

Comparative Clinical and Laboratory Profile of Dengue, Leptospirosis, and Scrub Typhus.

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Abstract

Background: Dengue, leptospirosis, and scrub typhus are common causes of acute undifferentiated febrile illness in tropical countries and often present with overlapping clinical features, making early diagnosis challenging. **Objectives:** To compare the clinical manifestations and laboratory profiles of patients with dengue, leptospirosis, and scrub typhus and identify distinguishing features useful for early diagnosis. **Methods:** This prospective comparative observational study included 160 laboratory-confirmed patients, comprising 60 dengue, 50 leptospirosis, and 50 scrub typhus cases. Demographic characteristics, clinical findings, laboratory parameters, complications, and outcomes were recorded and analyzed using appropriate statistical tests, with $p < 0.05$ considered statistically significant. **Results:** Dengue predominantly affected younger patients and was characterized by thrombocytopenia, leukopenia, hemoconcentration, rash, and bleeding manifestations. Leptospirosis showed significantly higher frequencies of jaundice, conjunctival suffusion, acute kidney injury, elevated bilirubin, serum creatinine, and liver enzymes. Eschar was observed exclusively in scrub typhus patients, who also demonstrated elevated inflammatory markers and hepatic dysfunction. Hospital stay and complication rates were highest among patients with leptospirosis. Several clinical manifestations and laboratory parameters differed significantly among the three groups ($p < 0.05$). **Conclusion:** Although dengue, leptospirosis, and scrub typhus share many presenting features, careful evaluation of characteristic clinical signs and routine laboratory investigations enables early differentiation. Prompt recognition of these distinguishing profiles facilitates timely disease-specific treatment and improves patient outcomes, particularly in resource-limited settings.

Keywords: Dengue, Leptospirosis, Scrub typhus, Acute febrile illness, Tropical infections, Clinical profile, Laboratory profile.



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INTRODUCTION

Acute undifferentiated febrile illness (AUFI) is a major cause of hospital admissions in tropical and subtropical countries, particularly during the monsoon and post-monsoon seasons. Among the various etiologies, dengue fever, leptospirosis, and scrub typhus are the most common infectious diseases that present with overlapping clinical manifestations, making early diagnosis and appropriate management challenging. These infections are associated with significant morbidity and mortality if not recognized and treated promptly. Early differentiation is therefore essential to initiate disease-specific therapy, reduce complications, and improve patient outcomes.[1-3]

Dengue is a mosquito-borne viral infection caused by the dengue virus (DENV), transmitted primarily by *Aedes aegypti* mosquitoes. The disease spectrum ranges from asymptomatic infection and uncomplicated dengue fever to severe dengue characterized by plasma leakage, hemorrhage, shock, and multiorgan dysfunction. The global burden of dengue has increased substantially over the past few decades owing to rapid urbanization, climate change, and expansion of vector habitats. India continues to report seasonal outbreaks with considerable healthcare burden, especially during the rainy season.[1,4,5]

Leptospirosis is a widespread zoonotic disease caused by pathogenic *Leptospira* species. Human infection occurs through direct or indirect exposure to urine of infected animals, particularly in environments contaminated by floodwater or moist soil. Clinical manifestations vary from a mild febrile illness to severe disease involving hepatic dysfunction, acute kidney injury, pulmonary hemorrhage, and circulatory collapse. Because its initial presentation often resembles other tropical

infections, laboratory confirmation is essential for accurate diagnosis.[2,6,7] Scrub typhus, caused by *Orientia tsutsugamushi* and transmitted through the bite of infected chigger mites, has emerged as an important re-emerging cause of acute febrile illness across the Asia-Pacific region, including India. Patients commonly present with fever, headache, myalgia, lymphadenopathy, and gastrointestinal symptoms, while the characteristic eschar may not always be present. Delayed diagnosis may lead to serious complications such as acute respiratory distress syndrome, myocarditis, meningoencephalitis, acute kidney injury, and multiple organ dysfunction syndrome. Fortunately, early treatment with doxycycline or azithromycin results in rapid clinical improvement.[3]

Despite their different etiologies, dengue, leptospirosis, and scrub typhus share several common clinical and laboratory features including fever, thrombocytopenia, leukocyte abnormalities, elevated liver enzymes, and multiorgan involvement. This overlap frequently delays definitive diagnosis, particularly in resource-limited settings where advanced diagnostic facilities may not be readily available. Comparative evaluation of their clinical presentation and laboratory characteristics may help clinicians identify distinguishing features and facilitate timely diagnosis and appropriate management.[7,8] Therefore, the present study was undertaken to compare the clinical manifestations and laboratory profiles of patients with dengue, leptospirosis, and scrub typhus presenting to a tertiary care hospital and to identify distinguishing parameters that may aid in their early differentiation.

MATERIALS AND METHODS

Study Design

This was a hospital-based, prospective, comparative observational study.

Study Setting

The study was conducted in the Department of General Medicine in collaboration with the Departments of Microbiology and Pathology at a tertiary care teaching hospital.

Study Duration

The study was carried out over a period of 24 months after obtaining approval from the Institutional Ethics Committee.

Study Population

Adult patients admitted with acute febrile illness who were subsequently diagnosed with dengue, leptospirosis, or scrub typhus by appropriate laboratory investigations were included in the study.

Sample Size

A total of 160 patients were enrolled in the study:

- Dengue: 60 patients
- Leptospirosis: 50 patients
- Scrub typhus: 50 patients

The sample size was calculated assuming a confidence level of 95%, statistical power of 80%, and an anticipated moderate difference in major clinical and laboratory parameters among the three disease groups.

Inclusion Criteria

- Patients aged 18 years or older.
- Patients presenting with acute febrile illness (duration ≤ 14 days).
- Laboratory-confirmed diagnosis of dengue, leptospirosis, or scrub typhus.
- Patients willing to provide written informed consent.

Exclusion Criteria

- Patients with co-infection involving more than one tropical infectious disease.
- Patients with chronic liver disease, chronic kidney disease, autoimmune disorders, malignancy, or hematological disorders affecting laboratory parameters.
- Patients already receiving specific antimicrobial therapy before admission for more than 72 hours.
- Pregnant women.
- Patients with incomplete clinical records or refusal to participate.

Diagnostic Criteria

Diagnosis was established using standard laboratory methods:

- Dengue: NS1 antigen and/or dengue IgM ELISA.
- Leptospirosis: IgM ELISA and/or Microscopic Agglutination Test (MAT), where available.
- Scrub Typhus: IgM ELISA and/or Immunofluorescence Assay (IFA), where available.

Data Collection

A structured proforma was used to record demographic characteristics, duration of illness, presenting symptoms, physical examination findings, and associated complications. Detailed clinical examination was performed at admission.

Laboratory Evaluation

The following investigations were performed:

- Complete blood count (hemoglobin, total leukocyte count, differential count, platelet count)
- Hematocrit
- Erythrocyte sedimentation rate
- Liver function tests (AST, ALT, bilirubin, alkaline phosphatase)
- Renal function tests (serum urea and creatinine)
- Serum electrolytes
- C-reactive protein
- Urinalysis
- Chest radiography, abdominal ultrasonography, and other imaging studies whenever clinically indicated.

Outcome Measures

The primary outcome was comparison of the clinical features and laboratory parameters among patients with dengue, leptospirosis, and scrub typhus. Secondary outcomes included comparison of complications, duration of hospitalization, intensive care unit admission, and in-hospital mortality.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using SPSS version 25.0. Continuous variables were expressed as mean $\pm$ standard deviation (SD) or median (interquartile range) depending on data distribution. Categorical variables were presented as frequencies and percentages. Comparisons among the three groups were performed using one-way ANOVA or Kruskal-Wallis test for continuous variables and Chi-square test or Fisher's exact test for categorical variables. A p-value <0.05 was considered statistically significant.

RESULTS

A total of **160 patients** with laboratory-confirmed tropical febrile illnesses were included in the study. Of these, **60 (37.5%)** had dengue fever, **50 (31.3%)** had leptospirosis, and **50 (31.3%)** had scrub typhus. The demographic characteristics, clinical features, laboratory findings, and outcomes were compared among the three groups.

Table 1. Demographic Characteristics of Study Participants

Variable	Dengue (n=60)	Leptospirosis (n=50)	Scrub Typhus (n=50)	p-value
Mean age (years)	31.8 $\pm$ 12.6	42.5 $\pm$ 14.1	39.7 $\pm$ 13.5	<0.001
Male	36 (60.0%)	34 (68.0%)	29 (58.0%)	0.54
Female	24 (40.0%)	16 (32.0%)	21 (42.0%)	
Rural residence	28 (46.7%)	36 (72.0%)	33 (66.0%)	0.018
Mean duration of fever (days)	5.2 $\pm$ 1.6	6.8 $\pm$ 2.1	7.1 $\pm$ 2.3	<0.001

Patients with leptospirosis and scrub typhus were significantly older than those with dengue. Rural residence was significantly more common among patients with leptospirosis and scrub typhus. Duration of fever before presentation was longest in scrub typhus and shortest in dengue ($p<0.001$).

Table 2. Comparison of Clinical Features

Clinical Feature	Dengue (n=60)	Leptospirosis (n=50)	Scrub Typhus (n=50)	p-value
Fever	60 (100%)	50 (100%)	50 (100%)	NS
Headache	46 (76.7%)	26 (52.0%)	29 (58.0%)	0.012
Myalgia	48 (80.0%)	39 (78.0%)	38 (76.0%)	0.89
Rash	18 (30.0%)	3 (6.0%)	6 (12.0%)	0.004
Bleeding manifestations	15 (25.0%)	5 (10.0%)	3 (6.0%)	0.011
Jaundice	3 (5.0%)	20 (40.0%)	11 (22.0%)	<0.001
Conjunctival suffusion	2 (3.3%)	18 (36.0%)	4 (8.0%)	<0.001
Eschar	0	0	19 (38.0%)	<0.001
Hepatomegaly	11 (18.3%)	18 (36.0%)	17 (34.0%)	0.041
Splenomegaly	7 (11.7%)	9 (18.0%)	14 (28.0%)	0.083

Although fever was universal in all groups, dengue patients had significantly higher frequencies of headache, rash, and bleeding manifestations. Jaundice and conjunctival suffusion were significantly associated with leptospirosis, while eschar was exclusively observed in scrub typhus patients.

Table 3. Comparison of Laboratory Parameters

Laboratory Parameter	Dengue	Leptospirosis	Scrub Typhus	p-value
Hemoglobin (g/dL)	13.4 ± 1.8	12.6 ± 2.0	12.9 ± 1.9	0.072
Total leukocyte count (/mm ³)	4,650 ± 1,520	11,920 ± 3,480	10,480 ± 2,950	<0.001
Platelet count (×10 ³ /mm ³)	64 ± 28	112 ± 46	98 ± 41	<0.001
Hematocrit (%)	43.8 ± 4.5	38.9 ± 4.8	39.7 ± 5.0	<0.001
AST (IU/L)	112 ± 48	146 ± 72	138 ± 69	0.009
ALT (IU/L)	86 ± 37	118 ± 56	103 ± 49	0.006
Total bilirubin (mg/dL)	1.0 ± 0.4	3.5 ± 1.8	2.2 ± 1.1	<0.001
Serum creatinine (mg/dL)	0.9 ± 0.3	2.3 ± 1.1	1.5 ± 0.8	<0.001
CRP (mg/L)	18 ± 10	72 ± 28	68 ± 24	<0.001

Dengue patients demonstrated significantly lower platelet counts and leukocyte counts with higher hematocrit values. Leptospirosis was associated with markedly elevated bilirubin, serum creatinine, and liver enzymes. Scrub typhus also showed raised inflammatory markers and liver enzymes but less severe renal dysfunction than leptospirosis.

Table 4. Clinical Outcome and Complications

Outcome	Dengue (n=60)	Leptospirosis (n=50)	Scrub Typhus (n=50)	p-value
ICU admission	8 (13.3%)	14 (28.0%)	11 (22.0%)	0.087
Acute kidney injury	2 (3.3%)	16 (32.0%)	7 (14.0%)	<0.001
Hepatic dysfunction	12 (20.0%)	23 (46.0%)	18 (36.0%)	0.006
Shock	7 (11.7%)	8 (16.0%)	6 (12.0%)	0.79
Mechanical ventilation	3 (5.0%)	6 (12.0%)	5 (10.0%)	0.35
Mean hospital stay (days)	5.8 ± 2.1	8.7 ± 3.4	7.9 ± 2.8	<0.001
Mortality	1 (1.7%)	3 (6.0%)	2 (4.0%)	0.42

Patients with leptospirosis experienced significantly higher rates of acute kidney injury, hepatic dysfunction, and longer hospital stays. Scrub typhus had intermediate severity, while dengue patients generally had shorter hospitalization and fewer complications. Mortality was highest in leptospirosis, although the difference among groups was not statistically significant.

DISCUSSION

Acute undifferentiated febrile illness remains a major diagnostic challenge in tropical countries because dengue, leptospirosis, and scrub typhus share several overlapping clinical manifestations. Early differentiation based on clinical and laboratory findings is essential for prompt initiation of appropriate therapy and prevention of severe complications. The present study compared the demographic profile, clinical presentation, laboratory abnormalities, and outcomes among patients with these three common tropical infections. In the present study, dengue predominantly affected younger individuals, whereas leptospirosis and scrub typhus were more common among middle-aged adults, particularly those from rural areas. These findings are consistent with the epidemiological observations reported by Xu et al. and Reller and Dumler, who noted that occupational exposure, agricultural activities, and rural environmental conditions increase the risk of leptospirosis and scrub typhus, while dengue affects all age groups in endemic urban and peri-urban regions. (9-11)

Fever was the universal presenting symptom in all three diseases, highlighting the difficulty of differentiating these infections on clinical grounds alone. However, certain clinical manifestations were significantly associated with specific diseases. Rash and bleeding manifestations were more frequent in dengue, jaundice and conjunctival suffusion were characteristic of leptospirosis, while eschar was observed exclusively in scrub typhus. Similar distinguishing clinical features have been described by Gupta et al. and the National Centre for Disease Control (NCDC) guidelines, which emphasize that although eschar is highly suggestive of scrub typhus, it is absent in a substantial proportion of patients, necessitating a high index of clinical suspicion. (12,13) The laboratory findings further demonstrated important differences among the three infections. Dengue patients had marked thrombocytopenia, leukopenia, and hemoconcentration, reflecting plasma leakage and bone marrow suppression. In contrast, leptospirosis was associated with leukocytosis, hyperbilirubinemia, elevated liver enzymes, and significantly increased serum creatinine, indicating hepatic and renal involvement. Patients with scrub typhus also exhibited elevated inflammatory markers and hepatic dysfunction, although renal impairment was generally less severe than in leptospirosis. These observations are in agreement with the reports of

Wilder-Smith et al., Taylor et al., and Reller and Dumler, who demonstrated that laboratory profiles can provide valuable clues for differentiating tropical febrile illnesses before confirmatory serological testing becomes available.(9-11)

Regarding outcomes, leptospirosis showed the highest frequency of acute kidney injury, hepatic dysfunction, intensive care admission, prolonged hospitalization, and mortality, whereas dengue generally had a more favorable clinical course with shorter hospital stay. Scrub typhus demonstrated intermediate disease severity, and most patients responded well to timely doxycycline therapy. Similar outcome patterns have been reported by Taylor et al., Gupta et al., and the NCDC national guidelines, emphasizing that delayed diagnosis and treatment are the principal determinants of adverse outcomes in leptospirosis and scrub typhus. (8,12,13) Overall, the present study highlights that although significant overlap exists among these tropical infections, careful assessment of characteristic clinical signs together with routine laboratory parameters can substantially improve early diagnostic accuracy. Such differentiation is particularly valuable in resource-limited settings where advanced diagnostic facilities may not be immediately available, allowing clinicians to initiate appropriate therapy while awaiting confirmatory investigations.

CONCLUSION

Dengue, leptospirosis, and scrub typhus are important causes of acute febrile illness with considerable overlap in clinical presentation. However, characteristic clinical features such as bleeding manifestations in dengue, jaundice and conjunctival suffusion in leptospirosis, and eschar in scrub typhus, together with distinct laboratory abnormalities including thrombocytopenia, leukopenia, elevated liver enzymes, hyperbilirubinemia, and renal dysfunction, facilitate early differentiation. Leptospirosis was associated with the greatest disease severity and longest hospital stay, whereas dengue generally had a more favorable outcome. Recognition of these distinguishing clinical and laboratory profiles can aid early diagnosis, prompt initiation of disease-specific treatment, and reduction in morbidity and mortality, especially in resource-constrained healthcare settings.

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