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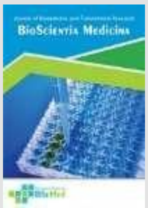

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Therapeutic Plasma Exchange as Adjuvant Rescue Therapy for Weil's Disease-Associated Acute Liver Failure in a Hemodialysis-Dependent Patient: A Case Report

Ardana Tri Arianto[1*], Aura Ihsaniar[1], Lichte Christian Purbono[1]

[1]Department of Anesthesiology and Intensive Therapy, Universitas Sebelas Maret, Surakarta, Indonesia

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***Corresponding author:**
Ardana Tri Arianto

E-mail address:
ardana@staff.uns.ac.id

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A B S T R A C T

Background: Weil's disease, the severe form of leptospirosis, manifests as a triad of jaundice, renal failure, and hemorrhage. In patients with pre-existing end-stage renal disease (ESRD), the management of superimposed acute liver failure (ALF) is exceptionally challenging due to altered pharmacokinetics, fluid intolerance, and the inability of standard hemodialysis to clear protein-bound hepatic toxins. **Case presentation:** We present a 32-year-old anuric male with ESRD on maintenance hemodialysis who presented with fever, jaundice, and altered mental status following floodwater exposure. He developed severe metabolic encephalopathy (GCS E2V2M4), profound coagulopathy (INR 6.04), and hyperbilirubinemia (Total Bilirubin 18.31 mg/dL). Following the failure of broad-spectrum antibiotics and sustained low-efficiency dialysis (SLED) to halt clinical deterioration, two sessions of therapeutic plasma exchange (TPE) were initiated as salvage therapy. The intervention utilized 100% fresh frozen plasma (FFP) replacement to address hemostatic failure. TPE resulted in rapid biochemical clearance and clinical stabilization. Post-intervention, the INR decreased from 6.04 to 1.57 (74% reduction), Total bilirubin declined from 18.31 to 5.57 mg/dL (69.5% reduction), and platelet counts recovered from 45,000 to 142,000/µL. Neurological status normalized (GCS 15) within 48 hours of the second session. **Conclusion:** TPE served as an effective bridge to recovery by clearing albumin-bound toxins and restoring coagulation factors in a high-risk patient where standard renal replacement was insufficient.

1. Introduction

Leptospirosis, a ubiquitous zoonotic infection caused by the pathogenic spirochete *Leptospira interrogans*, persists as a formidable public health challenge, particularly within the equatorial belt where climatic conditions favor its transmission.[1] While historically categorized as an occupational hazard affecting agricultural workers and veterinarians, the epidemiological landscape of leptospirosis has shifted dramatically. It has emerged as a disease of urbanization and climate change, frequently precipitating outbreaks in the wake of heavy rainfall and flooding in densely populated tropical regions.[2] The clinical presentation of this spirochetosis is notoriously protean, ranging from a subclinical, flu-like illness to a catastrophic multi-system failure. While the vast majority of infections are self-limiting and resolve with minimal intervention, a critical subset of patients—approximately 10% to 15%—progress to the fulminant manifestation historically eponymized as Weil's disease. This severe syndrome is clinically defined by a devastating triad: profound hepatic dysfunction manifesting as deep jaundice, acute kidney injury

(AKI) often requiring dialysis, and a hemorrhagic diathesis resulting from severe coagulopathy.[3] The mortality trajectory of Weil's disease is alarming; while baseline fatality rates hover between 10% and 50%, the superimposition of pulmonary hemorrhage or sepsis-associated liver dysfunction (SALD) can elevate mortality to levels exceeding 70%, rendering it one of the most lethal infectious syndromes in critical care medicine.

To understand the gravity of severe leptospirosis, one must dissect the complex pathophysiological cascade that follows the spirochetemia phase. The virulence of *Leptospira* is not merely a consequence of direct bacterial invasion but is significantly driven by a dysregulated and exuberant host immune response.[4] Upon entering the bloodstream, the spirochetes trigger a massive release of pro-inflammatory mediators, including tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-1 beta (IL-1β). This phenomenon, widely termed a "cytokine storm," mirrors the immunopathology seen in severe bacterial sepsis, leading to systemic endothelial activation. The endothelium, usually a regulator of vascular tone and hemostasis, transforms into a pro-coagulant and pro-inflammatory surface. This results in widespread vasculitis, capillary leakage, and catastrophic microcirculatory collapse. At the cellular level, mitochondrial dysfunction ensues, depriving vital organs of oxidative phosphorylation capability. In the liver, this pathological sequence manifests uniquely. Unlike viral hepatitis, which causes massive hepatocellular necrosis, leptospirosis typically induces severe cholestasis through the disruption of hepatocyte intercellular junctions and transporter downregulation. This results in "sepsis-associated cholestasis," characterized by hyperbilirubinemia that is disproportionate to the elevation of liver enzymes, coupled with a profound failure of synthetic function. The clinical sequelae are life-threatening: the accumulation of neurotoxic bilirubin leads to hepatic encephalopathy, while the failure to synthesize clotting factors precipitates a consumptive coagulopathy, leaving the patient defenseless against spontaneous hemorrhage.[5]

The management of severe leptospirosis, already a Herculean task in healthy individuals, becomes exponentially more complex when superimposed upon pre-existing comorbidities. Among these, end-stage renal disease (ESRD) presents the most intricate therapeutic dilemma. Patients with ESRD are not merely individuals with failed kidneys; they possess a unique and fragile physiological phenotype characterized by "uremic milieu." Chronic uremia induces a state of persistent, low-grade inflammation and oxidative stress, leading to profound structural alterations in the vascular bed. This phenomenon, often described as chronic uremic endothelial dysfunction, acts as a "first hit" to the patient's physiology. The endothelium in these patients is already stiffened, permeable, and prone to dysfunction. When the acute vasculitis of leptospirosis provides the "second hit," the cumulative insult leads to a rapid and often irreversible disintegration of microcirculatory integrity. Consequently, the risk of multi-organ dysfunction syndrome (MODS) in ESRD patients is significantly higher than in the general population. Furthermore, the presence of anuria (total absence of urine output) strips the clinician of the primary tool used in sepsis management: aggressive fluid resuscitation. In a standard patient, hypotension is countered with fluids to restore perfusion; in an ESRD patient, such fluid loading risks precipitating immediate pulmonary edema and hypoxic respiratory failure. Thus, the clinician is trapped between the Scylla of septic shock and the Charybdis of volume overload.[6]

When an ESRD patient develops Weil's disease, the immediate reflex is to optimize renal replacement therapy. However, this approach exposes the fundamental limitations of standard extracorporeal platforms in the setting of liver failure. Conventional therapies, such as high-flux hemodialysis (HD) or sustained low-efficiency dialysis (SLED), rely predominantly on the physical principles of diffusion and convection across a semi-permeable membrane.

These modalities are exceptionally efficient at removing small, water-soluble toxins with low molecular weights, such as urea, creatinine, and potassium.[7] However, the toxic milieu of Weil's disease is dominated by a different class of molecules. The primary drivers of toxicity—bilirubin, bile acids, hydrophobic endotoxins, and aromatic amino acids—are protein-bound, specifically circulating tightly attached to albumin. The albumin-bilirubin complex has a molecular mass of approximately 66,000 Daltons (66 kDa), which far exceeds the pore size and molecular weight cut-off of standard high-flux dialysis membranes (typically restricted to 15-20 kDa). Consequently, while SLED effectively corrects the uremic component of the disease, it is bio-physically incapable of clearing the hepatic toxins. As these protein-bound toxins accumulate, they exert direct neurotoxicity, driving the patient deeper into metabolic encephalopathy, and perpetuate vasodilation, worsening hemodynamic instability. This creates a therapeutic ceiling where the patient remains encephalopathic and coagulopathic despite biochemically "adequate" dialysis numbers.

Faced with the failure of standard renal support, clinicians must look toward alternative extracorporeal blood purification therapies (EBPT). Therapeutic plasma exchange (TPE) has emerged as a promising, albeit underutilized, modality in this context.[8] Unlike hemodialysis, which filters the blood, TPE functions on the principle of separation and extraction. By centrifuging blood to separate cellular components from plasma, TPE removes the patient's entire plasma volume and replaces it with a physiological substitute, such as fresh frozen plasma (FFP) or albumin. This mechanism confers a distinct advantage: the removal is non-selective regarding molecular size. TPE effectively eliminates large molecular weight substances (>50,000 kDa), immune complexes, and, crucially, albumin-bound toxins. In the context of Weil's disease, TPE theoretically achieves three simultaneous goals: "cytokine debulking" by physically removing the circulating mediators of the cytokine storm; "hepatic detoxification" by extracting the albumin-bound bilirubin and bile acids; and "hemostatic resuscitation" by replacing the depleted plasma with FFP rich in coagulation factors and natural anticoagulants. While the American Society for Apheresis (ASFA) guidelines currently recognize TPE as a Category III indication for liver failure and sepsis—implying that the optimum role of apheresis is not established and decision-making should be individualized—its application in the specific intersection of leptospirosis and ESRD remains a frontier of critical care medicine.[9]

The intersection of these three clinical entities—severe leptospirosis, acute liver failure, and pre-existing end-stage renal disease—creates a "perfect storm" of physiological derangement that is rarely documented in medical literature. To our knowledge, fewer than five cases describing this specific triad have been published in the last decade, and even fewer have detailed the granular kinetics of recovery following apheresis in an anuric patient. This paucity of data leaves clinicians without a clear roadmap when standard therapies fail.[10] Therefore, this case report aims to bridge this significant knowledge gap by describing the successful implementation of Therapeutic Plasma Exchange as an adjuvant rescue therapy in a hemodialysis-dependent patient presenting with life-threatening Weil's disease. By providing a detailed analysis of the clinical timeline, biochemical response, and fluid management strategy, we seek to demonstrate the efficacy of TPE in reversing severe coagulopathy and encephalopathy. The novelty of this study lies in its proof-of-concept that TPE can serve as a critical "immunological and toxicological reset," successfully bridging a patient to recovery in a scenario where standard renal replacement therapies are physiologically insufficient.

2. Case Presentation

A 32-year-old Asian male presented to the Emergency Department (ED) of Dr. Moewardi Regional General Hospital with a three-day history of high-grade fever (39.5°C), progressive dyspnea, and rapidly deteriorating consciousness. Family members reported that the patient had become increasingly lethargic and confused over the preceding 24 hours. Notably, the patient had a history of end-stage renal disease (ESRD) secondary to chronic glomerulonephritis and had been strictly anuric on maintenance hemodialysis (twice weekly) for three years. The patient resided in a flood-prone urban area. Two weeks prior to symptom onset, he participated in community flood-relief activities, involving prolonged wading through stagnant water with visible skin abrasions on his lower extremities. This history was highly suggestive of leptospiral exposure.

Upon admission to the Intensive Care Unit (ICU), the patient appeared toxic and critically ill. Glasgow Coma Scale (GCS) was initially 14 (E4V4M6) but deteriorated within 6 hours to 10 (E2V3M5). Pupils were isochoric but sluggish. Asterixis was present. Hemodynamics evaluation revealed blood pressure 110/70 mmHg (Mean Arterial Pressure 83 mmHg), Heart Rate 105 beats/min (sinus tachycardia). Respiratory examination showed tachypneic (28 breaths/min), oxygen saturation (SpO_2) 94% on 4 L/min nasal cannula. Lung auscultation revealed bibasilar rhonchi. Sclerae were deeply icteric. Skin examination showed diffuse petechiae on the shins and generalized jaundice. Hepatomegaly was noted with a liver span of 16 cm.

Initial laboratory investigations unveiled a catastrophic picture of multi-system organ failure consistent with severe sepsis. Hematological analysis demonstrated a marked leukocytosis (WBC 22,000/µL) with neutrophil predominance and profound thrombocytopenia (Platelets 45,000/µL), suggesting a consumptive process superimposed on anemia (Hb 9.2 g/dL). The hepatic profile was indicative of fulminant injury, characterized by deep jaundice with a Total Bilirubin of 18.31 mg/dL (Direct 9.80 mg/dL) and massive hepatocellular necrosis, with both AST (1,011 U/L) and ALT (1,085 U/L) exceeding 1,000 U/L. This liver dysfunction was accompanied by life-threatening coagulopathy, evidenced by a prothrombin time of 68.8 seconds, an INR of 6.04, and hypofibrinogenemia (120 mg/dL), raising concern for Disseminated Intravascular Coagulation (DIC) or severe synthetic failure. Renal parameters showed acute deterioration on the background of ESRD, with a BUN of 163 mg/dL and a Creatinine of 4.8 mg/dL, slightly elevated from the patient's baseline of 4.5 mg/dL. Definitive diagnosis was established via serology; Leptospira IgM ELISA was reactive, and the patient met the definition for presumptive leptospirosis with a Faine's Criteria score of 26 (Clinical: 12, Epidemiological: 10, Bacteriological: 4), while screening for Hepatitis A, B, C, Dengue, and Malaria returned negative results.

The clinical management commenced with a standard sepsis protocol, initiating Intravenous Ceftriaxone 2g daily to address the underlying leptospiral infection. Recognizing the patient's anuric end-stage renal disease (ESRD) status and admission hyperkalemia (5.8 mmol/L), urgent renal replacement therapy was prioritized. Sustained low-efficiency dialysis (SLED) was initiated at Hour 12 utilizing a low-velocity protocol—blood flow at 150 mL/min and dialysate flow at 300 mL/min—over a six-hour duration, achieving a net ultrafiltration of 1.5 liters to alleviate pulmonary congestion. However, this initial strategy proved insufficient to arrest the fulminant hepatic deterioration. By Hour 24, despite effective potassium correction, the patient's clinical trajectory worsened significantly: the Glasgow Coma Scale plummeted to 8 (E2V2M4), the INR remained critical at 5.8, and total bilirubin surged to 19.1 mg/dL. This rapid decline underscored the failure of standard diffusive clearance to mitigate the burden of protein-bound toxins and necessitated an immediate escalation to extracorporeal salvage therapy. Consequently, a multidisciplinary consensus was reached to initiate therapeutic plasma exchange (TPE) via a right internal jugular vein double-lumen catheter using the COBE® Spectra Apheresis System. The rescue prescription was aggressive, targeting a large-volume exchange of 1.5 plasma volumes (calculated as approximately 3,200 mL) per session to maximize toxin removal.

Table 1. Clinical Findings Summary
Admission Data: Severe Multi-Organ Involvement

Day 1 ICU

PARAMETER	VALUE	INTERPRETATION
I. HEMATOLOGY PROFILE		
WBC	**22,000** /µL	Leukocytosis (Neutrophilic)
Platelets	**45,000** /µL CRIT	Severe Thrombocytopenia
Hemoglobin	**9.2** g/dL	Normocytic Anemia
II. HEPATIC FUNCTION		
Total Bilirubin	**18.31** mg/dL CRIT	Deep Jaundice
Direct Bilirubin	**9.80** mg/dL	Cholestatic pattern
AST (SGOT)	**1,011** U/L	Massive necrosis (>1k)
ALT (SGPT)	**1,085** U/L	Massive necrosis (>1k)
III. COAGULATION PROFILE		
INR	**6.04** HIGH RISK	Imminent Hemorrhage
PT	**68.8** sec	Significantly prolonged
aPTT	**40.5** sec	Moderately prolonged
Fibrinogen	**120** mg/dL	Hypofibrinogenemia
IV. RENAL (ESRD BACKGROUND)		
BUN	**163** mg/dL	Acute-on-chronic
Creatinine	**4.8** mg/dL	Baseline (4.5 mg/dL)
V. MICROBIOLOGY		
Lepto IgM	**Reactive**	Acute Infection
Faine's Score	**26** Points	Presumptive Positive
Viral Screen	**Negative**	Hep A/B/C, Dengue neg

Crucially, 100% fresh frozen plasma (FFP) was selected as the replacement fluid—a strategic decision designed to simultaneously replenish depleted coagulation factors (II, VII, IX, X) and natural anticoagulants (Protein C and S) in the setting of profound synthetic liver failure. Given the patient's complete anuria, fluid mechanics were managed with precision; the device was programmed for a strictly isovolemic balance (Input equals Output). To counteract the obligatory volume load from citrate anticoagulation and line flushes (approximately 300 mL), a contingency for sequential ultrafiltration (SCUF) was established immediately post-procedure. Anticoagulation safety was paramount due to the risk of impaired hepatic citrate metabolism; Citrate-Dextrose Solution A (ACD-A) was administered at a reduced citrate-to-blood ratio of 1:40, with continuous hourly monitoring of the calcium gap (Total/Ionized Calcium ratio < 2.5) and concurrent calcium gluconate titration to prevent citrate toxicity. Two successful sessions were completed at Hour 36 (processing 3,250 mL with 12 units FFP) and Hour 60 (processing 3,269 mL with 12 units FFP) to address toxin rebound, with the patient maintaining hemodynamic stability throughout without the need for vasopressor support (Figure 1).

The completion of the second TPE session marked a definitive inflection point in the patient's clinical trajectory, precipitating a rapid and profound recovery. Neurologically, the severe metabolic encephalopathy resolved swiftly; the patient regained full consciousness and orientation, achieving a normalized Glasgow Coma Scale of 15 (E4V5M6) by Hour 72, a finding indicative of the effective clearance of neurotoxic accumulation. This clinical awakening was paralleled by substantial physiological restitution, evidenced biochemically by the precipitous decline in hepatic retention markers and the restoration of hemostatic integrity. With the imminent threat of fulminant liver failure resolved and hemodynamic stability assured, the patient was transferred out of the Intensive Care Unit on Day 5. He continued to demonstrate sustained improvement and was discharged from the hospital on Day 10, successfully resuming his pre-morbid maintenance hemodialysis regimen without residual sequelae.

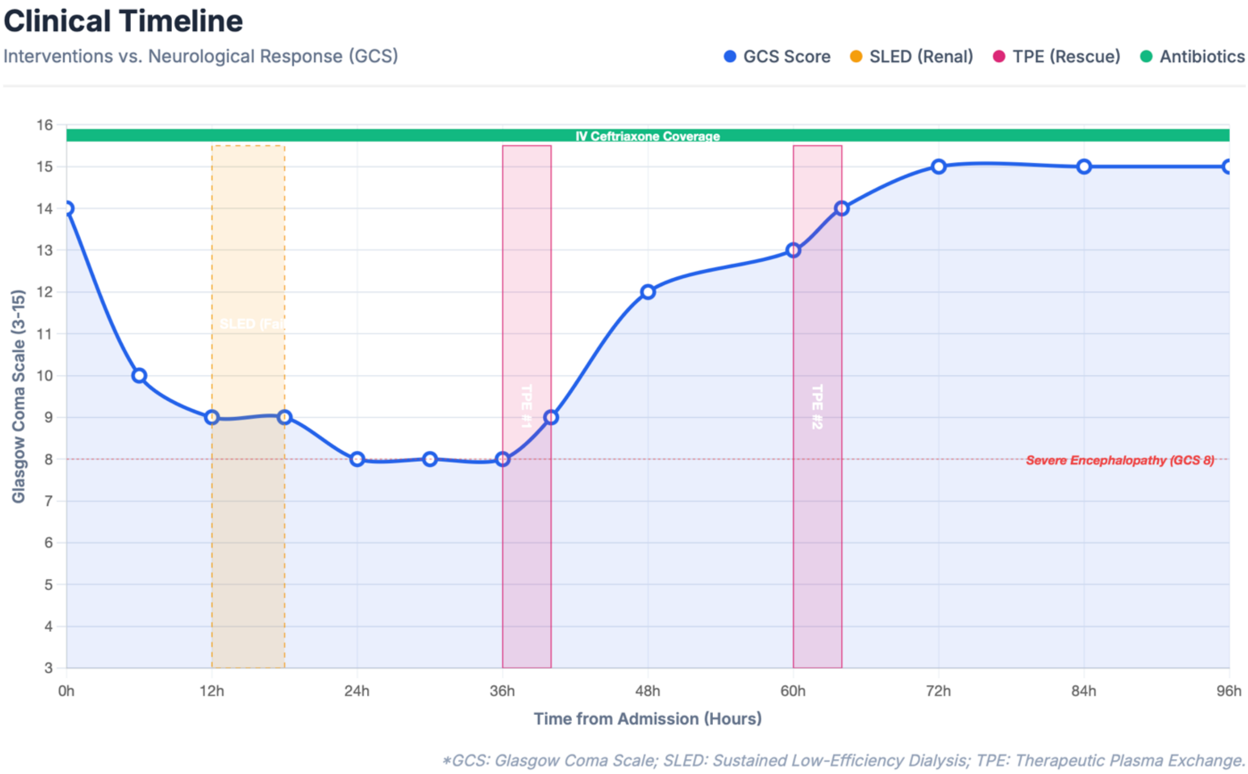

Figure 1. Clinical timeline of interventions and response.

Table 2. Evolution of Laboratory Parameters

Pre- and Post-Intervention Kinetic Analysis

SLED (Hour 12) | TPE x2 (Hour 36, 60)

PARAMETER	REF. RANGE	ADMISSION (PRE-SLED)	PRE-TPE 1 (HOUR 36)	POST-TPE 1 (HOUR 40)	PRE-TPE 2 (REBOUND)	POST-TPE 2 (HOUR 64)	FINAL OUTCOME (% REDUCTION)
COAGULATION PROFILE							
INR	0.8-1.2	6.04	5.92	1.85	2.10	1.57	74% Reduction
Platelets (µL)	150-450k	45,000	42,000	65,000	88,000	142,000	Normalized
Fibrinogen (mg/dL)	200-400	120	115	210	205	280	Normalized
HEPATIC FUNCTION							
Total Bilirubin (mg/dL)	0.3-1.2	18.31	19.10	12.40	14.50	5.57	69.5% Reduction
AST (U/L)	< 35	1,011	1,050	420	480	85	91.9% Reduction
ALT (U/L)	< 45	1,085	1,100	550	610	196	81.9% Reduction
RENAL & METABOLIC (ESRD)							
Creatinine (mg/dL)	0.6-1.2	4.8	3.2*	2.9	3.5	3.7	ESRD Baseline
INFLAMMATORY MARKERS							
CRP (mg/L)	< 5	145	152	88	95	32	78% Reduction
Procalcitonin (ng/mL)	< 0.05	12.4	12.8	6.5	7.2	2.1	83% Reduction

** Note: The reduction in Creatinine observed at Pre-TPE 1 was due to the SLED session performed at Hour 12. TPE itself does not significantly clear Creatinine.*

3. Discussion

This case report illuminates a successful navigational strategy through a clinical scenario often deemed insurmountable: the collision of fulminant Weil's disease, acute liver failure (ALF), and pre-existing end-stage renal disease (ESRD).[11] The survival of this patient serves as a proof-of-concept for the utility of therapeutic plasma exchange (TPE) not merely as a supportive measure, but as a decisive adjuvant rescue therapy. The clinical trajectory—characterized by a precipitous decline despite maximal standard care, followed by an immediate and sustained recovery post-apheresis—strongly suggests that TPE addressed specific pathophysiological derangements that standard renal replacement therapies (SLED) and antimicrobial agents could not mitigate. The key finding is the distinct temporal correlation between the initiation of TPE and the rapid reversal of "irreversible" coagulopathy and metabolic encephalopathy, a phenomenon that warrants a deep dive into the pharmacokinetics of toxin clearance and the hemodynamics of the anuric patient.[12]

The stark contrast between the failure of Sustained Low-Efficiency Dialysis (SLED) and the success of TPE in this patient can be elucidated by examining the molecular characteristics of the toxic milieu in severe leptospirosis (Figure 2).[13] In the setting of ALF, the circulating plasma becomes saturated with a complex array of neurotoxins (including ammonia, endogenous benzodiazepines, and aromatic amino acids), bile acids, and inflammatory mediators. Crucially, the most potent of these—specifically unconjugated bilirubin and hydrophobic bile salts—are highly protein-bound, circulating predominantly in tight association with serum albumin.

Standard renal replacement modalities, such as high-flux hemodialysis or SLED, operate fundamentally on the principles of diffusion and convection across a semi-permeable membrane. These synthetic membranes are engineered with specific pore sizes designed to mimic the glomerular filtration barrier, typically allowing the passage of small to middle-sized molecules.[14] The molecular weight cut-off for a standard high-flux membrane generally hovers between 15 to 20 kilodaltons (kDa). While this is sufficient for clearing water-soluble uremic retention solutes like urea (0.06 kDa) and creatinine (0.11 kDa), it is wholly inadequate for clearing albumin-bound toxins. The albumin-bilirubin complex, which drives the severe cholestatic jaundice and encephalopathy in Weil's disease, has a molecular mass of approximately 66 kDa [12]. This size discrepancy creates an absolute biophysical barrier; the toxic complex is simply too large to traverse the dialysis membrane. Consequently, while the SLED session in our patient effectively managed hyperkalemia and volume status, it left the protein-bound toxic load virtually untouched. This explains the clinical paradox observed at Hour 24: the patient was "renally optimized" (normal potassium, controlled urea) yet remained deeply encephalopathic and progressively icteric.[15]

Therapeutic plasma exchange overcomes this diffusive limitation by employing a fundamentally different separation logic. Rather than filtering blood based on pore size, TPE utilizes centrifugal force or large-pore filtration to separate the cellular components (red cells, white cells, platelets) from the plasma entirely. By removing the plasma, TPE indiscriminately eliminates all non-cellular components regardless of their molecular weight, encompassing everything from small ions to massive immune complexes and albumin-bound toxins. We analogize this to the "Squid Effect": if a tank of water is contaminated with ink (toxins), filtering it through a mesh (dialysis) might remove solid debris, but the water remains colored. TPE effectively drains the "ink-stained" water and replaces it with fresh, clear water (Fresh Frozen Plasma). By exchanging 1.5 plasma volumes, we effectively removed the "carrier" molecule (albumin) itself, along with its entire payload of associated toxins. This aligns with the "bio-logic" of artificial liver support systems, providing a rapid reduction in total bilirubin (from 18.31 to 5.57 mg/dL) that would be pharmacokinetically impossible with dialysis alone.[16]

The pathophysiology of severe leptospirosis is driven heavily by a dysregulated host immune response, often termed a "cytokine storm." The spirochetemia triggers a massive release of pro-inflammatory cytokines, particularly Interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and IL-1β, which mediate endothelial activation and microcirculatory collapse.[17] While specific cytokine assays were not performed in this case due to resource constraints, the drastic reduction in surrogate inflammatory markers—C-Reactive Protein (CRP) falling from 152 to 32 mg/L and Procalcitonin dropping from 12.4 to 2.1 ng/mL—strongly implies a dampening of the systemic inflammatory response. Theoretically, TPE achieves this via "cytokine debulking." By physically removing a large volume of plasma, the procedure eliminates the circulating pool of cytokines. This sudden reduction in intravascular concentration creates a steep concentration gradient between the extravascular tissue compartment and the blood, drawing cytokines out of the tissues and into the circulation where they can be cleared (or metabolized). This "washout" effect likely mitigated the direct cytotoxic effects of the inflammatory storm on hepatocytes and cerebral tissue, contributing to the rapid neurological recovery. Perhaps the most critical and clinically distinct benefit of TPE in this specific case was its role in hemostatic regulation. The patient presented with an INR of 6.04 and severe hypofibrinogenemia, placing him at imminent risk of fatal pulmonary or intracranial hemorrhage. In a patient with normal renal function, such coagulopathy might be managed via the "massive transfusion protocol"—the rapid infusion of multiple units of fresh frozen plasma (FFP).[18]

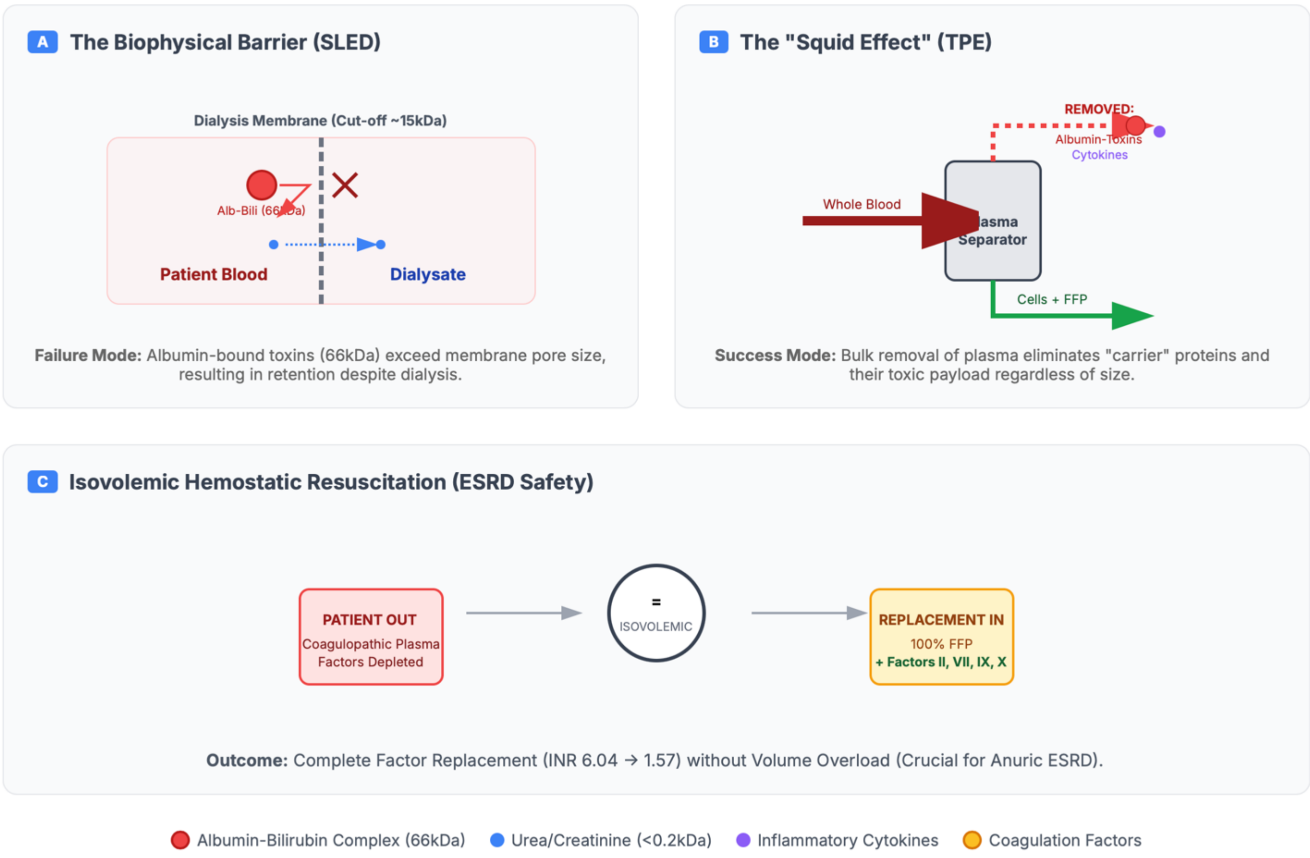

Figure 2. Mechanistic rationale of TPE.

However, in an anuric ESRD patient, this standard approach is fraught with peril. To correct an INR of >6.0 using simple transfusion would likely require 15-20 mL/kg of FFP, equating to a volume load of approximately 1200 to 1500 mL. In a patient with zero urine output who is already prone to pulmonary congestion, such a rapid volume expansion would almost certainly precipitate flash pulmonary edema and acute hypoxic respiratory failure. The clinician is thus trapped in a lethal dilemma: transfuse and cause lung failure, or withhold transfusion and risk fatal hemorrhage.[19] TPE provided an elegant physiological solution to this dilemma by decoupling factor replacement from volume expansion. By utilizing an isovolemic exchange protocol (Input = Output), we were able to remove 3,250 mL of coagulopathic, factor-deficient patient plasma and replace it simultaneously with 3,250 mL of factor-rich FFP. This massive exchange effectively replaced the patient's entire coagulation proteome. It replenished not only the pro-coagulant factors (II, VII, IX, X, and Fibrinogen) but also the essential anticoagulant proteins (Protein C and S) and ADAMTS13, which are synthesized in the liver and depleted in ALF. We observed a correction of INR from 6.04 to 1.57 within hours, a degree of correction that is difficult to achieve even with Prothrombin Complex Concentrates (PCC). PCCs typically contain only specific factors (II, VII, IX, X) and lack Factor V or fibrinogen, making them incomplete solutions for the broad synthetic failure of Weil's disease. Thus, TPE served as the only viable modality to restore hemostasis safely in this volume-intolerant patient.

A rigorous scientific analysis must address the potential confounders of antimicrobial therapy. *Leptospira interrogans* is highly sensitive to beta-lactams, and Intravenous Ceftriaxone was initiated immediately upon admission.[20] The natural history of treated leptospirosis often involves defervescence and gradual clinical improvement within 3 to 5 days. Skeptics might argue that the patient's recovery was merely the natural result of antibiotic efficacy rather than the TPE intervention.

However, the granular timeline of this case argues strongly against antibiotics being the sole driver of recovery. The "antibiotic window" usually shows a linear or gradual improvement. In contrast, our patient exhibited a distinct "U-shaped" clinical course. Between Hour 12 and Hour 36—well after the initiation of antibiotics—the patient continued to deteriorate significantly: his GCS dropped from 10 to 8, bilirubin rose, and coagulopathy worsened. This deterioration occurred despite the clearance of the bacteremia, suggesting that the organ failure was now being driven by the downstream toxic and inflammatory sequelae rather than the active infection itself. The sharp inflection point in the clinical curve occurred strictly after TPE Session 1 (Figure 1). The rapid normalization of the GCS and the immediate correction of the INR within hours of the procedure provide a temporal association that is too tight to be explained by the gradual mechanism of antibiotic-mediated bacterial clearance. This suggests that while antibiotics successfully treated the root cause (the infection), TPE was necessary to manage the overwhelming toxic payload that was perpetuating the organ failure.[16,17]

The implications of this case extend beyond the intensive care unit to the broader context of global health. Leptospirosis is a disease of poverty, disproportionately affecting low-to-middle-income countries (LMICs) in tropical regions where advanced medical infrastructure is often scarce. In high-resource settings, "Artificial Liver Support" might involve proprietary albumin-dialysis systems such as the Molecular Adsorbent Recirculating System (MARS) or Prometheus. While effective, these systems are prohibitively expensive, often costing in excess of $3,000 to $5,000 USD per session for the specific filters and circuits alone. Furthermore, they require specialized machinery and technical expertise that may not be available in rural or district hospitals. TPE, by contrast, utilizes standard apheresis equipment (or even manual exchange techniques in extreme settings) and widely available fluids (albumin or FFP). It is significantly more cost-effective and accessible in tertiary centers across the developing world. By demonstrating that TPE can match or exceed the theoretical benefits of MARS (toxin removal + hemostatic correction) in this context, this case supports the positioning of TPE as a pragmatic "bio-artificial liver" for severe tropical infections in resource-limited health systems.[19,20]

We acknowledge several limitations inherent to this report. First, as a single-case study (N=1), the findings limit broad causal inference and generalization. While the physiological rationale is sound, individual variations in response to TPE can be significant. Second, the "cytokine clearance" hypothesis remains theoretical in this specific case, as we lacked the laboratory capacity to perform serial assays of IL-6, TNF-α, or IL-10. Our conclusions regarding immunomodulation are inferred from the rapid decline in downstream markers (CRP, Procalcitonin) and clinical stabilization. Finally, the phenomenon of "toxin rebound" was evident in our data, where Total Bilirubin rose from 12.4 mg/dL post-Session 1 to 14.5 mg/dL pre-Session 2. This occurs because TPE clears only the intravascular compartment; toxins stored in the extravascular tissue re-equilibrate into the blood over time. This highlights that TPE is not a definitive "cure" but a temporizing bridge. It underscores the necessity of serial sessions to maintain the "toxicological window" open long enough for the liver's intrinsic regenerative capacity to recover. Future research should focus on establishing protocolized triggers—such as specific bilirubin thresholds or MELD scores—to guide the initiation and frequency of TPE in this population.

4. Conclusion

The management of severe Weil's disease in the presence of end-stage renal disease represents a formidable clinical challenge where standard treatment algorithms often falter. This case demonstrates that when the clinical picture is dominated by protein-bound toxemia and synthetic failure, standard renal replacement therapy is mechanistically insufficient. Therapeutic plasma exchange (TPE) with FFP replacement served not merely as a supportive measure but as a decisive adjuvant rescue therapy. Its success in this case was underpinned by three distinct physiological pillars: (1) Enhanced toxin clearance: It bypassed the molecular weight limitations of hemodialysis, effectively clearing the albumin-bound bilirubin and bile acids that were driving metabolic encephalopathy; (2) Isovolemic Hemostatic resuscitation: It allowed for the massive replenishment of coagulation factors and physiological anticoagulants, correcting a fatal coagulopathy without subjecting an anuric patient to the risks of volume overload and pulmonary edema; (3) The "Bridge to Recovery": It provided a critical temporal bridge, stabilizing the patient's multi-organ failure long enough for antibiotics to clear the infection and for intrinsic hepatic regeneration to occur. In the complex landscape of critical care, where sepsis-associated liver dysfunction or acute liver failure complicates the course of patients with contraindications to aggressive fluid resuscitation (such as ESRD or severe heart failure), TPE should be elevated from a "last-ditch" consideration to an early, standard-of-care rescue intervention. Its unique ability to simultaneously detoxify the plasma and restore hemostasis makes it an indispensable tool in the intensivist's armamentarium against "irreversible" multi-organ failure.

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