $30.0–50.0 \times 10^3/\mu L$, or no improvement within 24–48 hours, could prompt consideration of ASFA Category III rescue TPE with FFP replacement. (5) Arrange structured cardiovascular and renal follow-up after discharge. The limitations are plain. This is a single-patient case report, so it cannot give population-level comparative risk ratios. Larger registries are needed. Specialized assays for the serum sFlt-1/PlGF ratio, quantitative ADAMTS13 activity, and genetic complement or LCHAD mutations were unavailable in the acute emergency setting. After TPE, fractionated direct and indirect bilirubin and leukocyte sub-panels at T_1–T_4 were followed only through total bilirubin and core clinical recovery endpoints. Future prospective multicenter trials in Indonesian academic centers should standardize biomarker-guided thresholds for starting TPE in obstetric critical care.

5. Conclusion

Postpartum Mississippi Class 1 HELLP syndrome that overlaps with Swansea-positive acute fatty liver of pregnancy (Swansea score 6/15) and intrauterine fetal death is a life-threatening obstetric thrombotic microangiopathy. It can progress quickly. Delivery, magnesium sulfate neuroprotection, and high-dose corticosteroids may not stop it. This case report shows what serial monitoring can detect. In our patient, refractory microangiopathic deterioration appeared as a −40.43% platelet drop to a nadir of $28.0 \times 10^3/\mu L$ and persistent bilirubin of 11.16 mg/dL at 24 hours after delivery. Single-session rescue Therapeutic Plasma Exchange (TPE) with Fresh Frozen Plasma (FFP), started within 24 to 48 hours after delivery, was followed by rapid reversal of the laboratory features of the thromboinflammatory cascade. Platelets rebounded by +310.71% to $115.0 \times 10^3/\mu L$ (+144.68% above admission). LDH fell by −56.28% (549.0 to 240.0 U/L), AST by −90.35% (425.0 to 41.0 U/L), and ALT by −86.42% (265.0 to 36.0 U/L). Total bilirubin cleared by −84.19% (13.60 to 2.15 mg/dL). She recovered fully. She left hospital on Day 5 without end-organ sequelae. Prospective multicenter studies should define standardized kinetic triggers for early extracorporeal plasma exchange in refractory obstetric thrombotic microangiopathies.

Declarations

Ethics Approval and Consent to Participate

This case report was reviewed and approved by the CMHC Research Center Ethics Committee, Indonesia (protocol number 2026/0418) and followed the Declaration of Helsinki and the institutional guidelines of Dr. Moewardi Regional General Hospital.

Consent for Publication

Written informed consent was obtained from the patient and her legal next-of-kin for publication of de-identified clinical data, serial laboratory measurements, and sonographic findings.

Availability of Data and Materials

All longitudinal clinical, hemodynamic, hematological, and biochemical data analyzed in this report are included in the article (Tables 1–5; Figures 1–5).

Competing Interests

The authors declare no financial, commercial, or professional conflicts of interest related to the research, authorship, or publication of this article.

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Authors' Contributions

ES: Conceptualization, Methodology, Validation, Supervision, and Writing – review & editing; MARH: Investigation, Data curation, Formal analysis, Visualization, and Writing – original draft.

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Generative Artificial Intelligence Disclosure

No generative artificial intelligence was used in the study design, data collection, analysis, or interpretation of the findings.

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