


CASE REPORT

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# Dengue and leptospirosis coinfection: a case series



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## Abstract

**Background** Both dengue and *Leptospira* infections are endemic to tropical and subtropical regions, with their prevalence increasing in recent decades. Coinfection with these pathogens presents significant diagnostic challenges for clinicians due to overlapping clinical manifestations and laboratory findings. This case report aims to elucidate two clinical scenarios where the coinfection of dengue and leptospirosis complicates the disease course, creating a diagnostic conundrum.

**Case presentation** We present the clinical scenarios of two Bangladeshi males, aged 25 and 35 years, who were admitted to our hospital with acute febrile illness. The first patient exhibited hepatic and renal involvement, while the second presented with symptoms initially suggestive of meningoencephalitis. Both cases were initially managed under the presumption of dengue infection based on positive serology. However, further evaluation revealed coinfection with *Leptospira*, complicating the disease course. Both patients received appropriate treatment for dengue and antibacterial therapy for leptospirosis, ultimately resulting in their recovery.

**Conclusion** These case scenarios underscore the critical importance for clinicians in regions where dengue and *Leptospira* are endemic to consider both diseases when evaluating patients presenting with acute febrile illness.

**Keywords** Dengue fever, Leptospirosis, Coinfection, Encephalopathy, Case report

## Background

Dengue is one of the fastest-growing mosquito-borne viral diseases and poses a significant public health threat. It is an arthropod-borne disease transmitted through the bite of infected mosquitoes and is highly prevalent in tropical and subtropical regions. According to the World Health Organization (WHO), approximately half of the world's population is now at risk of dengue infection, with an estimated 100–400 million infections occurring annually [1]. While dengue incidence was historically limited

to the monsoon season, recent epidemics in Bangladesh indicate a shift, with longer transmission periods resulting in increased human infections. Climate change, with its associated rise in global temperatures, is likely to expand the geographic range and incidence of dengue by promoting viral reproduction and survival [2, 3].

Leptospirosis is a zoonotic disease with a higher incidence in tropical and subtropical regions. Human infection occurs through accidental exposure to the urine of infected animals or contaminated soil and water. According to the Centers for Disease Control and Prevention (CDC), an estimated 1 million cases occur globally each year, resulting in nearly 60,000 deaths [4]. The incidence of leptospirosis has increased in recent decades, largely due to climate change [3, 5] and natural disasters [6]. While most infections are subclinical, a minority result in

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severe disease involving multiple organs such as the kidneys, liver, lungs, and brain.

Given the overlapping geographic distribution of dengue and leptospirosis, coinfection is a likely occurrence and poses a significant public health concern. The reported prevalence of coinfection ranges from 0.9% to 5.9% [7–10]. The overlapping symptoms and signs in the early phase can create a diagnostic challenge, potentially leading to fatal consequences, particularly during dengue epidemics [11].

In the year 2023, Bangladesh, a densely populated nation, confronted its most significant dengue outbreak in history, recording 316,411 confirmed cases of infection and 1650 fatalities [12]. Conversely, Bangladesh has a high annual occurrence of leptospirosis [13].

In this report, we delineate the concurrent occurrence of dengue and *Leptospira* infections in two patients initially admitted to our dengue ward with suspected dengue fever.

## Case presentation

### Case 1

A 25-year-old Bangladeshi male, residing in a rural village and employed as an agricultural worker, presented to our health center with a 3-day history of high-grade fever. Additionally, the patient complained of myalgia, severe bodily pain, and episodes of vomiting. Over the past day, he had experienced abdominal pain and loose, watery stools. Notably, the patient observed yellow discoloration of both his urine and eyes for the past day.

During the physical examination, the patient appeared conscious and oriented, without any signs of meningeal irritation. He presented with a temperature of 103 °F, dehydration, jaundice, and leg edema. His pulse was recorded at 90 beats per minute (bpm), and his blood pressure measured 130/80 mmHg. Skin examination revealed petechial rash on the chest and extremities, as well as subconjunctival hemorrhage in both eyes. The tourniquet test yielded a positive result. Considering the ongoing outbreak, dengue serology was performed, confirming positivity. Further investigations revealed elevated serum bilirubin levels and thrombocytopenia.

We started management for dengue fever with guideline (DGHS, 2018)-directed cautious fluid resuscitation and frequent clinical and biochemical monitoring. The patient was doing well for the next 2 days; however, on the fourth day since admission, the temperature spiked again, accompanied by an increase in liver biochemistry and serum creatinine levels (Table 1). Considering the differential diagnoses, we subsequently conducted testing for leptospirosis, which yielded a positive result. Treatment was augmented to incorporate intravenous administration of Ceftriaxone at a dosage of 2 g per day.

Subsequent monitoring revealed gradual improvement in both clinical and biochemical parameters over time. The patient was discharged in a stable condition.

On the tenth day, a follow-up serological test for leptospirosis was conducted, revealing an elevated titer of 3600, suggestive of recent infection with leptospirosis.

### Case 2

A 35-year-old previously healthy Bangladeshi male was transferred to our facility from a distant district, presenting with a 3-day history of high-grade fever and altered consciousness. The patient's attendant reported fresh rectal bleeding occurring over the past day. The patient had no documented systemic illnesses. The physical examination revealed impairment in higher cognitive function, as indicated by a Glasgow Coma Scale score of 9 (E2V4M3). The patient exhibited a pulse rate of 100 beats per minute, blood pressure of 90/60 mmHg, and normal jugular venous pressure. Additionally, the patient presented with a temperature of 100 °F and jaundice. Pupillary examination demonstrated bilaterally equal and reactive pupils. The neurological assessment revealed a stiff neck and bilateral extensor plantar response. Abdominal examination detected the presence of ascites, as indicated by shifting dullness and a palpable liver. Additionally, bilateral subconjunctival hemorrhage was observed. The patient was transferred to the dengue ward on the same day of admission after receiving a positive result for dengue infection. A tentative diagnosis of expanded dengue syndrome was made and supportive management was started accordingly. The patient was then shifted to intensive care unit for better monitoring and relevant laboratory investigations were sent. Chest X-ray showed normal radiological appearance of lung with no cardiomegaly (cardiothoracic ratio 0.45). Initial investigations unveiled leukocytosis, thrombocytopenia, elevated alanine transaminase (ALT), and increased serum creatinine levels. Additionally, cerebrospinal fluid (CSF) analysis revealed pleocytosis, with normal protein and glucose concentrations which prompted us to do test for *Leptospira* and it came as positive on day 3. A reevaluation of leptospirosis serology on the ninth day revealed an increasing titer of 1:3200, signifying a recent infection with leptospirosis.

Injection ceftriaxone 2 g/daily was then added to ongoing treatment. All parameters gradually started to return to normal and he was stable without additional fluid support. On day 7, the patient suddenly developed palpitation, respiratory distress, and orthopnea. Physical examination revealed tachycardia, tachypnea, hypotension, and elevated jugular venous pressure, accompanied by crackles over both lung fields. A repeat chest X-ray showed an enlarged cardiac silhouette, prominent

**Table 1** Time trends of investigations of the first patient

Name	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8
Hemoglobin (gm/dL)	11.4	11.1	8.9	11.1	10.7	10.8	10.6	10.2
TC WBC ( $\times 10^9/L$ )	8.1	9.54	4.25	12.66	14.14	15.61	13.19	10.37
Neutrophil (%)	82	89	46.3	56.6	59.6	59.4	66.1	64.6
Lymphocyte (%)	12	7.8	40.0	23.8	22.6	26.8	24.2	29.6
HCT	35.1%	33%	29.4%	31.8%	31.3%	31.4%	31.8%	32.1%
Platelet ( $\times 10^9/L$ )	27,000	38,000	265,000	81,000	70,000	107,000	148,000	269,000
S. creatinine (mg/dL)		6.8	7.72		2.8	2.1	1.55	1.4
S. bilirubin (mg/dL)	3.9	4.9						
Leptospiral antibody				Positive				
Dengue-NS1	Positive							
Dengue-IgM	Positive							
Dengue-IgG	Negative							
ALT	56		61	120		78		40
Blood urea (mg/dL)			177					
S. lipase (IU/L)			732 IU/L					
Chest X-ray	No abnormalities							
USG of whole abdomen			No abnormalities described					
S. electrolytes								
Sodium (mmol/L)	128		130					
Potassium (mmol/L)	5.1		5.3					
Chloride (mmol/L)	90		109					
Bicarbonate (mmol/L)	28		19					
Urine RME	No abnormalities							

TC WBC Total WBC Count, HCT Hematocrit, ALT Alanine transaminase, USG Ultrasonography, Urine RME Urine Routine Microscopic Examination

\*Day 1 means first day of hospital admission

vascular markings, and opacities in the lower regions of both lungs, indicative of pulmonary edema. The electrocardiogram (ECG) revealed sinus tachycardia, reduced R-wave amplitude, depressed ST segments, and T-wave inversion in chest leads, alongside an elevated serum troponin I level (refer to Table 2). Subsequent 2D-echocardiography demonstrated features suggestive of global hypokinesia, with an ejection fraction of 40%. Based on the ESC 2013 criteria proposed by Caforio *et al.*, a diagnosis of probable myocarditis was established. Management involved oxygen inhalation and diuretic therapy. The patient's condition showed gradual improvement over the subsequent days, eventually resulting in discharge in a stable hemodynamic state on day 14.

To facilitate a better understanding and a clear comparison of the clinical features and outcomes of these cases, we have created a table that summarizes key aspects of each case (Table 3).

#### Follow-up

The patient presented for a follow-up appointment 2 months postdischarge. The patient exhibited stable hemodynamic status and normal physical functioning.

Follow-up echocardiography demonstrated the absence of regional wall motion abnormalities.

#### Discussion

Acute febrile illness (AFI) represents a frequent cause of hospitalization, especially prevalent in tropical and subtropical regions. The diagnostic process poses challenges for clinicians, especially in low-income countries such as Bangladesh, where appropriate diagnostic tools may be limited. Clinicians often adopt a syndrome-based approach to address this diagnostic dilemma. Among the spectrum of AFI etiologies, including malaria, scrub typhus, enteric fever, and Rickettsia diseases, dengue and leptospirosis hold considerable significance in India, an adjacent nation to Bangladesh [14, 15]. Correspondingly, outpatient studies conducted in Bangladesh have reported similar findings [16].

Dengue virus infection ranks as the most prevalent arthropod-borne illness globally, with widespread distribution. While typically sporadic in developing nations, cases often arise from travel to endemic regions. However, rising global temperatures are fostering the ecological persistence of the virus, leading

**Table 2** Time trends of investigations of the second patient

Name	Day 1	Day 2	Day 3	Day 5	Day 6	Day 7	Day 8	Day 9
Hemoglobin	12.5	11.1	11.3		10.8		11.5	12.2
TC WBC	21.12	11.8	10.21		7.54		6.44	5.86
Neutrophil	75.7%	85.6%	71.2%		67.3%		59.7%	55.7%
Lymphocyte	5.8%	12.3%	15.3%		18.3%		23.7%	29.6%
HCT	38.3	31.9	34.2		34.0		36.9	39.8
Platelet	53,000	108,000	75,000		77,000		113,000	151,000
S. creatinine	4.47 mg/dL	7.1 mg/dL	6.7 mg/dL	5.10	3.68			0.8
S. bilirubin		4.65 mg/dL		2.01 mg/dL	0.8			
Dengue-NS1	Positive							
Dengue-IgM	Positive							
Leptospiral antibody			Positive					
Blood film for malarial parasite			Negative					
ALT (IU/L)			1882		830			30
Blood glucose			7 mmol/L					
S. albumin	2.1							
Prothrombin time			16.6 seconds					
Troponin-I (Reference 0.04 ng/mL)						2.12 ng/mL		
ECG						Sinus tachycardia, depressed ST segment, and T-wave inversion in chest leads		
Echocardiography						Global hypokinesia with ejection fraction of 40%		
D-Dimer			3.5 mg/dL					
USG of W/A			Ascites					
Chest X-ray						Cardiomegaly, prominent vascular marking, pulmonary edema		
CSF study		15 leukocytes/ $\mu$ L, glucose 60 mg/dL, protein 50 mg/dL						

TC WBC Total WBC Count, HCT Hematocrit, ALT Alanine transaminase, ECG Electrocardiogram, USG Ultrasonography, CSF Cerebrospinal fluid

\*Day 1 means first day of hospital admission

to shifts in epidemiology. Bangladesh is currently facing the largest dengue outbreak with an unprecedented rise in infection rate and case fatality rate (CFR) of 0.47%. Notably, Dengue virus serotype 2 (DENV2) has reemerged as the predominant circulating serotype in 2023, following its prevalence in 2018 [17].

The clinical presentation typically features a marked increase in body temperature, severe myalgia, often termed as “break-bone fever,” and retro-orbital pain. Key characteristics of this infection include capillary leakage and hemorrhagic manifestations, which are pivotal in the development of severe complications such as shock syndrome and subsequent multiorgan failure.

The typical biochemical alterations are dynamic, characterized by leukopenia, significant thrombocytopenia, and an elevation in hematocrit levels during the critical phase. These parameters gradually normalize during the recovery phase.

Conversely, leptospirosis, a zoonotic infection caused by *Leptospira* spp., poses a substantial risk of mortality [18]. It is known to precipitate recurrent outbreaks, particularly in tropical regions, attributable to favorable epidemiological shifts [19, 20]. In addition to fever, characteristic symptoms at presentation include abdominal pain, jaundice, and oliguria. Unlike dengue infection, leukocytosis is commonly observed in leptospirosis. Organ dysfunction features, such as elevated

**Table 3** Comparison of two cases

Traits	Case 1	Case 2
Age and gender	25 years, male	35 years, male
Presenting complaints	High-grade fever for 3 days, myalgia, severe body pain and vomiting, abdominal pain, yellow discoloration of his urine and eyes	High-grade fever, altered consciousness and fresh rectal bleeding
On physical examination	Conscious, oriented without any signs of meningeal irritation. Temperature 103 °F Dehydration, jaundice, leg edema were present Petechial rash on the chest and extremities; subconjunctival hemorrhage	Glasgow coma scale scores of 9 (E2V4M3), Temperature 100 °F and presence of jaundice, stiff neck with a bilateral extensor plantar response Ascites present, just palpable liver and subconjunctival hemorrhage
Dengue serology	Positive (on the day of admission)	Positive (on the day of admission)
Second spike of temperature	Day 4 since admission	No second spike
Leptospiral serology	Positive (on the day 4 of admission)	Positive (on the day 3 of admission)
Occurrence of probable myocarditis	No	Yes
Discharge	On day 10	On day 14
Follow-up	Fully recovered, no residual sequelae	Fully recovered, no residual sequelae

bilirubin and ALT levels, along with increased serum creatinine levels, are prominent in leptospiral infection.

While dengue is traditionally not recognized as a neurotropic virus, recent findings indicate its neurotropic potential. Neurological complications have been documented in 0.5–6.2% of cases [21, 22]. A surveillance study conducted in India identified dengue as the causative agent in 5% of acute encephalitis syndrome cases [23]. In our second case, the presentation likely stemmed from dengue encephalopathy.

The occurrence of probable myocarditis in the second case is likely due to leptospiral infection. Myocarditis associated with leptospirosis has been documented in both clinical cases [24, 25] and postmortem biopsies [26]. Alternatively, the myocarditis may also be attributable to dengue infection. A recent systematic review and meta-analysis reported a pooled prevalence of myocarditis in dengue fever of 12.4% [27].

As both diseases peak during the monsoon season, coinfection is expected to occur frequently. Without a strong clinical suspicion, the diagnosis of coinfection may be delayed, resulting in fatal outcomes. Dengue management primarily revolves around timely and adequate fluid resuscitation, while leptospirosis requires antibiotic therapy along with appropriate organ support if warranted.

Several studies have endeavored to investigate clinical and biochemical indicators that could aid clinicians in promptly diagnosing coinfection with dengue and leptospirosis [28, 29]. It was observed that abdominal discomfort and fatigue were more prevalent in the dengue–*Leptospira* coinfection group, while symptoms such as headache, arthralgia, epigastric pain, retro-orbital pain, acute kidney injury, and gum bleeding were more commonly reported in cases of dengue infection alone.

Additionally, in the coinfection group, the typical progression from febrile to critical and convalescent phases of dengue was less clearly delineated [9].

The documented cases discussed here had certain noteworthy characteristics that led us to consider possibilities other than dengue: jaundice, disruption of the classical phase of dengue, leukocytosis, and a marked deterioration in liver and renal function. Both cases respond dramatically after addition of antibiotic.

#### Limitations

Owing to the unavailability of resources at our facility, we were unable to conduct polymerase chain reaction (PCR) testing on cerebrospinal fluid (CSF) for Japanese encephalitis and herpes simplex virus. Furthermore, cardiac magnetic resonance imaging (MRI) was not feasible to provide enhanced confirmation of myocarditis.

#### Conclusions

The convergence of clinical syndromes during the initial undifferentiated phase of leptospirosis and dengue fever may result in its under-recognition, particularly amid dengue fever epidemics, potentially leading to a poorer prognosis.

#### Guidelines

The case report presentation followed CARE guidelines [30].

#### Learning points for clinicians

Considering the strikingly similar clinical presentations of dengue and *Leptospira* infections, clinicians practicing in endemic areas should exercise heightened vigilance and include these conditions in the differential diagnosis

of acute febrile illnesses (AFI). Even in cases suspected or confirmed as dengue, leptospirosis should be actively excluded, given its specific antibiotic treatment, which can substantially enhance overall patient survival.

#### Abbreviations

WHO	World Health Organization
CDC	Centers for Disease Control and Prevention
DF	Dengue fever
JVP	Jugular venous pressure
CSF	Cerebrospinal fluid
AFI	Acute febrile illness
DENV2	Dengue virus serotype 2
CFR	Case fatality rate
ALT	Alanine transaminase

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#### Author contributions

MA and LK: involved in patient's care, conceptualization, data curation, literature review, and manuscript writing. AR, MSR, MAA: involved in patient's care, interpreted patient data, edited the final draft. SRC: involved in patient's care, conducted literature review, revised and edited the final draft. Each of the authors has meticulously reviewed and granted their approval for the final manuscript.

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#### Availability of data and materials

All data generated or analysed during this study are included in this published article.

#### Declarations

##### Ethics approval and consent to participate

Ethical approval was obtained from the Ethical Review Committee of Sylhet MAG Osmani Medical College, Sylhet, Bangladesh. Written consent, obtained after thorough information disclosure, has been acquired from both patients for the publication of this case report. We hereby confirm that informed consent was obtained from both patients for the publication of identifying information or images in this publication.

##### Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

##### Competing interests

The authors affirm that they do not possess any known competing financial interests or personal relationships that might have been perceived to influence the work presented in this paper.

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