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Case Report

# Acute Dengue Fever in a Neonate Secondary to Perinatal Transmission

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## ABSTRACT

***Background*:** Dengue in pregnancy is associated with adverse maternal and fetal outcomes, including perinatal transmission.

***Case report:*** We report a case of neonatal dengue in a baby born to a 29-year-old primigravida at 38 weeks of gestation. She developed acute dengue fever 2 days prior to delivery. Her dengue nonstructural protein 1 antigen was reactive. She delivered a term baby girl via spontaneous vaginal delivery. Her fever persisted in the post-partum period which was associated with post-partum hemorrhage, altered coagulation, and liver function. She was clinically diagnosed to have hemophagocytic lymphohistiocytosis complicated with disseminated intravascular coagulation and treated with intravenous (IV) dexamethasone and multiple blood products, including fresh frozen plasma and platelet concentrate. She recovered in over the next 5 days. The baby girl was born with a birth weight of 3040g and developed fever on the third day of life with poor perfusion, associated with mottling and hypotension. The baby was treated with IV fluids, inotropes, and supportive care. The fever subsided after 48 h, along with clinical improvement, but continued with thrombocytopenia. The baby did not have any bleeding. Platelet recovery started on the 11$^{th}$ postnatal day (i.e., the 8$^{th}$ day of illness), and platelet count was normalized at 2 weeks. Dengue serology immunoglobulin M by enzyme-linked immunosorbent assay was positive for both mother and baby. The clinical diagnosis was confirmed by laboratory tests.

***Conclusion:*** Dengue fever in mothers very late in pregnancy can cause symptomatic dengue infection in neonates.

***Keywords:*** Neonatal dengue, Pregnant, Thrombocytopenia, Vertical transmission

## Introduction

Dengue is a flavivirus infection transmitted to humans by *Aedes aegypti*. It is a self-limiting systemic infection. About 3.9 billion people in the world are at risk of dengue infection, and most of the reported cases are from tropical and subtropical countries making dengue infection a global health burden (1). Dengue infection has a wide range of clinical manifestations, varying from asymptomatic self-limiting illness to hemorrhagic fever and dengue shock syndrome.

As the incidence of dengue infection is increasing in adults, pregnant women have also become the vulnerable population regarding dengue virus infection. Dengue infection during pregnancy is associated with various complications affecting the mother and baby, including perinatal death, miscarriage, preterm delivery, intrauterine growth retardation, and neonatal intensive care unit (NICU) admission (2).

Studies have shown that the intrauterine transfer of the dengue virus can be proved by the isolation of virus from fetal or cord blood samples (3). Most of the reported neonatal dengue cases demonstrated dengue infection in mothers very late in pregnancy. Vertical transmission is commonly associated with dengue virus serotype 2. This is due to the high circulation of this serotype and its ability to cross fetoplacental barrier (4).

As the vertical mode of transmission of dengue has not been frequently reported globally, there has been limited knowledge about this mode of transmission. We report a rare case of neonatal dengue in a baby born to 29-year-old

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primigravida who was diagnosed to have dengue infection 2 days prior to delivery.

## Case report

A 29-year-old primigravida of 38 weeks of gestation who is a known case of asthma and gestational diabetes mellitus was admitted with the complaint of fever for one day. Her dengue nonstructural protein 1 was positive. Fever was not associated with rash, bleeding, or abdominal pain. On admission, she was febrile with a temperature of 101.3°F, heart rate of 110 bpm, and blood pressure of 150/86 mmHg.

On the 3rdday of fever, she delivered a term baby girl via vaginal route. She continued to have a fever, and atonic postpartum hemorrhage was noted on the postnatal 2ndday. Blood investigations showed an altered coagulation profile, low platelet count, elevated serum ferritin, and elevated liver enzymes. Abdominal ultrasound showed ischemic hepatitis. She had the features of hemophagocytic lymphohistiocytosis (HLH) and disseminated intravascular coagulation (DIC). She was treated with intravenous (IV) dexamethasone, fresh frozen plasma, and platelet concentrate. She showed clinical improvement in 5dayswith her platelets on an improving trend as well.

The baby girl cried soon after birth with the Apgar scores of 9/10 and 9/10 at the 1st and 5th min of life with a birth weight of 3040 g. She was kept under observation in the NICU, and the mother was ill. On the 4thday of life, the baby developed fever, mottling of the skin, feeding intolerance, poor perfusion, and hypotension. There was no organomegaly. Peripheral smear showed neutrophilia with left shift and presence of toxic granules. In addition, dengue immunoglobulin M (IgM) by enzyme-linked immunosorbent assay (ELISA) was negative on the 4thday of life.

C-reactive protein and procalcitonin were negative. The chest X-ray was normal. The baby was treated with IV antibiotics, IV fluids, inotropes, and other supportive measures with a clinical diagnosis of neonatal sepsis. The fever subsided after 48 h gradually, along with the clinical improvement; however, there was a persistent drop in platelet count from 198,000cells/µL to 13,000cells/µL by the 10th day of life with rising packed cell volume, which required multiple platelet transfusions.

On the 11thday of life, dengue IgM by ELISA was positive confirming the diagnosis of neonatal dengue infection. The baby was afebrile from the 6thday of life, and platelet recovery started from the 11thday of life. The administration of antibiotics stopped after 7 days. Initial blood culture grew *Staphylococcus haemolyticus*; however, repeat culture was sterile. Serial platelet count showed an increasing trend since the 11thday (Figure 1). Breast feeding started for the baby, and serial weight gain was noted. The baby was discharged on the 15thday of life with normal platelet count and weight of 2860 g.

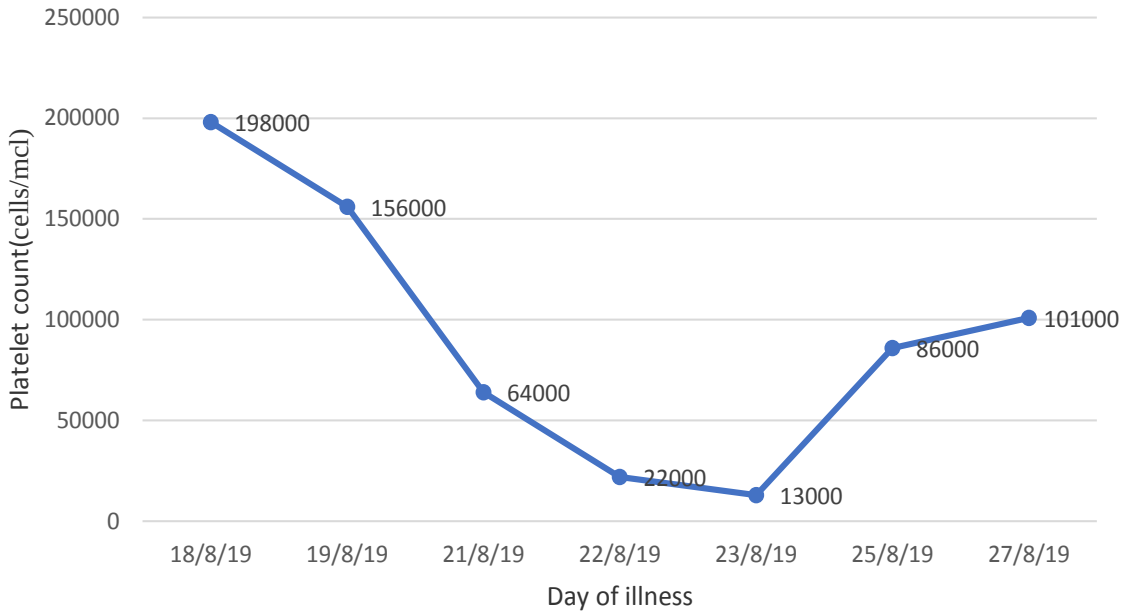


**Figure 1.** Serial platelet count of neonate with acute dengue

## Discussion

The vertical transmission of dengue virus is not a common mode of transmission; however, few case series and isolated case reports have emerged from dengue-endemic regions. Dengue infection can be transmitted in all trimesters. There are reported cases worldwide showing the presence of dengue virus in fetal and cord blood samples explaining the intrauterine transmission of dengue. However, this mode of transmission was not considered common (3).

The incidence rates of dengue infection were reported as 3.8%, 7.7%, 77%, and 11.5% in the first trimester, second trimester, third trimester, and during the immediate postpartum period in a study carried out by Waduge et al., respectively (5). A higher incidence of pre-eclampsia, premature deliveries, cesarean deliveries, and low birth-weight babies were observed in a systematic review conducted by Sawyer et al. (6).

The effects of maternal dengue on neonates are due tothe increased production of cytokines, such as tumor necrosis factor-alpha and interleukin 6, which are pro-inflammatory and have an effect on the uterus by stimulating the increased production of proteins acting on the uterus. These proteins stimulate premature uterine contractions, resulting in preterm delivery. Thrombocytopenia, plasma leakage, and bleeding tendency may result in damage to the placental circulation with consequences for the fetus, such as stillbirth and intrauterine growth retardation (7).

The cases of neonatal dengue are rarely reported due to infections occurring in early pregnancy and most commonly reported in maternal infection during late pregnancy. This has been postulated on the basis that when infections occur later in pregnancy, there is insufficient time for the production of antibodies, and viremia from the mother is directly transferred to the neonate (8). In our case, the mother was symptomatic close to delivery, and she delivered vaginally on the 3$^{rd}$day of fever.

The incubation period of dengue virus is about 3 to 10 days, and its half-life was noted as 40 days in neonates. The symptoms may vary in new-borns and pregnant women. In our case, the mother had a fever 3 days before delivery and developed the features of HLH and disseminated DIC following delivery, while the infant was febrile with the features of sepsis.In a review carried out by Sirinivan on the vertical transmission of dengue, it was observed that the onset of fever may vary from the 1$^{st}$day to the 11$^{th}$day. In addition, babies will remain symptomatic for 3-5 days (9). In our case, the infant was symptomatic on the 4$^{th}$day of life with fever, mottling, and poor perfusion.

Since the initial ELISA IgM was negative, a clinical diagnosis of sepsis was considered, and the neonate was accordingly treated. However, the infant had a serial drop in platelet count with the mother suffering from dengue hemorrhagic fever, and a clinical diagnosis of neonatal dengue was considered. A repeated dengue ELISA IgM was performed which was strongly positive. This can be attributed to the fact that dengue IgM levels rise quickly, and detectable levels appearwithin3-5 days onwards, with peak levels observed 2 weeks after the onset of symptoms (10). In the case of strong clinical suspicion, dengue serology needs to be repeated for negative cases.

## Conclusion

Based on our case and available literature, we concluded that a clinical diagnosis of neonatal dengue should be considered in febrile symptomatic neonates with a history of maternal febrile illness before delivery, especially in places with endemic dengue fever. Early recognition, diagnosis, and appropriate management of neonatal dengue reduce the mortality rate to a great extent.

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## Conflicts of interest

The authors have no conflicts of interest.

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