ORIGINAL ARTICLE

Beyond Fever—The Changing Face of Acute Leptospirosis: A Retrospective Observational Study from Western India

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Abstract

Background: Leptospirosis is a zoonotic infection caused by pathogenic *Leptospira* species and remains a significant cause of acute febrile illness in tropical regions. Its clinical spectrum ranges from mild, self-limiting illness to severe multi-organ dysfunction. The disease is broadly classified into anicteric and icteric (Weil's disease) forms, the latter associated with jaundice and increased morbidity. In India, diagnosis is often challenging due to overlapping features with other endemic infections such as dengue and scrub typhus. Coinfections and changing epidemiological patterns, including increasing urban cases, further complicate clinical assessment. This study evaluated the demographic profile, clinical characteristics, organ involvement, coinfections, severity, management, and outcomes of adults hospitalized with acute leptospirosis, with comparison between icteric and anicteric phenotypes.

Materials and methods: This retrospective observational study included 78 adults with laboratory-confirmed acute leptospirosis admitted over 30 months to a tertiary care hospital in Rajasthan, India. Diagnosis was established by positive *Leptospira*-specific immunoglobulin M (IgM) serology (>11 NTU) and/or polymerase chain reaction (PCR). Data regarding demographics, comorbidities, clinical features, organ involvement, coinfections, treatment, and outcomes were extracted from medical records.

Organ involvement was defined using predefined clinical and laboratory criteria across major systems. Severe disease was defined as dysfunction of two or more organ systems. Icteric leptospirosis was defined by clinical jaundice and/or serum bilirubin ≥3 mg/dL. Coinfections were confirmed through appropriate laboratory testing. Continuous variables were expressed as median (interquartile range) and categorical variables as frequency (%). Subgroup comparisons were performed using the Mann–Whitney *U* test and Fisher's exact test.

Results: The median age was 57 years (interquartile range 41–68), with slight male predominance (52.6%). Although 59% of patients were from rural areas, 41% were urban residents. Hypertension (25.6%) and diabetes mellitus (29.5%) were common comorbidities, while 42.3% had no prior illnesses. Anicteric disease predominated (84.6%), and 15.4% had icteric leptospirosis. Fever was present in 93.6% of patients. Hepatic (69.2%) and respiratory (66.7%) involvement were most frequent, and multi-organ dysfunction occurred in 61.5%. Coinfections were identified in 52.6% of cases, most commonly dengue (17.9%) and scrub typhus (14.1%). Coinfected patients were younger and had fewer comorbidities, with lower rates of renal, respiratory, and neurological involvement and reduced need for ventilatory support. Icteric patients were significantly younger (median 31.5 vs 58 years) and had longer hospital stays (10.5 vs 7 days). Hepatic involvement was universal in the icteric group, and secondary hemophagocytic lymphohistiocytosis (HLH) was markedly more frequent. Mortality was higher among icteric patients but did not reach statistical significance. Mechanical ventilation was required in 10.3% of patients. The median hospital stay was 7 days, and overall mortality was 2.6%, with both deaths occurring in patients with severe multi-organ dysfunction.

Conclusion: Acute leptospirosis exhibits diverse clinical presentations with frequent multi-organ involvement in hospitalized adults. Coinfections are common but did not consistently worsen outcomes. Icteric disease represents a more severe phenotype associated with greater complications and prolonged hospitalization. Early diagnosis and timely supportive management are critical to achieving favorable outcomes in endemic settings.

Keywords: Acute febrile illness, Coinfection, Icteric leptospirosis, Leptospirosis, Mortality, Multi-organ dysfunction, Tropical infections.

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Introduction

Leptospirosis is a widespread zoonotic infection caused by pathogenic *Leptospira* species, presenting with a broad spectrum ranging from mild, self-limiting febrile illness to severe multi-organ disease.[1,2] Clinically, it is classified as anicteric or icteric (Weil's disease), the latter associated with jaundice, higher morbidity, and increased risk of complications.[1,3]

In India, leptospirosis remains underreported due to overlapping symptoms with other endemic febrile illnesses, low clinical suspicion, and limited diagnostic resources.[2,4] Traditionally linked to rural occupational exposures, recent studies report increasing urban cases, likely reflecting environmental changes and evolving epidemiology.[3,5]

Comorbidities such as diabetes and hypertension are common, but healthy individuals are also frequently affected.[2]

Coinfections with pathogens such as dengue and scrub typhus further complicate diagnosis and management and may influence organ involvement and disease severity.[5–8] Despite effective antibiotics and supportive care, severe leptospirosis with multi-organ involvement continues to carry significant morbidity and mortality, particularly in icteric cases.[1,3,9]

This study aims to describe the demographic and clinical spectrum, organ involvement, coinfections, and outcomes of 78 acute leptospirosis patients admitted to a tertiary care center in Rajasthan, India, with emphasis on differences between icteric and anicteric phenotypes. The findings aim to inform clinical management and highlight evolving epidemiological patterns in endemic regions.

Materials and Methods

Study Design and Setting

This was a retrospective observational study conducted at Fortis Escorts Hospital, Jaipur, India, a tertiary care hospital, over a period of 30 months (time period, e.g., July 2023 to December 2025). The study

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was approved by the Institutional Ethics Committee vide letter No. FEHJ/IEC/25/004, and the requirement for informed consent was waived due to the retrospective nature of the study. The aim of this study was to assess the varied clinical manifestations, including demographics, comorbidities, coinfections (if any), organ involvement, severity, complications, and outcomes of patients with icteric and anicteric leptospirosis.

Study Population

All patients with a confirmed diagnosis of leptospirosis admitted to the Department of Medicine in the authors' unit during the study period were included. As this was a retrospective observational study, all consecutive eligible patients admitted during the study period were included. A formal sample size estimation was not performed.

Leptospirosis was diagnosed based on positive serology [*Leptospira*-specific immunoglobulin M (IgM) antibody] or a positive molecular test [polymerase chain reaction (PCR)]. A *Leptospira*-specific IgM value >11 NTU was considered positive, 9–10.9 borderline, and <9 negative. Patients with incomplete medical records were excluded. A total of 78 patients met the inclusion criteria and were included in the final analysis.

Data Collection

Data were extracted from patient case files procured from the Medical Records Department using a standardized data collection form. The following variables were recorded.

Demographics

Age, gender, and background (rural/urban).

Comorbidities

Preexisting conditions documented in the medical history, including hypertension (HTN), diabetes mellitus (DM), coronary artery disease (CAD), hypothyroidism, chronic obstructive pulmonary disease (COPD)/asthma, chronic kidney disease (CKD), cerebrovascular accident (CVA), and chronic liver disease (CLD)/fatty liver.

Clinical Presentation

Symptoms at admission, including fever, cough, breathlessness, abdominal pain, body aches, nausea/vomiting, weakness, headache, jaundice, loose stools, chills, reduced appetite, altered sensorium, rash, chest pain, bleeding manifestations, oliguria, and other symptoms.

Leptospirosis Phenotype

Classified as icteric (Weil's disease) or anicteric based on the presence of clinical jaundice and/or explicit diagnosis in the medical records.

Organ System Involvement

Hepatic, respiratory, hematological, renal, neurological, cardiac, rhabdomyolysis, uveitis, and secondary hemophagocytic lymphohistiocytosis (HLH), as documented in the case files or diagnosis notes. The following features were used to identify organ involvement, and the presence of at least one feature indicated involvement of the respective organ:

Respiratory—Shortness of breath, cough, hemoptysis, abnormal respiratory auscultation, partial pressure of arterial oxygen/fraction of inspired oxygen (PaO_2/FiO_2) <300.

Hepatic—Icterus, hepatomegaly, serum bilirubin >2 mg/dL, transaminitis.

Renal—Oliguric or nonoliguric renal failure, need for supportive renal replacement therapy.

Cardiac—Findings of cardiogenic shock, myocarditis, elevated cardiac enzymes, two-dimensional echocardiography correlation, and heart failure.

Nervous system—Neck stiffness or rigidity, seizures, Glasgow Coma Scale score <15/15.

Hematological—Bleeding manifestations, thrombocytopenia, and findings consistent with disseminated intravascular coagulation (DIC).

Uveitis—Pain/tenderness with redness in the eye, visual changes such as floaters or decreased visual acuity.

Rhabdomyolysis—Muscle tenderness, elevated creatine phosphokinase.

Coinfections

Presence of other pathogens, including dengue, scrub typhus, hepatitis A, enteric fever (typhoid), brucellosis, tuberculosis (TB), influenza A, coronavirus disease 2019 (COVID-19), human immunodeficiency virus (HIV), and varicella (chickenpox), was diagnosed using standard laboratory methods, including serology, PCR, nucleic acid amplification tests (NAAT), or culture, where available. Efforts were made to correlate laboratory findings with the clinical presentation to improve diagnostic accuracy.

Severity Indicators

Multi-organ dysfunction (defined as involvement of ≥2 organ systems), acute respiratory distress syndrome (ARDS), shock, intensive care unit (ICU) admission, need for noninvasive ventilation (NIV), and need for invasive mechanical ventilation.

Treatment

Antibiotics, corticosteroids, intravenous immunoglobulin (IVIG), plasmapheresis (PLEX), hemodialysis, and ventilatory support.

Outcomes

Outcome was measured as discharge to home, left against medical advice (LAMA), or death. Length of stay included days of stay in the medical intensive care unit (MICU) and/or hospital floor.

Definitions

Severe leptospirosis was defined as involvement of ≥2 organ systems based on the organ involvement documented in the medical records.

Multi-organ dysfunction was defined as involvement of two or more of the following organ systems: hepatic, respiratory, hematological, renal, neurological, cardiac, or others (rhabdomyolysis, uveitis, and HLH).

Icteric leptospirosis (Weil's disease) was defined by the presence of clinical jaundice (serum bilirubin ≥3 mg/dL or clinical diagnosis) along with other systemic features.

Statistical Analysis

Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 26.0. Continuous variables were assessed for normality using appropriate methods, and as most variables showed nonnormal distribution, they are presented as median (interquartile range). Categorical variables are presented as frequency (%). Comparisons were performed using the Mann–Whitney *U* test and Fisher's exact test. A *p*-value <0.05 was considered statistically significant.

Ethical Considerations

The study was conducted in accordance with the Declaration of Helsinki. Patient confidentiality was maintained by anonymizing all data prior to analysis. The Institutional Ethics Committee waived the need for informed consent due to the retrospective design.

Results

Demographic and Baseline Characteristics

Table 1 provides the foundation of the study cohort. The median age of 57 years (interquartile range 41–68) indicates that leptospirosis affects a wide age range, with a slight male predominance (52.6%). The

rural predominance (59.0%) suggests the traditional understanding of leptospirosis as an occupationally acquired disease, although a significant urban proportion (41.0%) suggests changing epidemiology.

Hypertension (25.6%) and diabetes mellitus (29.5%) were the most common comorbidities, reflecting the background burden of noncommunicable diseases. Notably, 42.3% of patients had no comorbidities, highlighting that leptospirosis can affect previously healthy individuals.

Clinical Symptoms and Laboratory Features

Table 2 and Figure 1 capture the *Leptospira* phenotype, severity indicators, and clinical spectrum of leptospirosis. The majority (84.6%) presented with anicteric disease, while 15.4% had the icteric (Weil's) form. Although fever was present in 93.6% of patients, detailed characteristics such as duration, pattern, and peak temperature were inconsistently documented in the records and could not be reliably analyzed. It was followed by cough (48.7%) and breathlessness (44.9%).

Table 1: Demographic and baseline characteristics of patients with leptospirosis (*N* = 78)

Characteristic	*N = 78*
Age (years)	
Median (IQR) [range]	57 (41–68) [18–83]
Gender, *n* (%)	
Male	41 (52.6)
Female	37 (47.4)
Background, *n* (%)	
Rural	46 (59.0)
Urban	32 (41.0)
Comorbidities, *n* (%)	
Hypertension	20 (25.6)
Diabetes mellitus	23 (29.5)
Coronary artery disease/ischemic heart disease	9 (11.5)
Hypothyroidism	11 (14.1)
Chronic obstructive pulmonary disease/asthma	18 (23.1)
Chronic kidney disease	6 (7.7)
Cerebrovascular accident	2 (2.6)
Chronic liver disease/fatty liver	3 (3.8)
Number of comorbidities, *n* (%)	
0	33 (42.3)
1	20 (25.6)
2	8 (10.3)
≥3	17 (21.8)

IQR, interquartile range

Jaundice was present in 15.4%, correlating exactly with the icteric cases. Hepatic (69.2%) and respiratory (66.7%) involvement were the most common, highlighting the hepatopulmonary predominance. Figure 2 depicts the organ systems involved in these patients. Multi-organ dysfunction (≥2 organs) occurred in 61.5%, indicating significant disease severity. All included patients had laboratory-confirmed leptospirosis based on predefined diagnostic criteria. The median *Leptospira*-specific IgM value was 13.4 NTU.

Table 2: Distribution of patients with *Leptospira* phenotype (*N* = 78), severity indicators and IgM titers

Characteristic	*N = 78*
Leptospirosis phenotype, *n* (%)	
Icteric (Weil's disease)	12 (15.4)
Anicteric	66 (84.6)
Severity indicators, *n* (%)	
Multi-organ dysfunction (≥2 organs)	48 (61.5)
Acute respiratory distress syndrome	8 (10.3)
Shock	11 (14.1)
ICU admission	13 (16.7)
Noninvasive ventilation	10 (12.8)
Invasive mechanical ventilation	7 (9.0)
Leptospira IgM	
IgM positive, *n* (%)	78 (100)
IgM value, median (IQR)‡	13.4 (11.9–14.7)

ARDS, acute respiratory distress syndrome; HLH, hemophagocytic lymphohistiocytosis; ICU, intensive care unit; IQR, interquartile range; NIV, noninvasive ventilation; SOB, shortness of breath; ‡All 78 patients had quantitative immunoglobulin M (IgM) results; the median and IQR were calculated from all values

Coinfections

Figure 3 highlights that over half (52.6%) of patients had at least one coinfection. Dengue (17.9%) and scrub typhus (14.1%) were the most frequent, reflecting the endemicity

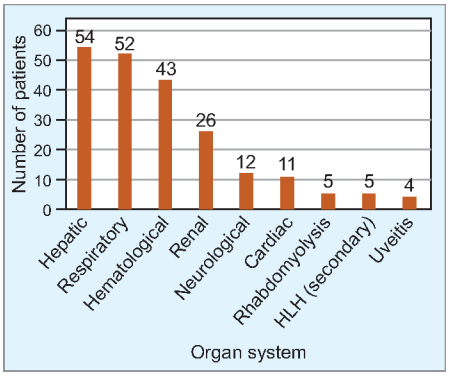

Fig. 2: Frequency of involvement of various organ systems (*N* = 78)

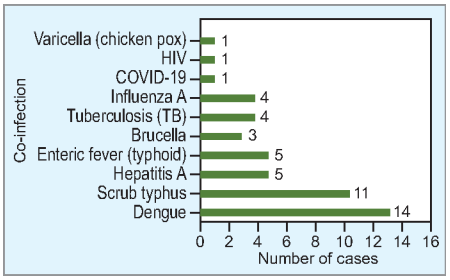

Fig. 3: Frequency of coinfection observed among all patients with leptospirosis

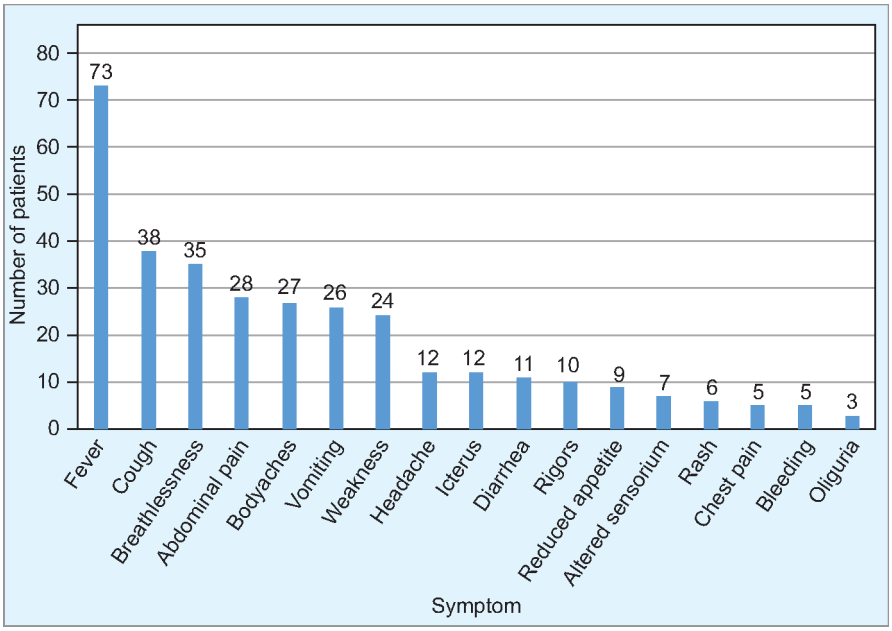

Fig. 1: Distribution of symptoms among all patients with leptospirosis (*N* = 78)

Table 3: Treatment and outcomes of patients with leptospirosis (*N* = 78)

Characteristic	*N = 78*
Treatment, *n* (%)	
Antibiotics	78 (100)
Corticosteroids	3 (3.8)
Intravenous immunoglobulin	1 (1.3)
Plasmapheresis	3 (3.8)
Hemodialysis (for acute kidney injury)	1 (1.3)
Mechanical ventilation/ noninvasive ventilation	8 (10.3)
Length of hospital stay, days—median (IQR)	7 (5–9)
Outcome, *n* (%)	
Discharged	73 (93.6)
Died	2 (2.6)
Left against medical advice	3 (3.8)

AKI, acute kidney injury; IQR, interquartile range; NIV, noninvasive ventilation

Table 4: Comparison of patients with icteric vs anicteric leptospirosis (*N* = 78)

Characteristic	*Icteric (n = 12)*	*Anicteric (n = 66)*	*p-value*	*OR (95% CI)*
Age, years—median (IQR)	31.5 (23–58)	58 (43–68)	<0.001[1]	–
Male gender—*n* (%)	7 (58.3)	34 (51.5)	0.76[2]	1.32 (0.38–4.56)
Rural background—*n* (%)	6 (50.0)	40 (60.6)	0.54[2]	0.65 (0.19–2.20)
Any comorbidity—*n* (%)	3 (25.0)	42 (63.6)	0.01[2]	0.19 (0.05–0.75)
Organ involvement—*n* (%)				
Hepatic	12 (100)	42 (63.6)	<0.001[2]	14.4 (1.7–121)[3]
Renal	6 (50.0)	20 (30.3)	0.20[2]	2.30 (0.66–7.98)
Respiratory	8 (66.7)	44 (66.7)	1.00[2]	1.00 (0.27–3.68)
Hematological	8 (66.7)	35 (53.0)	0.54[2]	1.77 (0.49–6.44)
Neurological	3 (25.0)	9 (13.6)	0.38[2]	2.11 (0.47–9.45)
Cardiac	3 (25.0)	8 (12.1)	0.36[2]	2.42 (0.53–11.0)
Rhabdomyolysis	2 (16.7)	3 (4.5)	0.15[2]	4.20 (0.62–28.5)
Uveitis	2 (16.7)	2 (3.0)	0.09[2]	6.40 (0.80–51.0)
HLH (secondary)	4 (33.3)	1 (1.5)	<0.001[2]	32.5 (3.5–304)
Multi-organ dysfunction (≥2 organs)—*n* (%)	9 (75.0)	39 (59.1)	0.36[2]	2.08 (0.51–8.47)
Any ventilation (NIV/ invasive)—*n* (%)	3 (25.0)	14 (21.2)	0.72[2]	1.24 (0.29–5.29)
Length of stay, days—median (IQR)	9.5 (7.5–13)	7 (5–9)	0.02[1]	–
Mortality—*n* (%)	1 (8.3)	1 (1.5)	0.27[2]	5.91 (0.34–101)

CI, confidence interval; HLH, hemophagocytic lymphohistiocytosis; IQR, interquartile range; NIV, noninvasive ventilation; OR, odds ratio; [1]Mann–Whitney *U* test; [2]Fisher's exact test; [3]Odds ratio calculated using the Haldane–Anscombe correction because of a zero cell count

of these infections in the region. Hepatitis A (6.4%) and enteric fever (6.4%) were also notable. The high rate of coinfections (11.5% had two, and 2.6% had three or more) underscores the complex diagnostic and clinical challenges in tropical febrile illnesses and is a unique contribution of this series.

Treatment and Outcomes

Table 3 highlights that all patients received antibiotics, reflecting the standard of care. Antibiotics included doxycycline, ceftriaxone, azithromycin, piperacillin–tazobactam, and meropenem, selected based on clinical severity and physician discretion. Antibiotic escalation was required in a subset of patients with worsening clinical status or suspected secondary infections. Adjunctive therapies were used selectively: corticosteroids (3.8%), intravenous immunoglobulin (IVIG) (1.3%), plasmapheresis (PLEX) (3.8%), and hemodialysis (1.3%). The three patients who required PLEX had diffuse alveolar hemorrhage, severe jaundice, and secondary thrombotic microangiopathy, respectively. Mechanical ventilation was required in 10.3% of patients. The median length of stay was 7 days (interquartile range 5–9). Outcomes were favorable overall, with 93.6% discharged, 2.6% mortality (2 deaths), and 3.8% leaving against medical advice. The low mortality rate suggests good clinical outcomes with timely management.

Icteric vs Anicteric Leptospirosis

Table 4 shows that patients with icteric disease (Weil's disease) were younger (median 30 vs 57.5 years, $p < 0.001$) and had fewer comorbidities (25 vs 63.6%, $p = 0.01$). Hepatic involvement was universal in the icteric group (100 vs 63.6%, $p < 0.001$), and secondary hemophagocytic lymphohistiocytosis (HLH) was far more frequent (33.3 vs 1.5%, $p < 0.001$).

Renal involvement was higher in icteric cases (50 vs 30.3%) but was not statistically significant. Icteric patients had longer hospital stays (10.5 vs 7 days, $p = 0.02$). Mortality was higher (8.3 vs 1.5%) but was not statistically significant. Overall, Weil's disease represents a more severe phenotype requiring prolonged care and monitoring for complications such as HLH.

Coinfected vs *Leptospira* Alone

Table 5 shows that coinfected patients were significantly younger (median 44 vs 60 years, $p < 0.001$) and had fewer comorbidities (39 vs 78.4%, $p < 0.001$). Interestingly, they had less renal (22 vs 45.9%, $p = 0.03$), respiratory (56.1 vs 78.4%, $p = 0.04$), and neurological involvement (7.3 vs 24.3%, $p = 0.05$). They also required significantly less ventilatory support (7.3 vs 37.8%, $p = 0.001$). This suggests that coinfections may occur in a healthier, younger population but do not necessarily worsen organ dysfunction compared to *Leptospira* infection alone.

Dengue and Scrub Typhus Coinfections

Table 6 descriptively provides a detailed profile of patients with the two most common coinfections. Dengue-coinfected patients had universal hepatic and hematological involvement but no renal, neurological, or cardiac complications. Scrub typhus-coinfected patients had more varied organ involvement, including renal (44.4%), respiratory (55.6%), and cardiac (22.2%) manifestations. Both groups had zero mortality, although the small sample sizes preclude firm conclusions. This table highlights the distinct clinical patterns associated with different coinfections.

Severe vs Nonsevere Leptospirosis

Table 7 reveals that severe disease (≥2 organ involvement) occurred in 61.5% of patients. The only predictor of severity was coinfection (56.3 vs 46.7%, $p = 0.48$, odds ratio 1.47), although this did not reach statistical significance. The icteric phenotype showed a strong trend (18.8 vs 3.3%, $p = 0.08$). Severe cases had significantly longer hospital stays (8 vs 5 days, $p < 0.001$), and both deaths occurred in the severe group. This table underscores that while severe disease prolongs hospitalization, mortality remains low with appropriate care. The low mortality rate may reflect early diagnosis, prompt initiation of appropriate antibiotics, and access to advanced supportive care, including intensive care unit (ICU) monitoring and organ support.

Table 5: Comparison of patients with any coinfection vs *Leptospira* alone (*N* = 78)

Characteristic	*Coinfection (n = 41)*	*Leptospira alone (n = 37)*	*p-value*	*OR (95% CI)*
Age, years–median (IQR)	44 (29–60)	60 (50–70)	<0.001[1]	–
Male gender, *n* (%)	22 (53.7)	19 (51.4)	1.00[2]	1.10 (0.45–2.67)
Rural background, *n* (%)	23 (56.1)	23 (62.2)	0.65[2]	0.78 (0.31–1.94)
Any comorbidity, *n* (%)	16 (39.0)	29 (78.4)	<0.001[2]	0.17 (0.06–0.46)
Organ involvement, *n* (%)				
Hepatic	32 (78.0)	22 (59.5)	0.09[2]	2.42 (0.91–6.46)
Renal	9 (22.0)	17 (45.9)	0.03[2]	0.33 (0.12–0.90)
Respiratory	23 (56.1)	29 (78.4)	0.04[2]	0.36 (0.13–0.97)
Hematological	25 (61.0)	18 (48.6)	0.36[2]	1.65 (0.67–4.06)
Neurological	3 (7.3)	9 (24.3)	0.05[2]	0.24 (0.06–0.99)
Cardiac	3 (7.3)	8 (21.6)	0.10[2]	0.29 (0.07–1.20)
Rhabdomyolysis	1 (2.4)	4 (10.8)	0.18[2]	0.21 (0.02–1.95)
Uveitis	1 (2.4)	3 (8.1)	0.34[2]	0.28 (0.03–2.85)
Secondary HLH	4 (9.8)	1 (2.7)	0.36[2]	3.89 (0.41–36.5)
Multi-organ dysfunction (≥2 organs), *n* (%)	27 (65.9)	21 (56.8)	0.48[2]	1.47 (0.58–3.70)
Any ventilation (NIV/invasive), *n* (%)	3 (7.3)	14 (37.8)	0.001[2]	0.13 (0.03–0.50)
Length of stay, days—median (IQR)	7 (5–10)	7 (5–9)	0.65[1]	–
Mortality, *n* (%)	1 (2.4)	1 (2.7)	1.00[2]	0.90 (0.05–14.9)

CI, confidence interval; HLH, hemophagocytic lymphohistiocytosis; IQR, interquartile range; NIV, noninvasive ventilation; OR, odds ratio; [1]Mann–Whitney *U* test; [2]Fisher's exact test

Table 6: Clinical characteristics of patients with dengue and scrub typhus coinfections (*N* = 78)

Characteristic	*Dengue coinfection (n = 11)*	*Scrub typhus coinfection (n = 9)*	*All patients (N = 78)*
Age, years—median (IQR)	41 (36–51)	44 (28–60)	57 (41–68)
Male gender, *n* (%)	4 (36.4)	6 (66.7)	41 (52.6)
Rural background, *n* (%)	5 (45.5)	7 (77.8)	46 (59.0)
Any comorbidity, *n* (%)	3 (27.3)	4 (44.4)	45 (57.7)*
Organ involvement, *n* (%)			
Hepatic	11 (100)	8 (88.9)	54 (69.2)
Renal	0 (0)	4 (44.4)	26 (33.3)
Respiratory	4 (36.4)	5 (55.6)	52 (66.7)
Hematological	11 (100)	6 (66.7)	43 (55.1)
Neurological	0 (0)	1 (11.1)	12 (15.4)
Cardiac	0 (0)	2 (22.2)	11 (14.1)
Rhabdomyolysis	1 (9.1)	0 (0)	5 (6.4)
Uveitis	0 (0)	1 (11.1)	4 (5.1)
Secondary HLH	0 (0)	2 (22.2)	5 (6.4)
Multi-organ dysfunction (≥2 organs), *n* (%)	11 (100)	8 (88.9)	48 (61.5)
Any ventilation (NIV/invasive), *n* (%)	0 (0)	2 (22.2)	17 (21.8)
Length of stay, days—median (IQR)	7 (6–9)	9 (5–10)	7 (5–9)
Mortality, *n* (%)	0 (0)	0 (0)	2 (2.6)

HLH, hemophagocytic lymphohistiocytosis; IQR, interquartile range; NIV, noninvasive ventilation; Some patients had both dengue and scrub typhus (*n* = 1) and are counted in both columns; Any comorbidity denotes patients with at least one preexisting condition (refer to Table 1)

Discussion

This study provides a comprehensive overview of acute leptospirosis in a tertiary care center in Rajasthan, highlighting its diverse clinical spectrum and outcomes. The median age of 57 years and slight male predominance align with previous Indian and global reports demonstrating that leptospirosis commonly affects adults with a higher proportion of male patients; systematic reviews from India have similarly noted male predominance and a wide age distribution in clinical cohorts.[1,2]

Although leptospirosis has traditionally been considered a rural disease linked to agricultural exposures, the substantial proportion of urban patients (41%) in this cohort suggests a shift in epidemiology. Urban leptospirosis has been increasingly reported, including the influence of urban risk factors such as waterlogging and rodent exposure contributing to transmission.[3,10] While common comorbidities such as diabetes and hypertension were observed, 42% of patients were previously healthy, emphasizing that leptospirosis affects individuals across health backgrounds.[2]

Clinically, anicteric presentations predominated (84.6%), consistent with numerous studies showing that nonjaundiced leptospirosis is the more frequent clinical form; the disease's spectrum ranges from mild febrile illness to severe multi-organ involvement.[1,4] However, multi-organ involvement occurred in over 60% of cases in this cohort, underscoring the potential severity even in nonicteric patients. Gastrohepatic and pulmonary systems were often affected, reflecting the classic organ predilection of leptospiral infection.[1,11] Fever remained the most universal symptom, with respiratory manifestations and breathlessness commonly reported, highlighting the disease's systemic nature.[2,4]

A notable finding was the high rate of coinfections, present in more than half of the cohort, with dengue and scrub typhus

Table 7: Comparison of severe vs nonsevere leptospirosis (*N* = 78)

Characteristic	*Severe (n =48)*	*Nonsevere (n =30)*	*p-value*	*OR (95% CI)*
Age, years—median (IQR)	57 (41–68)	56 (40–66)	0.78[1]	–
Male gender—*n* (%)	25 (52.1)	16 (53.3)	1.00[2]	0.95 (0.38–2.39)
Rural background—*n* (%)	28 (58.3)	18 (60.0)	1.00[2]	0.93 (0.36–2.40)
Any comorbidity—*n* (%)	30 (62.5)	15 (50.0)	0.35[2]	1.67 (0.65–4.26)
Icteric phenotype—*n* (%)	9 (18.8)	3 (10.0)	0.53[2]	2.08 (0.51–8.38)
Any coinfection—*n* (%)	27 (56.3)	14 (46.7)	0.48[2]	1.47 (0.58–3.70)
Length of stay, days—median (IQR)	8 (6–11)	5 (4–7)	<0.001[1]	–
Mortality—*n* (%)	2 (4.2)	0 (0.0)	0.52[2]	–

Severe disease was defined as involvement of ≥2 organ systems; CI, confidence interval; IQR, interquartile range; OR, odds ratio; [1]Mann–Whitney *U* test; [2]Fisher's exact test

being the most frequent. Systematic analyses in India report coinfection of scrub typhus and leptospirosis as an important clinical consideration due to overlapping seasonal and geographic distributions.[5,8] Coinfections with dengue and leptospirosis occur globally, with pooled coinfection prevalence reported in meta-analytic studies, and can complicate diagnosis and management.[2,6,7] In the present cohort, these coinfections occurred predominantly in younger, healthier patients and were associated with less severe renal, respiratory, and neurological involvement, suggesting that coinfected patients may not necessarily develop more severe leptospirosis.[7,10] However, this finding should be interpreted cautiously given the small subgroup size and lack of multivariate adjustment. The possibility of serological cross-reactivity, particularly in endemic settings, cannot be excluded and may have led to overestimation of coinfection rates. Therefore, these findings should be interpreted with caution.

Distinct clinical patterns were observed with specific coinfections. For instance, dengue coinfection primarily affected the hepatic and hematological systems, while scrub typhus coinfection showed broader organ involvement, reinforcing pathogen-specific vigilance in endemic regions.[5,12,13] These findings are consistent with other acute febrile illness surveillance studies that show diverse organ involvement depending on the infectious agent.[6,8]

Icteric leptospirosis (Weil's disease) represented a younger, more severely affected subgroup with universal hepatic involvement, a higher incidence of hemophagocytic lymphohistiocytosis (HLH), longer hospital stays, and a trend toward increased mortality. Severe leptospirosis marked by jaundice and organ dysfunction is well documented as a distinct and serious clinical phenotype with higher morbidity and variable mortality rates across settings.[1,9]

Severe leptospirosis, defined by multi-organ involvement, was observed in over 60% of patients and was associated with prolonged hospitalization, although mortality remained low (2.6%), highlighting the effectiveness of timely antibiotic therapy and supportive care in modern clinical settings.[2,3,11] Despite this low mortality, global data indicate that severe forms, especially with pulmonary hemorrhage or renal failure, are associated with a significantly higher risk of death—up to 50% in some contexts without prompt care.[1,9]

Overall, these findings underscore the heterogeneity of leptospirosis presentations, the importance of recognizing icteric and coinfected subgroups, and the critical role of early diagnosis and comprehensive management in improving outcomes. Additionally, the study highlights evolving epidemiology, including increasing urban cases and high rates of coinfections, emphasizing the need for region-specific surveillance and clinical awareness to improve timely diagnosis and tailored therapeutic strategies in endemic and emerging settings.[2,5,6,14] The findings of this study are broadly consistent with previous Indian studies demonstrating male predominance, multi-organ involvement, and the predominance of anicteric disease. However, compared to earlier reports, our study shows a higher proportion of urban cases and coinfections, suggesting evolving epidemiological patterns.

Strengths and Limitations

This study provides a comprehensive real-world evaluation of acute leptospirosis, including the clinical spectrum, organ involvement, coinfections, and outcomes in a tertiary care setting. Inclusion of only laboratory-confirmed cases and the use of predefined criteria enhance diagnostic reliability. The comparative analysis of icteric and anicteric phenotypes and the high burden of coinfections offer clinically relevant insights into disease heterogeneity and evolving epidemiology, including a notable urban contribution.

However, limitations include the retrospective, single-center design with potential selection bias and limited generalizability. The modest sample size and lack of multivariate analysis restrict the identification of independent predictors. Incomplete documentation limited the detailed assessment of some clinical parameters. Additionally, reliance on serology for coinfections raises the possibility of cross-reactivity. Despite these constraints, the study highlights important trends in the clinical profile of leptospirosis in an endemic setting.

Conclusion

Acute leptospirosis in adults demonstrates marked clinical heterogeneity with frequent multi-organ involvement and a substantial burden of coinfections in endemic settings. Icteric disease represents a distinct and more severe clinical phenotype associated with prolonged hospitalization and higher complication rates. Early diagnosis, vigilant monitoring for organ dysfunction, and timely supportive care are key determinants of favorable outcomes. Greater awareness of overlapping tropical infections is essential for improving diagnostic accuracy and management strategies in India.

Learning Points

Acute leptospirosis shows wide clinical variability, with frequent hepatic and respiratory involvement and multi-organ dysfunction in many hospitalized adults.

Anicteric disease is more common, while icteric (Weil's) disease represents a more severe phenotype with greater complications and longer hospital stays.

Coinfections, especially dengue and scrub typhus, are common but do not consistently worsen outcomes.

Early diagnosis and timely supportive management result in low mortality and favorable outcomes.

Urban cases of leptospirosis show a rising trend.

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