

# Acute Liver Failure in Postpartum Period—A Rare Complication of Dengue Infection: A Case Report

Shilpa Sapre<sup>1</sup>, Henil Upadhyay<sup>2</sup>, Charmy Parikh<sup>3</sup>

## ABSTRACT

**Aim:** Successful management of acute liver failure in a case of dengue infection in postpartum patient by a multidisciplinary approach.

**Background:** Dengue fever is a viral infection transmitted by the bite of *Aedes aegypti* mosquito. It is a major public health problem in developing countries like India. Symptomatology of dengue ranges from mild self-limiting illness to fulminant liver failure. Hepatic dysfunction is a known complication in dengue fever that ranges from mild to moderate elevation of serum transaminases to catastrophic fulminant liver failure. Acute liver failure is a rare complication of dengue infection with high mortality rate.

**Case description:** We report here a case of 19-year-old female who was referred to our center for management of primary postpartum hemorrhage with acute febrile illness. Laboratory investigations revealed anemia, thrombocytopenia, and positive dengue NS1 antigen test. The patient was managed in the critical care unit for pulmonary edema, acute kidney injury, and deranged coagulation profile secondary to hepatic dysfunction. Postpartum hemorrhage was another challenge tackled conservatively. The spectrum of liver involvement varied from a modest rise in transaminases in the early phase and culminating finally in acute hepatic failure by the end of 2 weeks. Multiple blood and blood products were transfused during her 1 month stay in intensive care. There was no perinatal transmission. A multidisciplinary approach involving obstetricians, intensivists, and gastroenterologists resulted in successful recovery of the patient from acute liver failure.

**Conclusion:** Clinicians should have a high index of suspicion for dengue fever in endemic areas in a case of acute febrile illness with/without the classical signs and symptoms of dengue fever. Pregnancy poses a special challenge for the obstetrician as delivery during this period can have devastating complications. A multidisciplinary approach with cautious fluid management is advisable in patients with severe dengue infection. Postpartum hemorrhage can be one of the life-threatening complications due to thrombocytopenia and deranged coagulation profile. Acute liver failure is a rare complication but can develop in patients with severe hepatitis.

**Clinical significance:** Dengue infection in pregnancy can mimic other causes of thrombocytopenia like HELLP syndrome, megaloblastic anemia, and gestational thrombocytopenia; hence, a detailed evaluation is warranted in pregnant women presenting with acute febrile illness with thrombocytopenia. Liver involvement in dengue infection can have devastating consequences leading to severe hepatitis and acute liver failure.

**Keywords:** Acute liver failure, Dengue infection, Postpartum, Pregnancy.

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## BACKGROUND

Dengue fever is a viral infection transmitted by the bite of *Aedes aegypti* mosquito. It is caused by dengue virus (DENV) serotypes 1, 2, 3, and 4 with varied geographical distribution. Dengue, a major public health problem in tropical countries like India, is endemic in more than 100 countries.<sup>1</sup> The effects of dengue infection on pregnant women and its fetus have been reported in literature. Miscarriages, preterm labor, oligohydramnios, obstetric hemorrhage, risk of the cesarean section, and neonatal infection have been found to be associated with dengue infection.<sup>2,3</sup> Minimal to severe hepatitis is known in dengue infection; however, acute liver failure is rare. Incidence of dengue-associated acute liver failure ranges from 0.44 to 0.66%.<sup>4</sup> Dengue infection may predispose patients to massive postpartum hemorrhage due to associated thrombocytopenia and coagulation abnormalities secondary to hepatic dysfunction.<sup>5</sup> Acute liver failure is associated with a high mortality rate due to deranged coagulation, encephalopathy, renal failure, and metabolic derangements.<sup>6,7</sup>

We report here a case of acute liver failure in a postpartum patient with dengue infection.

## CASE DESCRIPTION

A 19-year-old female was referred to our hospital for management of primary postpartum hemorrhage following a full-term vaginal

<sup>1-3</sup>Department of Obstetrics and Gynecology, Pramukhswami Medical College, Karamsad, Anand, Gujarat, India

**Corresponding Author:** Shilpa Sapre, Department of Obstetrics and Gynecology, Pramukhswami Medical College, Karamsad, Anand, Gujarat, India, Phone: +91 7043010502, e-mail: shilpasapre14@gmail.com

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delivery 2 hours back. She gave history of high-grade fever with chills since past 2–3 days. On admission, she was conscious, pale, afebrile on touch with pulse rate 90 beats/minute, blood pressure 110/70 mm Hg, respiratory rate 20/minute, and SpO<sub>2</sub> 98% on room air. Systemic examination findings were normal. On per abdomen examination, the uterus was well retracted. Per speculum examination revealed a 2 cm cervical tear on the left side, which was repaired. There was no active bleeding. Laboratory examination showed: hemoglobin (Hb) 9.6 g%, total leukocyte count 16,400/mm<sup>3</sup>, and platelet count 30,000/mm<sup>3</sup>. In view of

**Table 1:** Laboratory investigations

Parameter	Day 1	Day 2	Day 7	Day 14	Day 28
Hb (g/dL)	9.6	8.6	6.4	6.7	8.1
WBC count (×1000/μL)	16.4	26.7	5.2	12.4	11.9
Platelets(×1000/μL)	33	45	36	80	502
PT (seconds)	12.6	28.9	23.5	22.7	12.8
APTT (seconds)	58	57	65.5	60	22.3
INR	1.07	2.5	2.02	1.7	1.09
Creatinine (mg/dL)	2.04	1.62	1.10	0.79	0.71

**Table 2:** Liver function tests

Parameter	Day 1	Day 7	Day 14	Day 28
S. Total bilirubin (mg/dL)	3.01	13.21	18.81	6.03
S. Direct bilirubin (mg/dL)	2.13	8.53	14.83	5.12
S. Indirect bilirubin (mg/dL)	0.88	4.68	3.98	0.91
S. AST(U/L)	619	2111	970	191
S. ALT(U/L)	135	78	60	53

positive history of fever and low platelet count, the dengue NS1 antigen was sent which was positive. Her liver function tests, renal function tests, and coagulation profile were also deranged; hence, a diagnosis of dengue with warning signs was made as per the WHO 2009 classification. Ultrasonography was normal.

On the 2nd day of admission, the patient developed sudden-onset breathlessness and a bout of heavy bleeding per vaginum. Her pulse rate was 110/minute, BP 100/60 mm Hg, respiratory rate was 40/minute, and  $spO_2$  was 97% on room air. On respiratory system examination, bilateral basal crepitations were present. Laboratory investigations showed hemoglobin (Hb) 8.6 g%, total leukocyte count 26,700/mm<sup>3</sup>, and platelet count 45,000/mm<sup>3</sup>. The ABG analysis revealed severe metabolic acidosis (pH = 7.17,  $HCO_3^-$  = 4.4,  $pCO_2$  = 12, lactate > 15). The patient was managed in the critical care unit for acute pulmonary edema with worsening laboratory and clinical parameters. Laboratory parameters of the patient are summarized in Table 1. Postpartum hemorrhage in the background of thrombocytopenia and DIC was managed conservatively. At the end of 2 weeks, she developed acute liver failure and hepatic encephalopathy and was put on ventilatory support. There was improvement in her platelet count over the due course of stay. Lab reports were negative for hepatitis A, B, C, and E. Liver function tests are summarized in Table 2. Broad-spectrum antibiotics were started along with lactulose solution, IV acetylcysteine, and IV Hepamerz infusion. Gastroenterologist opinion was taken for acute liver failure. During the whole course of 1 month of hospital stay, she was transfused with 6 units of PCV, 16 units of platelet, 12 units of FFP, and 10 units of cryoprecipitate. Perinatal transmission was ruled out. Conservative measures resulted in complete recovery of the patient and her newborn by the end of 1 month.

## DISCUSSION

Dengue fever is a major public health problem in the tropical and subtropical regions particularly in Southeast Asia and the western Pacific regions. The burden of dengue infection in India is heterogeneous with high seroprevalence in southern, western, and northern areas.<sup>8</sup> Dengue infection may manifest with influenza like self-limiting illness to life-threatening organ involvement. Dengue

has an incubation period of 5–7 days after which it suddenly manifests. It runs through three phases—febrile, critical, and convalescence phases.<sup>9</sup> In our case, the patient presented with fever of short duration and thrombocytopenia. There were no other classical features of dengue but the endemic nature of the disease in India with thrombocytopenia warrants for strong clinical suspicion and laboratory investigations for detection of dengue antigens and/or immunoglobulins in cases of acute febrile illness (AFI). Hepatic dysfunction is a well-recognized feature of dengue infection, accompanied by hepatomegaly, mild-to-moderate increases in transaminase levels, and anicteric jaundice. The rise in the levels of aspartate aminotransferase is higher than that of alanine aminotransferase. Similarly, in our case the AST levels were higher than the ALT levels during the whole duration of admission. The etiopathogenesis of hepatic dysfunction in dengue fever is multifactorial and is related to direct viral invasion of hepatocytes, immunological factors, and hypoxia particularly in cases of shock; however, hepatic injury has also been reported in patients without shock. The pathologic findings in patients with dengue fever include centrilobular necrosis, fatty change, Kupffer cell hyperplasia, acidophilic bodies, and monocyte infiltration of the portal tracts.<sup>10</sup>

Acute liver failure is generally uncommon; however, it is more commonly seen in patients with severe hepatitis as seen in our patient. Elevation of any one of the transaminases to almost 10 times of the normal value is a feature of severe hepatitis. American Association for the study of Liver Disease (AASLD) defines acute liver failure as evidence of coagulopathy (international normalized ratio  $\geq$  1.5) and presence of an altered sensorium (encephalopathy) without preexisting cirrhosis and with duration of symptoms of less than 26 weeks.<sup>11</sup> The mean duration of development of acute liver failure from onset of symptoms is 7–14 days,<sup>12</sup> which was seen in our case as well. Our patient also developed hepatic encephalopathy, coagulopathy, with high transaminase levels by 7–14 days. A study by Karoli et al.<sup>13</sup> found that a significant proportion of patients with classical dengue fever had thrombocytopenia and altered coagulation profile, which is similar to the findings in our case as well. This is indicative of the activation of both coagulation and fibrinolysis during acute dengue infection. Postpartum hemorrhage is complication occurring in 10% cases; however, the study by Sharma et al. reported that 19%<sup>14</sup> postpartum hemorrhage in our patient was managed conservatively with uterotonics and blood and blood products.

It is known that N-acetylcysteine may benefit patients with nonacetaminophen-induced acute liver failure by improving systemic hemodynamics, tissue oxygen delivery, or via other favorable effects on the acutely injured liver.<sup>15</sup> The standard dosage and duration for NAC regimens remain controversial, but have been suggested as IV N-acetylcysteine 100 mg/kg/day infusion for 5 days in adult patients. Conservative measures coupled with

judicious fluid management are the key in the management of dengue infection.

## CONCLUSION

Acute febrile illness with/without the classical manifestations of dengue fever should be a differential diagnosis in patients with thrombocytopenia. Other causes of thrombocytopenia like HELLP syndrome, vitamin B12 deficiency, etc., may complicate the diagnosis. As no specific antiviral therapy is available for dengue fever, the main aim of treatment should be symptomatic and fluid resuscitation. Liver involvement is not uncommon in dengue fever and such patients should be closely monitored in intensive care for signs of acute liver failure.

## CLINICAL SIGNIFICANCE

Dengue infection in pregnancy can mimic other causes of thrombocytopenia like HELLP syndrome, megaloblastic anemia, and gestational thrombocytopenia; hence, a detailed evaluation is warranted in pregnant women. Acute liver failure is a rare complication of dengue infection in pregnancy but a close supervision is advocated in patients with high transaminase levels.

This case report highlights the importance of multidisciplinary approach in managing patients of severe dengue.

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## REFERENCES

1. Ganeshkumar P, Murhekar MV, Poornima V, et al. Dengue infection in India: a systematic review and meta-analysis. *PLoS Negl Trop Dis* 2018;12(7):e0006618. DOI: 10.1371/journal.pntd.0006618.
2. Bopeththa BVKM, Hemapriya S, Gayan Niranga KK, et al. A case report of dengue haemorrhagic fever during the peripartum period: challenges in management and a case of vertical dengue transmission. *BMC Infect Dis* 2018;18(1):427. DOI: 10.1186/s12879-018-3352-x.
3. Prabhat A, Ruchika G, Soumya S, et al. Pregnancy outcome in women with dengue infection in Northern India. *Indian J Clin Pract* 2014;24(11):1053–1056.
4. Trung DT, Thao LeTT, Hien TT, et al. Liver involvement associated with dengue infection in adults in Vietnam. *Am J Trop Med Hyg* 2010;83(4):774–780. DOI: 10.4269/ajtmh.2010.10-0090.
5. Phi Hung L, Diem Nghi T, Hoang Anh N, et al. Case report: postpartum hemorrhage associated with dengue with warning signs in a term pregnancy and delivery. *F1000 Res* 2015;4:1483. DOI: 10.12688/f1000research.7589.1.
6. Malavige GN, Ranatunga PK, Jayaratne SD, et al. Dengue viral infections as a cause of encephalopathy. *Indian J Med Microbiol* 2007;25(2):143–145. DOI: 10.4103/0255-0857.32722.
7. Kye Mon K, Nontprasert A, Kittitrukul C, et al. Incidence and clinical outcome of acute liver failure caused by dengue in a hospital for tropical diseases, Thailand. *Am J Trop Med Hyg* 2016;95(6):1338–1344. DOI: 10.4269/ajtmh.16-0374.
8. Wilder-Smith A, Rupali P. Estimating the dengue burden in India. *The Lancet Global Health* 2019;7(8):e988–e989. DOI: 10.1016/S2214-109X(19)30249-9.
9. WHO. *Dengue Guidelines for Diagnosis, Treatment, Prevention and Control*. Geneva, Switzerland: World Health Organization; 2009.
10. Seneviratne SL, Malavige GN, de Silva HJ. Pathogenesis of liver involvement during dengue viral infections. *Trans R Soc Trop Med Hyg* 2006;100(7):608–614. DOI: 10.1016/j.trstmh.2005.10.007.
11. Bernal W, Wendon J. Acute liver failure. *N Engl J Med* 2013;369(26):2525–2534. DOI: 10.1056/NEJMra1208937.
12. Gasperino J, Yunen J, Guh A, et al. Fulminant liver failure secondary to haemorrhagic dengue in an international traveller. *Liver Int* 2007;27(8):1148–1151. DOI: 10.1111/j.1478-3231.2007.01543.x.
13. Karoli R, Fatima J, Siddiqi Z, et al. Clinical profile of dengue infection at a teaching hospital in North India. *The Journal of Infection in Developing Countries* 2012;6(07):551–554. DOI: 10.3855/jidc.2010.
14. Sharma S, Jain S, Rajaram S. Spectrum of maternofetal outcomes during dengue infection in pregnancy: an insight. *Infect Dis Obstet Gynecol* 2016;2016:5046091. DOI: 10.1155/2016/5046091.
15. Nabi T, Nabi S, Rafiq N, et al. Role of N-acetylcysteine treatment in non-acetaminophen-induced acute liver failure: a prospective study. *Saudi J Gastroenterol* 2017;23(3):169–175.