

Neonatal Dengue- A Case Series

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ABSTRACT

Dengue is one of the commonest arboviral infections seen in children but in neonates, it is a disregarded entity. It can be acquired either through vertical (transplacental) or horizontal transmission (mosquito bite). It usually presents with fever, lethargy, poor feeding, and thrombocytopenia which can be accompanied by hepatosplenomegaly, transaminitis, fluid leak, petechiae, bleeding, Acute Respiratory Distress Syndrome (ARDS), shock and Acute Kidney Injury (AKI). Dengue shock in neonates responds well to dopamine if used early. A retrospective review of case records of five neonates admitted with dengue fever from October 2021 to October 2022 showed the neonates average age was 10 days and male:female ratio of 3:2. Three cases had horizontal and two cases had vertical transmission. All neonates presented with fever and were admitted within one week of illness. Petechial rashes and refusal of feeds were observed in two cases. Four cases had leukopenia whereas, all cases had thrombocytopenia. Sepsis was ruled out. Dengue Nonstructural protein 1 (NS1) antigen was positive in four cases. Immunoglobulin GM (IgM) antibody was positive in all while Immunoglobulin G (IgG) was negative in all cases. None of the cases had hepatic derangement except for mild transaminitis in three cases. Only two cases had severe thrombocytopenia requiring platelet transfusion, but none developed bleeding, plasma leakage, shock requiring inotropes or fluid overload. Mortality due to neonatal dengue was nil and the duration of hospital stay ranged between 6-12 days. In the vertically transmitted cases, isolation of the virus from the breast milk or cord blood was not done due to logistics. Therefore, dengue fever can be suspected as one of the differentials in any neonate presenting with fever, leukopenia, and thrombocytopenia mimicking sepsis, especially during the epidemic season.

Keywords: Leukopenia, Sepsis, Thrombocytopenia, Transaminitis

INTRODUCTION

Dengue fever is caused by a flavivirus belonging to the flaviviridae family [1]. *Aedes aegypti* a day-biting mosquito is the vector that carries the flavivirus. World Health Organisation (WHO) defines dengue infection as an acute febrile illness with two or more of the following signs and symptoms like retro-orbital pain, severe headache, arthralgia, myalgia, haemorrhagic manifestations, leukopenia, and skin rash. Earlier dengue was an infection of children, but now even adults including pregnant women are infected by the dengue virus. The routes of dengue infection are by mosquito bites, maternal-foetal, mucocutaneous and by blood [1].

Dengue infection in the mother can cause severe complications like preterm delivery, low birth weight, miscarriage, and perinatal death. If the mother is affected late in pregnancy, the neonate can develop dengue infection [2,3]. With the emergence of dengue fever as an epidemic, more and more pregnant women are affected by the disease. Secondary dengue is said to be more serious and dangerous than primary dengue. If a pregnant mother gets dengue fever in the latter half of pregnancy and delivers during the febrile phase where viraemia is highest, both, mother and neonate can get severe dengue with life-threatening complications even with the primary infection [4]. The present case series presents five cases of neonatal dengue in a span of one year duration [Table/Fig-1].

Parameters	Case 1	Case 2	Case 3	Case 4	Case 5
Dengue NS1 antigen	Positive	Positive	Positive	Negative	Positive
Dengue IgM antibody	Positive	Positive	Positive	Positive	Positive
Dengue IgG antibody	Negative	Negative	Negative	Negative	Negative

[Table/Fig-1]: Dengue serology among the neonates.

Case 1

A 7-year-old boy was referred to the Paediatric Department of Sree Balaji Medical College and Hospital, Chrompet, Chennai, Tamil Nadu, India from outside with complaints of fever, cough, headache and vomiting for three days. On admission, he was afebrile with a heart rate of 105/minute and blood pressure of 98/60 mmHg. He had leukopenia, thrombocytopenia with a platelet count of 55000 cells/cumm and normal haemoglobin. NS1 antigen and dengue IgM antibody was positive and he was diagnosed for dengue fever. He was treated with intravenous fluids and paracetamol following which he recovered. On follow-up, he was afebrile with normal blood counts. His sister an eight-day-old female infant, also had fever since three days. She was born from non consanguineous marriage by Lower Segment Caesarean Section (LSCS) with an Appearance, Pulse, Grimace, Activity, and Respiration (APGAR) score of nine in one minute. On examination, she was febrile (100° F), her peripheral pulses were well felt, capillary refill time was less than two seconds. Petechial rashes were seen on her body. Laboratory examination showed low platelet count (87000 cells/cumm), low total leukocyte count (2000 cells/cumm), and elevated Serum Glutamic Pyruvic Transaminase (SGPT) (447 unit/L) and Serum Glutamic-oxaloacetic Transaminase (SGOT) (1023 unit/L). Blood culture was sterile and cranial Ultrasonography (USG) did not show any intracranial haemorrhage. She was tested for NS1 antigen and dengue IgM that came out to be positive [Table/Fig-1]. A diagnosis of neonatal dengue fever was made. Prophylactic antibiotics namely ampicillin (50 mg/kg/dose, 12 hourly) and gentamycin (4 mg/kg/day) were given for neonatal sepsis. Platelet count dropped to 66000 on day 3. Antibiotics were stopped on fifth day and cultures were negative. Platelet count was checked everyday. On fifth day, platelet counts were increased to 100000 and liver enzymes started decreasing. She was discharged on the seventh day with weight of 3.2 kg. Follow-up period after five days was uneventful with no fever or rashes.

Case 2

A 15-day-old neonate girl, brought with complaints of fever since four days, rashes over the body and refusal of feeds since one day. Born out of non consanguineous marriage by LSCS with APGAR scores 8/10, 9/10 in one and five minutes, respectively and birth weight of 2.75 kg. Her mother was also admitted to the Medicine Department and was diagnosed with dengue and on treatment. Keeping this in mind, the baseline investigations from the neonate was done that showed (leukopenia 4500 cells/cumm), thrombocytopenia (95,000 cells/cumm), and normal haemoglobin. Blood culture was negative for any growth. She was kept on antibiotics and other supportive measures. Dengue NS1 antigen and IgM antibody was positive. Baby was treated symptomatically with antipyretics, intravenous fluids and discharged on the 10th day of admission without any complications.

Case 3

A 24-day-old inborn, term boy baby came with complaints of fever abdominal distension for the past six days. Baby born out of non consanguineous marriage by LSCS with APGAR scores 8/10, 9/10 in one and five minutes, respectively and birth weight of 3.1 kg. Child was exclusively on breastfeeds and there was no history of bad child rearing practices. Family history revealed that, grandmother was admitted two days before and was diagnosed with dengue. She was under treatment. On examination, the baby had fever (101.3° F), no petechiae, or bleeding manifestations was observed. The baseline investigations showed leukopenia (3700 cell/cumm), thrombocytopenia (83,000 cells/cumm), normal haemoglobin level. Blood culture showed no growth of organisms. USG abdomen showed moderate ascites. Dengue NS1 antigen and IgM antibody was positive [Table/Fig-1]. Baby was treated symptomatically with antipyretics and intravenous fluids. Serial ultrasound was done and found to be normal also thrombocytopenia gradually returned to normal range at the end and baby was discharged on the 12th day of admission. Follow-up period after five days of discharge was uneventful baby was alert, active, and feeding well with adequate weight gain.

Case 4

A one-day-old male neonate was admitted to Neonatal Intensive Care Unit (NICU) with fever at eight hours of life. The child was born to a primigravida mother at 38 weeks of gestation by a normal vaginal delivery with a birth weight of about 3.2 kg. The neonate cried at birth, started on direct breastfeeds within an hour of birth. The child was well, till eight hours of life but then started to have a fever with a temperature of about 38° C following which he was transferred to NICU. Family history revealed, mother also had fever for four days, was positive for dengue NS1 antigen, IgM, and IgG antibodies, and was on treatment. Child had normal vitals and normal skin perfusion. General and systemic examinations were unremarkable except a few petechiae on his face. Child was empirically started on antibiotics ampicillin (50 mg/kg/dose 12 hourly) and gentamycin (4 mg/kg/day). The blood culture was negative for any growth. Dengue IgM antibody came out to be positive [Table/Fig-1]. The child had fever for about four days, following which he entered the critical phase. Laboratory investigations showed normal White Blood Cells (WBC) count with thrombocytopenia (98,000/mm³) at the time of admission and platelet count was, as low as, 11,000/mm on day six of illness. Platelet transfusions and supportive management with intravenous fluids was provided. Except for a mild transaminitis, child did not have any complications. The child had defervescence on day seven then, he started to become alert and active. He was discharged after 10 days of admission. On follow-up after five days, child was active, feeding well and repeat investigations showed normal WBC and platelet counts (2,82,000/mm³).

Case 5

A two-day-old female neonate, who was delivered in the same hospital had developed fever. The baby had a birth weight of 2.9 kg with reassuring APGAR scores. She was born by vaginal delivery to a second gravida mother with a history of dengue fever at 39 weeks of pregnancy and was in recovery phase of illness. Baby had fever of about 37.9° C on day 2 of life, hence, child was empirically started on antibiotics ampicillin (50 mg/kg/dose 12 hourly) and gentamycin (4 mg/kg/day). Blood culture was negative for any growth. Chills was also evaluated for dengue NS1 antigen which was positive. However, dengue IgM and IgG antibody tests were negative [Table/Fig-1]. On day 5 of illness, baby entered the critical phase wherein, the neonate had refusal of feeds and lethargy and subsequently started on intravenous fluids. Petechial lesions were also noted. Platelet count was, as low as, 10,000/mm for which platelet transfusion (10 mL/kg) was provided. Followed which baby recovered well and was discharged on day 9 of life. On follow-up after five days, child was afebrile, alert, feeding well, no petechial rashes and repeat investigations showed normal WBC and platelet counts.

DISCUSSION

Dengue is a viral infection which affects people in endemic areas annually [5]. Neonatal dengue, most of the time is underdiagnosed, because it mimics neonatal sepsis and also due to less suspicion. Severe dengue is due to secondary heterotypic infections or primary infection in infants born from Dengue Virus (DENV)-immune mothers, due to Antibody-dependent Enhancement of infection (ADE) [6]. In the present case series, five cases of neonatal dengue are presented out of which, two cases had vertical transmission and three cases had horizontal transmission of dengue. The clinical course of dengue has three phases namely, febrile phase which lasts for about 2-7 days followed by critical phase ranging between 48-72 hours and finally, a convalescent phase of about 3-4 days. All the neonates presented within one week of illness during their febrile phase. The mean age of presentation was 10 days. Male to female ratio was 3:2. Petechial rashes and refusal of feeds were observed in two cases. Diagnosis of dengue fever can be done by using dengue virus isolation, virus nucleic acid detection, detection of NS1 antigen, or by detection of antibodies. Dengue virus isolation and virus nucleic acid detection are usually not preferred as they are time consuming and expensive [5]. In the present case series, four cases had leukopenia, and all of them had thrombocytopenia. Dengue NS1 antigen was positive in four cases, whereas, dengue IgM was positive in all cases. Surprisingly, all cases were found out to be negative for dengue IgG antibody, which can be explained as primary dengue infection. Neurosonogram did not reveal any bleeding despite low platelet counts. Sepsis screen including blood culture was negative in all cases.

Among the three vertically acquired dengue cases, all mothers had dengue NS1 antigen and IgG antibody positivity whereas, only 1 (33%) mother had dengue IgM positivity. Pregnant mothers can transmit the infection to the foetus if, she develops a fever 10 days prior to delivery to 10 hours post delivery. Intrauterine transmission is high, especially when the mother is in febrile phase as viraemia is observed highest in the febrile phase. The transmission is unaffected by the mode of delivery [6]. All neonates had a smooth hospital stay without any serious complications like shock requiring inotropes, severe plasma leakage and bleeding manifestations. According to literature review, newborns with low birth weight have a higher risk of getting severe forms of dengue [7]. In the present case series, all the neonates were term babies with normal birth weight. None of the cases had hepatic derangement except for mild transaminitis, which was observed in three cases. Only two cases had severe thrombocytopenia requiring platelet transfusion but, they did not develop any bleeding manifestations. Bleeding is due to mature immune system and repeated infections with various serotypes as

seen in older children and adults [8]. Although, neonates are one of the vulnerable groups, the lesser incidence of complications could be explained due to their immunological immaturity and also due to decreased production of mediators like Interleukin-1 (IL-1) 1 beta, IL-6 and tumour necrosis factor alpha by the neonate [9].

In the present case series, no newborn developed dengue shock syndrome, which is in contradiction to a study done by Pachauri A et al., where a neonate developed dengue shock syndrome on day three of life with a good outcome [8]. Age appears to be one of the most common epidemiological risk factors in dengue as the case fatality rate is higher in children compared to adults [10,11]. However, in the present case series, mortality due to neonatal dengue was nil and all cases recovered well. The duration of hospital stay ranged between 6-12 days with a mean duration of about nine days which is in contrast to the study done by Dalugama C et al., where they reported a longer hospital stay [12]. This could be explained as all the neonates were of term gestation and none of them had severe complications like shock requiring inotropes, fluid overload and organ failure. Maternal deaths were reported in 6%-18% of pregnant dengue patients in a study done by Machain-Williams C et al., whereas, in the present case series, there were no maternal death [13]. Reduced maternal death is due to the early diagnosis and management, as well as, prompt referral of sick mothers to a tertiary care centre for appropriate management. Supportive management like judicious use of fluids, inotropes and blood products, if required remains the main stay of treatment.

CONCLUSION(S)

It is recommended to suspect dengue fever in any neonate presenting with fever, leukopenia and thrombocytopenia mimicking sepsis, especially during the epidemic season. Dengue serology

should be done in both, the mother and child for early diagnosis and treatment. Neonate should be thoroughly evaluated for any serious complication and should be vigilantly monitored, till their second week of life, before discharging them.

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