

## CASE REPORT

# Congenital Dengue Infection: A Novel Case of Vertical Transmission of Dengue Virus in Karachi, Pakistan

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## ABSTRACT

Dengue is a viral infection that is transmitted generally among humans through mosquito bite. This article reports a less known mode of transmission i.e., vertical transmission of dengue virus. A male newborn with normal Apgar score developed fever on the 8<sup>th</sup> day of life. The fever progressed along with an erythematous rash. There was no evidence of mosquito exposure to the baby. However, the mother had mosquito bites two days prior to her delivery. The mother also developed fever on seventh day of delivery and a maculopapular rash during her ninth postpartum day. Baseline investigations of both the mother and the neonate showed thrombocytopenia, anemia, raised liver function tests and positive Dengue NS1 antigen test. The diagnosis of dengue fever was established. This case report demonstrates the possibility of congenital transmission of dengue virus. The health care providers should be aware of and adequately trained for handling such cases.

**Keywords:** Dengue; Blood Platelets; Infections; Thrombocytopenia; Antigens.

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## INTRODUCTION

Dengue is a viral disease that has rapidly spread in the world in recent years. The primary mode of transmission of dengue virus among humans is through the bites of infected female mosquito of species *Aedes Aegypti*<sup>1</sup>. However, there are summing evidences, supporting the possibility of intrauterine transmission of dengue virus from pregnant woman to her fetus. Though rates of vertical transmission seem low, the risk of transmission is associated with the timing of the infection during pregnancy<sup>2</sup>. This case is the first of its kind in terms of reporting of vertical transmission of dengue virus in this country.

## CASE PRESENTATION

An 8 days old male neonate, who was otherwise healthy, developed high-grade fever up to 102°F. He was taken to a nearby hospital. His initial investi-

gations showed hemoglobin (Hb) 14.3g/dL, hematocrit 42.1%, total leukocyte count (TLC)  $8.6 \times 10^9/L$  with 43% neutrophils and 44.5% lymphocytes. His platelet count was  $61 \times 10^9/L$ . Dengue NS1 Ag (dengue virus antigen detection) done through enzyme-linked immunosorbent assay (ELISA) turned out positive. The child was diagnosed as a case of Dengue fever and was admitted. Intravenous fluids and antipyretics were initiated. On 3<sup>rd</sup> day of fever, the baby developed maculopapular rashes all over his body. His platelets count dropped to  $32 \times 10^9/L$ . At this point, the parents brought the baby to the pediatric emergency of Ziauddin Hospital, Clifton, which is a well-equipped tertiary care setup.

On arrival, the temperature of the neonate was 98.7°F, his BP was 82/53, heart rate was 134/min and respiratory rate was 70/min. Physical examination revealed petechial rashes all over his body and chest recessions with equal bilateral air entry. On auscultation, pan systolic murmur was audible.

Abdominal and CNS examination were unremarkable. The patient was put on continuous positive airway pressure (CPAP 3/3). Complete blood count (CBC) done at Ziauddin hospital demonstrated a platelet count of  $26 \times 10^9/L$ . His liver function tests (LFTs) were raised with total bilirubin of 3.74mg/dl, direct bilirubin of 0.73mg/dl and alanine aminotransferase (ALT) of 48U/L. An intravenous (IV) bolus of normal saline injection was given and maintenance therapy of Dextrose saline was initiated. A pack of platelets (30 ml) was transfused. His chest X-rays showed mild infiltrates involving both suprahilar and infrahilar regions with intact costophrenic angles. Abdominal ultrasounds demonstrated streaks of pleural effusion bilaterally but were otherwise normal. Intravenous cefotaxime sodium and dextrose 1/5 saline were started. Nebulization with ipratropium bromide was also initiated to resolve respiratory distress. Echocardiography done for pan systolic murmur revealed a small perimembranous ventricular septal defect (VSD).

On second day of admission, the platelets improved to  $84 \times 10^9/L$  and petechiae started resolving. However, repeated platelets count again showed a level of  $51 \times 10^9/L$ . One more pack of platelets was transfused. Platelets count done on next day was  $59 \times 10^9/L$ . During the stay in hospital, four packs (120 ml) of platelets were transfused with daily monitoring. His petechiae became unnoticeable and his platelets improved from  $59 \times 10^9/L$  to  $77 \times 10^9/L$  and then through  $110 \times 10^9/L$  to  $135 \times 10^9/L$ . The C-reactive protein (CRP) was less than 0.5 mg/L. Blood culture revealed no growth. Patient improved clinically and started on demand feed. Daily platelet count and the course of treatment are shown in Table 1. Family history of the neonate revealed that his mother also developed high-grade fever one day before the baby got fever. She also developed a maculopapular rash on ninth postpartum day. Her laboratory investigations showed positive NS1Ag and she was managed along the national guidelines for dengue management.

**Table 1: Daily platelet count and clinical interventions with timeline.**

| Days of Illness | Daily Platelet Count | Clinical Interventions                              |
|-----------------|----------------------|---|
| Day 1           | $61 \times 10^9/L$   | IV fluids and anti-pyretics                         |
| Day 2           | $32 \times 10^9/L$   | CPAP 3/3  |
| Day 3           | $26 \times 10^9/L$   | Platelets transfusion, IV fluids and IV antibiotics |
| Day 4           | $84 \times 10^9/L$   | IV fluids and IV antibiotics                        |
| Day 5           | $51 \times 10^9/L$   | Platelets transfusion                               |
| Day 6           | $59 \times 10^9/L$   | Platelets transfusion                               |
| Day 7           | $110 \times 10^9/L$  | Platelets transfusion                               |
| Day 8           | $135 \times 10^9/L$  | -   |

Finally, the baby was discharged on sixth day of admission in clinically and vitally stable condition. The mother was advised not to get her baby circumscised until 6 weeks. All the laboratory and radiological investigations during the stay at hospital were done in the Ziauddin Hospital's Laboratory and Radiology Departments. The neonate was treated according to the national guidelines of dengue management that recommend fluid balance and monitoring of vital signs, blood parameters and any bleeding tendency in case of dengue fever.

## DISCUSSION

There are a number of increasing evidences of vertical transmission of dengue virus from mother to her fetus during pregnancy<sup>3</sup>. Worldwide multiple cases have demonstrated the antenatal acquisition of dengue infection as the presence of dengue

virus is found in blood samples collected from the fetus and the umbilical cord. However, to date, there have been no reports of transmission of antibodies against dengue virus infection in neonates, which are born to the mothers who acquired dengue infection near their term<sup>4,5</sup>. Negative results of IgM antibodies in mother do not exclude the diagnosis of dengue infection<sup>2</sup>. Therefore, there is an increasing likelihood that maternal dengue infection had been transmitted to the unprotected fetus.

Confirmation of dengue infections through laboratory tests is vital to establish the diagnosis. This can be done through various techniques like isolation of dengue virus, detection of dengue virus nucleic acid and NS1 antigen and determination of other blood markers, which are deranged in dengue infection. Hematological samples for detection of dengue virus must be taken within the initial four to



five days of appearance of symptoms i.e., during the febrile period. The Dengue NS1 antigen peaks about seven days after the initial clinical manifestation of symptoms. IgM levels rise rapidly, become detectable from three to five days, peak around two weeks after the onset of clinical symptoms and then become undetectable over the period of two to three months<sup>6</sup>. One feature of primary dengue infection is the high levels of anti-dengue IgM antibody and low levels of IgG antibody<sup>6,7</sup>. In this particular case, the diagnosis of dengue fever in the mother and the infant was confirmed by the dengue virus NS1 antigen test. The test was done through ELISA. Cord blood sampling was not done in this case, as there was no indication of this procedure at the time of delivery. If done, it could have helped in gathering more evidences for vertical transmission of any possible infection<sup>8</sup>. However, the symptomatic manifestation, clinical history and laboratory test results combined with the absence of any evidence of mosquito bite after birth give us an arena to formulate the suspicion of perinatal, intrauterine transmission of dengue infection, which presented itself after birth<sup>9</sup>.

This case is in the queue with other case reports available in the literature. Like all other mentioned cases of vertical transmission, dengue fever occurred in infants of mothers who acquired infection late in last trimester of pregnancy. In this particular case, the mother developed fever at seventh postpartum day, while the baby developed it on 8<sup>th</sup> day of life. Both the mother and the baby developed rash on the 3<sup>rd</sup> day of fever<sup>10</sup>. A study done by Chan and Johansson mentioned that the incubation period of dengue is between 3-10 days. Development of clinical signs in the neonate on 8<sup>th</sup> day after birth is a consistent finding with this parameter<sup>5</sup>. Thus, there is less likelihood that the neonate has acquired dengue fever through a direct mosquito bite, while it seems more probable that a vertical transmission has occurred in this scenario. Furthermore, there is a countrywide epidemic of dengue these days. So considering this information, the epidemiology of the present case accords the current scenario.

Such transmission of dengue virus from the mother to her newborn can result in variable outcomes in the neonatal period. The consequences may vary from asymptomatic infections to severe hematological, cardiac and pulmonary complications leading to neonatal mortality. A case of pulmonary hemorrhage due to acute left ventricular failure and cardiac arrest secondary to myocarditis leading to death *in utero* of the fetus to a mother who acquired dengue infection during the third trimester of pregnancy have also been reported<sup>3</sup>. There are now emerging evidences of association of dengue

fever during pregnancy with congenital brain anomalies and neurological manifestations in the newborns. Such incidences open the likelihood that Flaviviruses, other than Zika virus; can also cause neonatal malformations<sup>10</sup>. In addition to this some, researches also provide evidence that dengue infection with clinical manifestations during pregnancy constitute risk for stillbirth. This risk is amplified if the symptoms are severe when the infection is in acute phase. The likelihood of preterm birth is also increased if the women have clinical manifestations of dengue infection during their pregnancy<sup>11</sup>.

It is now imminent to highlight the importance of vertical transmission of dengue in neonates especially in the areas where it is endemic. Considering the fetal outcome of dengue infection, early diagnosis of congenital dengue will reduce maternal and infant mortality rates, significantly<sup>9</sup>. It is recommended to incorporate dengue control programs into health system, which consider pregnant women as an at-risk population so that public health measures can be taken to provide protection to pregnant women and decrease the infant mortality rate<sup>11</sup>.

## CONCLUSION

If a woman acquires dengue virus during pregnancy, clinicians should consider the possibility of vertical transmission, treat the mother and closely monitor the possible fetal outcomes. During pregnancy, women can also exercise the preventive measures such as more caution to avoid mosquito bites if they are living in areas where dengue is endemic. Further, more there is a need of more research and direct evidences to understand this mode of transmission and its outcomes.

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## CONFLICT OF INTEREST

There is no conflict of interest between the authors.

## PATIENT CONSENT

Verbal informed consent was obtained from the patients' legal guarding on telephone for publication of this case report after assuring him of confidentiality of identification and briefing him that how his sharing of information can help medical community in better understanding of this newly discovered mode of transmission of dengue.

### AUTHORS' CONTRIBUTION

SS was the primary author who wrote and compiled the manuscript. SE was the primary pediatrician and provided all the relevant information of the case.

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