The Clinical Spectrum of Weil's Disease: From Successful Management to Fatal Septic Shock

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ABSTRACT (times new roman, 10 pts, centered)

Weil's disease, the severe form of leptospirosis, poses a significant clinical challenge due to its potential for rapid multi-organ failure. This case series reports four patients presenting with fever, profound jaundice, myalgia, and dark urine. Laboratory evaluations revealed hyperbilirubinemia, thrombocytopenia, and leukocytosis in all subjects, with acute kidney injury complicating three cases. Diagnosis was confirmed via IgM Leptospira serology. Following empirical antibiotic treatment and supportive care, three patients achieved full recovery. However, one patient experienced rapid clinical deterioration leading to fatal septic shock. These cases underscore the diverse clinical spectrum of leptospirosis, ranging from manageable organ dysfunction to life-threatening systemic collapse. The findings emphasize that early clinical suspicion and prompt initiation of empirical therapy are paramount to reducing mortality, particularly in settings where distinguishing Weil's disease from other acute febrile illnesses remains difficult.

Keywords: Leptospirosis; Weil's disease; Acute Kidney Injury; Septic Shock; Hyperbilirubinemia

INTRODUCTION

Weil's disease, the severe manifestation of leptospirosis, presents a significant clinical challenge due to its diverse symptomatology and potential for rapid deterioration [1]. Caused by the spirochete Leptospira, the infection is primarily transmitted through contact with water or soil contaminated by the urine of reservoir animals, particularly rodents [2]. The clinical spectrum of leptospirosis ranges from a mild, self-limiting flu-like illness to severe forms characterized by the triad of jaundice, renal failure, and hemorrhagic diathesis, historically known as Weil's disease [2]. In non-tropical regions, the disease has often been underreported, leading to diagnostic delays and increased morbidity [3].

The clinical presentation of Weil's disease can be insidious, often mimicking other acute febrile illnesses such as dengue, malaria, or viral hepatitis, which complicates timely diagnosis. Patients typically exhibit nonspecific initial symptoms—including fever, myalgia, and gastrointestinal disturbances—before progressing to severe complications like acute kidney injury (AKI) and liver failure [4, 5]. Retrospective analyses indicate that prompt recognition and the initiation of empirical treatment are crucial for improving patient outcomes. Early administration of antibiotics, particularly doxycycline or penicillin, has been shown to significantly reduce mortality from severe leptospirosis [4, 6].

Recent literature emphasizes the importance of using diagnostic scoring systems, such as the Modified Faine's Criteria, to aid early identification of leptospirosis, especially in cases with atypical presentations [7]. These criteria integrate clinical history, epidemiological exposure, and laboratory findings to assess the probability of infection. Despite advances in diagnostic techniques, barriers to timely testing persist, particularly in resource-limited settings [9].

This case series highlights the complexities involved in diagnosing and managing Weill's disease through a detailed examination of four recent cases. By illustrating the varied clinical trajectories—ranging from successful recovery to fatal septic shock—we aim to underscore the necessity for heightened clinical awareness and prompt intervention strategies in combating this potentially life-threatening condition.

CASE PRESENTATION

Case 1

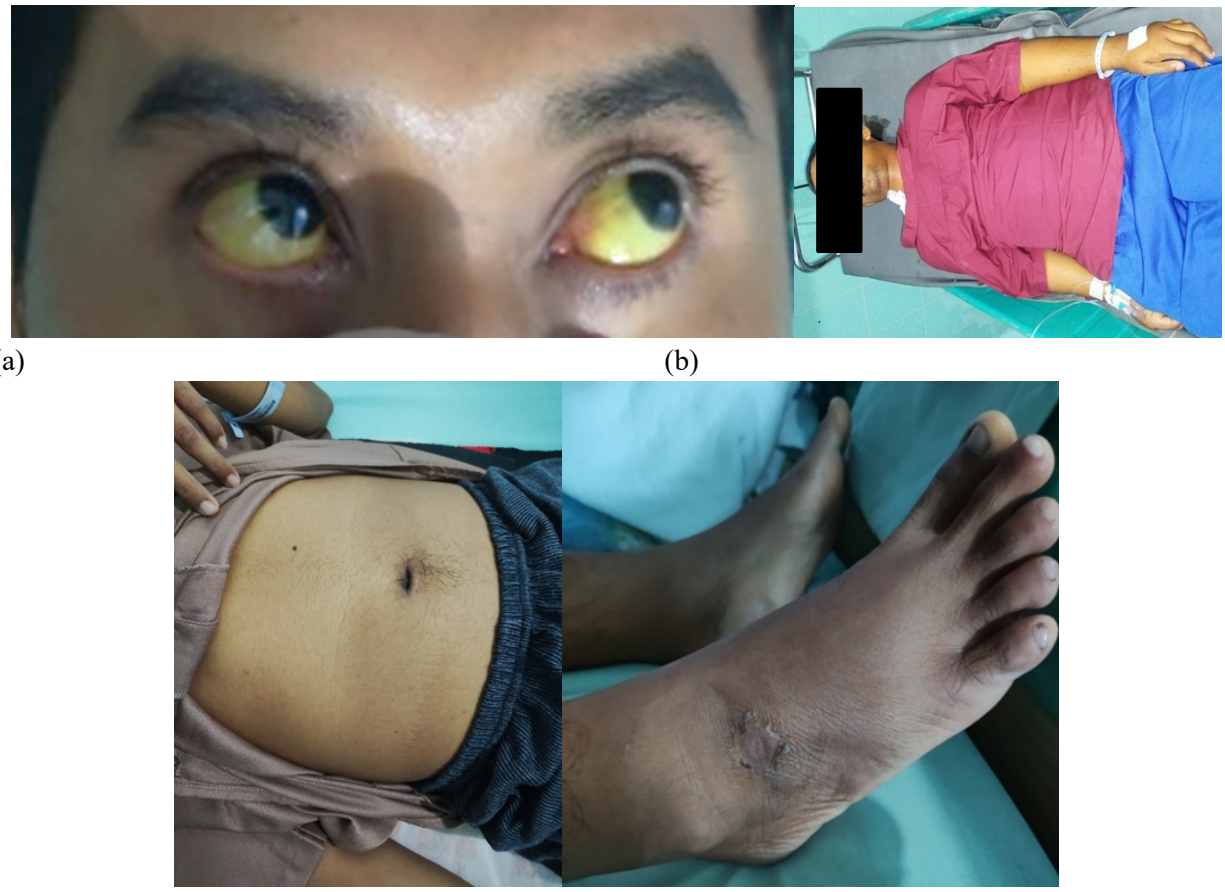
A 28-year-old male, employed as a sanitation and garden maintenance worker, was transferred from an outside hospital with suspected Weil's disease, acute kidney injury (AKI), and hypoalbuminemia. He presented with a one-week history of fever, headache, severe calf muscle pain (myalgia), progressive jaundice, and dark tea-colored urine. He also reported persistent shortness of breath that worsened with physical activity. Prior to transfer, he had received initial treatment with ampicillin-sulbactam (1.5 g every 8 hours) and methylprednisolone (62.5 mg/day), and had undergone one session of hemodialysis.

Upon admission, vital signs were notable for hypertension (144/75 mmHg) and tachypnea (24 breaths per minute), with an oxygen saturation of 95% on room air. Physical examination revealed marked scleral icterus, jaundiced skin, bilateral pulmonary rales, and peripheral edema affecting both upper and lower extremities.

Laboratory evaluation demonstrated anemia (Hemoglobin 11.6 g/dL), leukocytosis (21,700/µL) with neutrophilic predominance (87.8%), thrombocytopenia (95,000/µL), hyponatremia (130 mEq/L), and hypoalbuminemia (2.8 g/dL). The patient exhibited severe hyperbilirubinemia (Total Bilirubin 29.99 mg/dL) and AKI (Serum Creatinine 4.4 mg/dL). The International Normalized Ratio (INR) was 0.89. Urinalysis was significant for bilirubinuria (++). Chest radiography showed evidence of pulmonary edema (Figure 1), while a subsequent abdominal ultrasound revealed parenchymal liver disease and right renal insufficiency.

Given the high clinical suspicion, empirical intravenous ceftriaxone (1 g every 12 hours) was initiated pending serological results. Although initially planned for intermittent hemodialysis, the procedure was discontinued as the patient's condition stabilized. On the third day of admission, Leptospira IgM serology returned

positive. The patient responded well to antibiotic therapy, with significant improvement in clinical symptoms and laboratory parameters. He was educated regarding occupational risks and preventive measures and was discharged on the sixth day of hospitalization. Subsequent Microscopic Agglutination Testing (MAT) confirmed infection with Leptospira serogroups Bataviae (1:1280), Javanica (1:640), and Pomona (1:1280).



(a) (b)

(c) (d)

Figure 1. Clinical Photos of Patient (a. Conjunctival Suffusion, b. Edema of extremities, c. Skin appears icteric, d. Scar on dorsum pedis dextra)

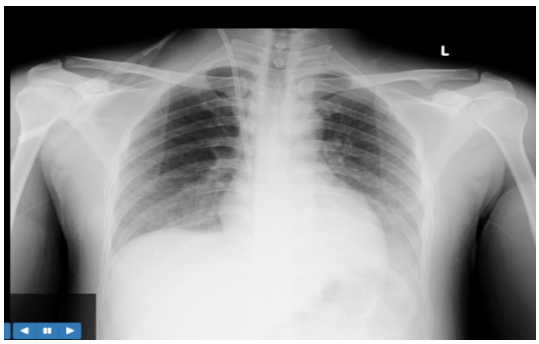


Figure 2. Chest X-ray

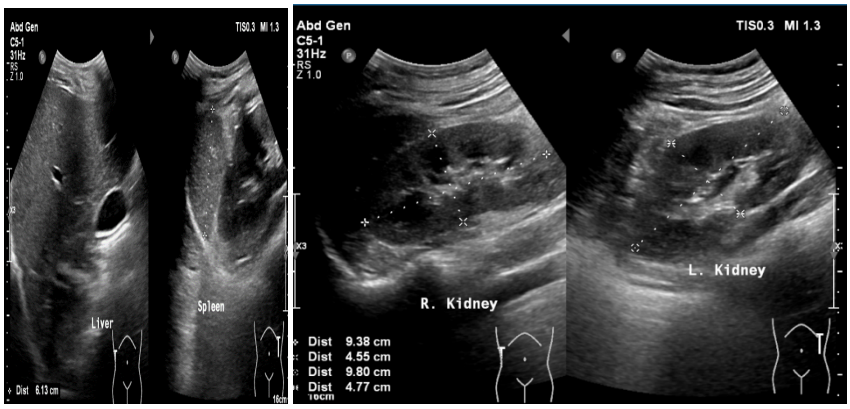


Figure 3. Liver and kidney ultrasound

Case 2

A 61-year-old female presented to the Emergency Room (ER) with a one-week history of abdominal bloating, nausea, vomiting, and progressive scleral icterus. She reported a fever lasting two days prior to admission, which had temporarily subsided with antipyretics. Her past medical history was significant for cerebrovascular disease four years prior, attributed to uncontrolled hypertension; she reported no residual neurological deficits but had been lost to follow-up.

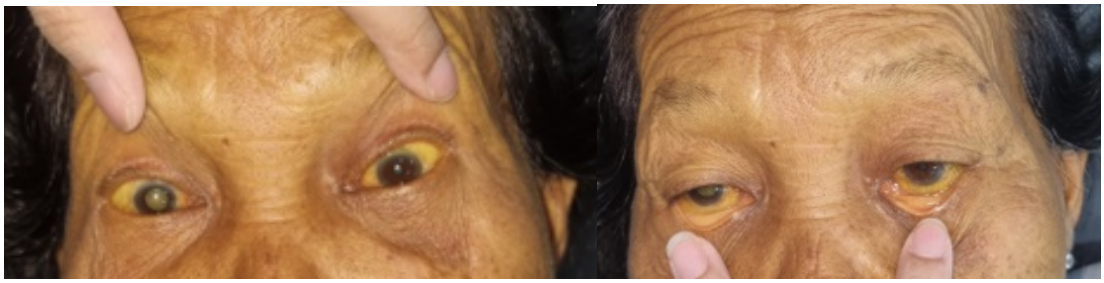
Upon presentation, the patient was hypertensive (145/98 mmHg), while other vital signs were within normal limits. Physical examination revealed conjunctival pallor, scleral icterus, and periumbilical tenderness. Initial lung auscultation was clear. Differential diagnoses at admission included acute hepatitis, acute cholangitis, community-acquired pneumonia, leptospirosis, and dengue fever. The patient was started on empirical intravenous ceftriaxone (2 g/day) alongside supportive care.

Initial laboratory investigations indicated anemia (Hemoglobin 10.5 g/dL), leukocytosis (26,000/µL) with neutrophilia (94%), and severe thrombocytopenia (18,000/µL). Coagulation studies showed a slightly prolonged Prothrombin Time (15.9 seconds) with a normal Activated Partial Thromboplastin Time. Biochemical analysis revealed hyperbilirubinemia (Total Bilirubin 10.49 mg/dL) and hypoalbuminemia (2.4 g/dL), while renal function (creatinine) was preserved. Viral hepatitis markers (HBsAg and anti-HCV) were non-reactive.

Chest radiography demonstrated aortic calcification, bilateral infiltrates with air bronchograms, and cardiomegaly (Figure 5). Abdominal ultrasonography revealed signs of cholecystitis, ascites, a benign ovarian cyst, and left pleural effusion.

On the second day of hospitalization, the patient developed diarrhea, bilateral pulmonary rhonchi, and palpable splenomegaly. Serological testing confirmed the diagnosis with a positive Leptospira IgM, while Hepatitis A IgM was negative. Urinalysis showed significant proteinuria (++2) and bilirubinuria (++3). By the fourth day, blood cultures remained negative, and a peripheral blood smear showed normochromic normocytic anemia with absolute neutrophilia and thrombocytopenia.

The patient's clinical condition gradually improved, and she was discharged after seven days of hospitalization. Discharge laboratory parameters showed a platelet count recovery to 253,000/µL and a reduction in total bilirubin to 7.01 mg/dL, though leukocytosis persisted. Three days post-discharge, Microscopic Agglutination Testing (MAT) confirmed infection with Leptospira serovars Javanica (1:1280) and Pomona (1:80)



(a) (b)

(c)

Figure 4. Clinical Photos of Patient (a. Scleral icterus, b. Anemic conjunctiva, c. Skin appears icteric)

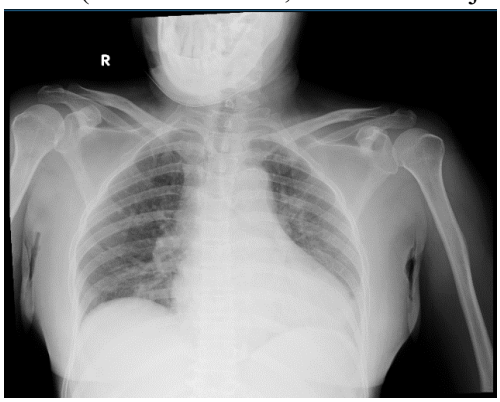


Figure 5. Chest X-ray

Case 3

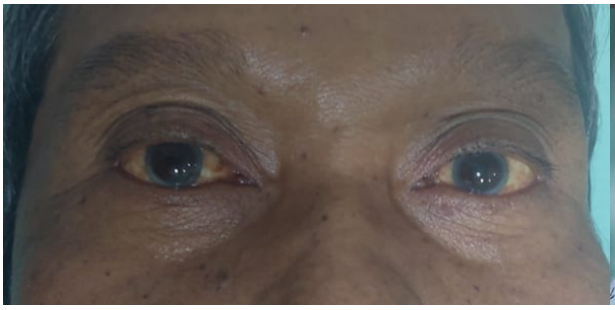
A 59-year-old male was transferred from an outside facility presenting with fever, headache, myalgia, and progressive jaundice that had evolved over one week. He denied any history of animal bites, exposure to floodwaters, or travel to malaria-endemic regions. Prior to transfer, he had completed a six-day course of levofloxacin (500 mg/day). Although the patient initially reported no known comorbidities, subsequent evaluation revealed underlying metabolic issues.

Upon admission, the patient was hypertensive, though other vital signs were stable. Physical examination was notable for bilateral conjunctival suffusion and marked generalized icterus. Initial abdominal examination revealed no hepatomegaly or specific tenderness.

Laboratory investigations revealed anemia (Hemoglobin 10.3 g/dL), leukocytosis (25,300/µL), and thrombocytopenia (67,000/µL). The patient exhibited significant renal and hepatic impairment, with a serum creatinine of 2.7 mg/dL, a blood urea nitrogen (BUN) of 199 mg/dL, and a Total Bilirubin of 15.8 mg/dL (Direct Bilirubin 7.95 mg/dL). Additionally, the patient was diagnosed with Type 2 Diabetes Mellitus during this admission, evidenced by a fasting blood glucose of 244 mg/dL and a 2-hour postprandial glucose of 269 mg/dL.

Diagnostic imaging performed at the previous hospital included an abdominal ultrasound showing hepatomegaly, gastritis, and multiple cholelithiasis. Chest radiography at our facility revealed cardiomegaly, aortosclerosis, and early signs of pulmonary edema.

The patient was treated empirically with intravenous ceftriaxone (2 g/day) and supportive therapy, alongside management for hypertension and diabetes. On the second day of admission, he developed rigors and epigastric pain with a positive Murphy's sign. While blood cultures and viral hepatitis markers (B and C) were negative , the diagnosis of leptospirosis was confirmed via a positive IgM Leptospira serology. The patient's condition gradually improved, and he was discharged without sequelae after eight days of hospitalization. No Microscopic Agglutination Test (MAT) was performed for this patient.



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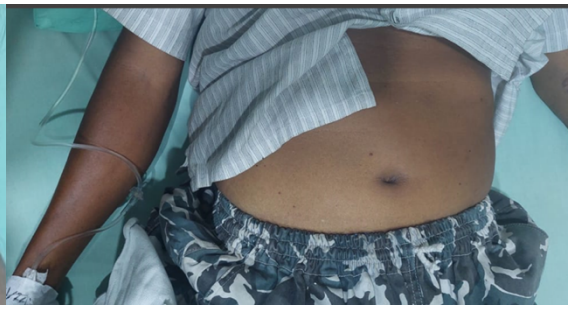

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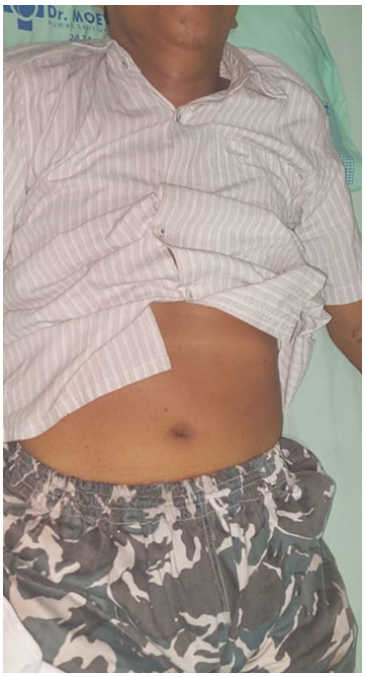


(c)

Figure 6. Clinical Photos of Patient (a. Conjunctival suffusion, b, c. Skin appears icteric)

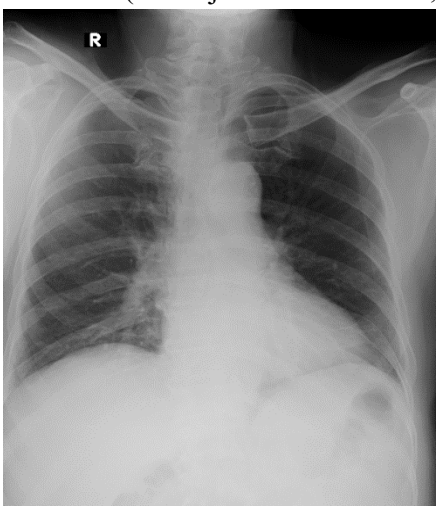


Figure 7. Chest X-ray

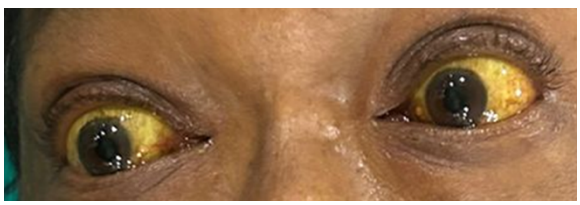
Case 4

A 34-year-old male presented to the Emergency Room (ER) with a five-day history of fever, nausea, and abdominal pain localized to the right upper quadrant and epigastrium. Systemic symptoms included progressive jaundice, abdominal bloating, shortness of breath, malaise, and the passage of tea-colored urine. Epidemiologically, he denied any recent travel, previous hospitalizations, or known exposure to rodents.

Upon admission, the patient was in a state of shock, with a blood pressure of 68/40 mmHg and a heart rate of 112 beats per minute. Physical examination revealed profound jaundice, conjunctival pallor, and bilateral basilar rales on lung auscultation. Abdominal palpation elicited tenderness in the upper quadrants, and generalized edema was noted in all extremities.

Laboratory evaluation indicated severe metabolic and hematological derangements: leukocytosis (19,000/µL) with neutrophilia (93%), thrombocytopenia (66,000/µL), and severe acute kidney injury (Creatinine 5.6 mg/dL). The patient exhibited extreme hyperbilirubinemia (Total Bilirubin 23.19 mg/dL) and metabolic acidosis (pH 7.34, HCO3 16 mmol/L). Chest radiography demonstrated bilateral paracardiac infiltrates with air bronchograms (Figure 9).

The patient was admitted to the intensive care unit (ICU) with a diagnosis of suspected Weil's disease complicated by septic shock. Management included aggressive fluid resuscitation and empirical intravenous ceftriaxone. On the second day, Leptospira IgM serology returned reactive, confirming the diagnosis. Despite treatment, the patient's condition deteriorated; total bilirubin rose to 27.98 mg/dL, and he developed hematemesis and tachypnea. By the fourth day of hospitalization, the patient became lethargic and hypoxic (saturation 67% on room air). He subsequently suffered massive hemoptysis and epistaxis, followed by refractory hypotension and death



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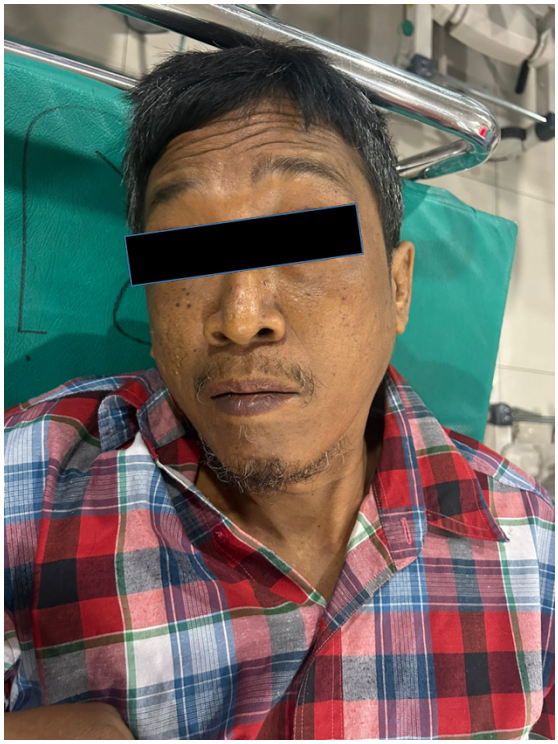

(b)

Figure 8. Clinical Photos of Patient (a. Conjunctival suffusion, b, c. Skin appears icteric)

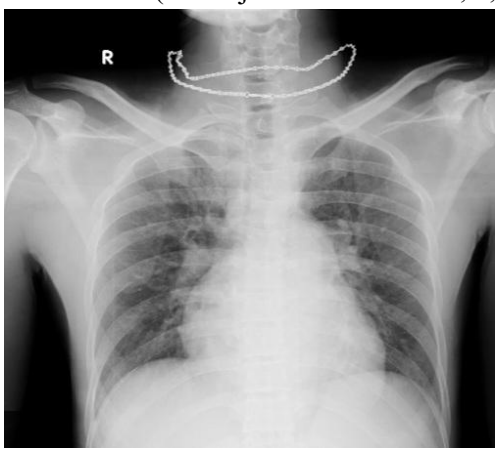

Figure 9. Chest X-ray

DISCUSSION

This case series illustrates the severe clinical spectrum of leptospirosis, known as Weil's disease, which is characterized by the triad of jaundice, renal failure, and hemorrhagic diathesis. While the majority of leptospirosis cases manifest as mild, self-limiting febrile illnesses, approximately 10% progress to this severe form, which carries a significantly higher mortality rate due to multi-organ dysfunction [1]. In our series, all four patients presented with advanced symptoms including fever, profound jaundice, and pulmonary involvement, underscoring the potential for rapid clinical deterioration.

The hallmark of Weil's disease is liver and kidney dysfunction. In this series, hyperbilirubinemia was a universal finding, likely resulting from hepatocellular damage and cholestasis, while acute kidney injury (AKI) complicated three of the four cases [4]. The pathophysiology of AKI in leptospirosis is multifactorial, involving direct nephrotoxic effects of the spirochete and hypovolemia from capillary leakage. Consistent with previous

studies, our patients exhibited significant thrombocytopenia [4]. This hematological abnormality is attributed to peripheral platelet consumption caused by extensive hemorrhage, immune-mediated destruction, and bone marrow suppression, all of which exacerbate the risk of bleeding complications such as the massive hemoptysis seen in Case 4 [4].

A critical observation in this series is the progression to septic shock, which proved fatal in one patient. Septic shock in leptospirosis is driven by a systemic inflammatory response syndrome (SIRS) and widespread vasculitis caused by the infection [13]. In Case 4, despite aggressive fluid resuscitation and vasopressor support, the patient succumbed to circulatory collapse. This aligns with literature suggesting that once the disease progresses to septic shock and multi-organ failure, the host immune response may shift to an immunosuppressive state, significantly increasing mortality [4]. Conversely, Case 1, who presented with severe AKI and pulmonary edema, recovered following the timely initiation of intermittent hemodialysis. This supports findings that renal replacement therapy is a life-saving intervention for patients with leptospirosis-associated renal failure [4].

Diagnosing Weil's disease remains a challenge in resource-limited settings due to its clinical resemblance to other tropical infections like dengue, malaria, and viral hepatitis [1]. In our series, the diagnosis relied on clinical suspicion and IgM serology. It is important to note that antibodies typically develop 3–10 days after symptom onset; thus, initial negative serology does not exclude infection [10]. The Microscopic Agglutination Test (MAT) remains the gold standard for serotype identification [11]. In our survivors, MAT confirmed infections with Bataviae, Javanica, and Pomona serovars. Unfortunately, MAT was not performed for the fatal case, limiting our ability to determine if a specific virulent serovar contributed to the severity of the outcome.

Effective management hinges on early recognition and the immediate initiation of antimicrobial therapy. Studies indicate that intravenous ceftriaxone is as effective as penicillin G for treating severe leptospirosis and is often more convenient to administer [5]. All patients in this series received empiric ceftriaxone. However, as demonstrated by the fatal outcome in Case 4, antibiotics alone may be insufficient in advanced stages. Comprehensive supportive care, including fluid resuscitation, correction of electrolyte imbalances, and mechanical ventilation for acute respiratory distress syndrome (ARDS), is vital [13].

CONCLUSION

This case series documents the variable clinical outcomes of Weil's disease, ranging from successful recovery to fatal progression. While three patients achieved complete recovery following appropriate antibiotic and supportive therapy , the death of one patient due to refractory septic shock highlights the disease's potential lethality. These findings reinforce that early clinical suspicion, prompt diagnosis, and aggressive intervention are critical to preventing severe complications—such as multi-organ failure—and improving survival rates in high-risk patients. Future research should focus on identifying early prognostic markers and optimizing management protocols for severe leptospirosis, particularly in resource-limited settings

Informed Consent Statement

Informed consent was obtained from all subjects involved in the study. Written informed consent has been obtained from the patients (or their legal guardians) to publish this paper, including the publication of accompanying clinical images.

Conflicts of Interest

The authors declare no conflict of interest.

Author Contributions

Conceptualization: D.R.H., S.B.S., T.S., and A.A.; Methodology: D.R.H. and I.K.K.; Validation: S.B.S., T.S., and A.A.; Formal Analysis: I.K.K., O.B.P., and T.N.N.; Investigation: I.K.K., F.P.P., and W.S.P.; Resources: D.R.H.; Data Curation: O.B.P., T.N.N., F.P.P., and W.S.P.; Writing – Original Draft Preparation: I.K.K., O.B.P., T.N.N., F.P.P., and W.S.P.; Writing – Review & Editing: D.R.H., S.B.S., T.S., and A.A.; Visualization: I.K.K. and T.N.N.; Supervision: D.R.H., S.B.S., T.S., and A.A.; Project Administration: D.R.H. All authors have read and agreed to the published version of the manuscript.

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