

# Vertical Transmission of Dengue Infection in Thai Infants : Two Case Reports

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## Abstract

Dengue infection is hyperendemic in tropical countries especially in Thailand. Most dengue infections occur during childhood but some adults may remain susceptible to infection. About 30 per cent of dengue infection are reported in patients > 15 years old. Some pregnant women may also be susceptible to dengue and if they experience dengue infection, they can transmit the dengue viruses to their babies. The authors report two babies who developed mild dengue illness, dengue hemorrhagic fever (DHF) grade II, beginning on their 6<sup>th</sup> day of life. Both of them had low grade fever, hepatomegaly and generalized petechial rash. The first baby had Hct ranging from 46 to 40 per cent with minimal right pleural effusion. The lowest platelet count was 19,000 cells/mm<sup>3</sup>. His mother had dengue shock syndrome with massive post partum bleeding. The second baby had dengue 2 infection while his mother had dengue fever. His Hct had also risen from 52 per cent to 61 per cent with right pleural effusion. His lowest platelet count was 7,000 cells/mm<sup>3</sup>. Both mothers and their babies had a complete recovery although the first baby had prolonged thrombocytopenia for two months.

**Key word :** Vertical Transmission, Dengue Infection

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Dengue infection is hyperendemic in tropical countries especially in Thailand<sup>(1)</sup>. It is the most important mosquito-borne Flavivirus infection. It is

one of the leading causes of death and hospitalization of children. The two important clinical manifestations are DF (dengue fever) and DHF (dengue hemorrhagic

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fever). DHF can be a fatal illness if no appropriate treatments are given<sup>(2)</sup>. The two hallmarks of DHF are plasma leakage that can lead to hypovolemic shock and abnormal hemostasis. Some children in Thailand who experience dengue infection may escape infection and contract it in adult life<sup>(3)</sup>.

Dengue infection has increased over the past 10 years especially in adults. About 30 per cent of infections are reported in > 15 years old patients compared to less than 5 per cent in the past. Pregnant women are also prone to dengue infections in this endemic country<sup>(4)</sup>. There are few reports of dengue virus vertical transmission so this is an additional 2 case reports<sup>(4-6)</sup>.

## CASE REPORT

### First case

A 25-year-old pregnant woman was admitted to Rajavithi Hospital at full-term in active labor. She was a gravida 1, para 0 with a history of uncomplicated antenatal care. A 3,450 gram male, full-term baby was delivered normally. She had complained of high grade fever and myalgia two days before and continued to have a high grade fever a few days after delivery. She had massive postpartum vaginal bleed-

ing which required transfusion of 4 units of fresh whole blood (FWB), 1 unit of packed red cells (PRC), 4 units of fresh frozen plasma (FFP), and 9 units of platelet concentrates. Her lowest platelet count was 26,000 cells/mm<sup>3</sup>. Although her liver enzymes, Aspartate aminotransferase/Alamine aminotransferase (AST/ALT) were elevated to 1,770 and 750 U respectively, she recovered completely and was discharged home after 6 days in the hospital with the diagnosis of dengue shock syndrome. She has serologically confirmed to have secondary dengue infection.

Her baby developed low grade fever 38.8°C on the 1<sup>st</sup> and 6<sup>th</sup> day after birth with generalized petechial rash. The liver was 2 cms below the right costal margin and the spleen tip was also palpated 0.5 cms below the left costal margin. His Hct ranged from 46 per cent to 40 per cent. Minimal right pleural effusion was shown on his chest film. The lowest platelet count was 19,000 cells/mm<sup>3</sup>. He was diagnosed as DHF gr II. He recovered well with good weight gain and normal development but had prolonged thrombocytopenia for two months. He had confirmed primary dengue infection. No viral study was done for this mother and infant.

	First mother	First infant
Age	25 years	1 and 6 day of life
Body weight (Kg)	NA	3.450
Day of fever	Two days before delivery	Day 1 and Day 6 of life
Temperature (°C)	38.5	38.8
Duration of fever (day)	5	5
Bleeding	Bleeding per vagina	No
Hepatomegaly (cm) below costal margin	3	2
Rash	MP, petechial	MP, petechial
Hb (g/dl)	10.4	16.5
Hct (%)	36 to 26	46 to 40
WBC (cells/mm <sup>3</sup> )	7,300	5,900
PMN (%)	74.6	39
Lymphocyte (%)	17.2	50
Lowest platelet (cells/mm <sup>3</sup> )	24,000	13,000
AST/ALT (U)	1,770/760	427/134
CXR	ND	Right pleural effusion
Duration in hospital (day)	6	12
Serology	Secondary dengue	Primary dengue
PCR	ND	ND
Diagnosis	DSS	DHF grII

## Second case

A 19-year-old pregnant woman was admitted to Rajavithi Hospital in active labor. She was gravida 2, parity 1 with uncomplicated antenatal care. A 3,045 gram male, full-term baby was delivered normally. She had complained of high fever just one day before and continued to have fever in the hospital for 3 days. She also had maculopapular rash with petechial rash over her body and extremities. She had stable hematocrit but the platelet count dropped from 182,000 to 16,000 cells/mm<sup>3</sup>. She was confirmed to have

secondary dengue infection and diagnosed as dengue fever. She was sent home after 5 days in the hospital.

Her baby developed low grade fever and generalized petechial rash all over his body on day 6 of life. His liver was 4 cms below the right costal margin. His hematocrit ranged from 54 per cent to 61 per cent. Minimal right pleural effusion was shown on his chest film. The lowest platelet count was 23,000 cells/mm<sup>3</sup>. He had confirmed primary dengue infection and dengue 2 was identified by reverse transcriptase polymerase chain reaction (PCR). He was sent home on the 10<sup>th</sup> day.

	Second mother	Second infant
Age	19 years	6 day of life
Body weight (kg)	54.3	3.045
Day of fever	One day before delivery	Day 6 of life
Temperature (°C)	38	38
Duration of fever (day)	4	3
Bleeding	No	No
Hepatomegaly (cm)	2	4
(below right costal margin)		
Rash	MP, petechial	MP, petechial
Hb (g/dl)	9.6	18
Hct (%)	29.6 to 34.3	48.7 to 61
WBC (cells/mm <sup>3</sup> )	6,500	3,400
PMN (%)	71	49
Lymphocyte (%)	12	45
Lowest platelet (cells/mm <sup>3</sup> )	16,000	7,000
AST/ALT (U)	ND	55/15
CXR	ND	Right pleural effusion
Duration in hospital (day)	5	10
Serology	Secondary dengue	Primary dengue
PCR	Negative	Dengue type 2
Diagnosis	DF	DHF grII

ND = not done, NA = not assessment, PCR = polymerase chain reaction

## DISCUSSION

These two babies began to have signs and symptoms of dengue infection on the 6<sup>th</sup> day of life. Since the incubation period of dengue is between 5-8 days<sup>(1,7)</sup>, it is less likely that these babies acquired dengue infections post natally. So these two cases are among a few cases in the world of vertical transmission from mother to their offspring. Unfortunately, virus studies were not done in the mothers and infants so that vertical transmission would be strongly supported when the same serotype and virus were identified in both the mother and infant.

The clinical presentation in infants do not depend on their mothers' illness as shown by the previous report<sup>(4,5)</sup>. The first mother had the most severe manifestation, dengue shock syndrome (DSS) while the second mother had the mildest form of disease, dengue fever (DF) and both their infants had the same disease manifestation, DHF grade II. In the previous reports of vertical transmission, all neonates had DF, so these are the first two neonates who had more severe diseases, DHF acquired through vertical transmission.

Clinical diagnosis of DHF in a newborn baby is very difficult and sepsis which is most common during this period of life is always ranked first in the differential diagnosis. The common signs and symptoms are that of not doing well with hepatomegaly and petechial rash, leukocytosis or leukopenia and thrombocytopenia are common findings in sepsis and DHF. Both babies had been treated as sepsis because the result of serological and virological confirmation takes a long time. Clinical presentation in the mothers play a vital role in the diagnosis in such newborns.

The first baby had prolonged thrombocytopenia for two months without any significant bleeding. There is no report of prolonged thrombocytopenia in a neonate with vertical transmission. The mechanism is likely to be viral induced bone marrow suppression but there is no proof in this case. Both infants had primary dengue infections while their mothers had secondary dengue infection. Both mothers had experienced dengue infection before as evidenced by secondary infections, so they should have antibodies to one or more serotypes of the dengue virus. At the time that the mothers had signs and symptoms of dengue infections, in these cases just about two and one day before delivery, they were sure to have viremia and sent dengue virus through the placenta to their infants. These infants were also sure to have received a significant number of their maternal antibodies (different from the newly infected ones) transplacentally since the beginning of the third trimester. As documented before those patients who presented with DHF are associated with secondary dengue infections(8-10). This may explain the most likely mechanism why infants who had primary dengue infections but had received dengue antibodies transplacentally had DHF.

Timing between the 2 dengue infections are also another important factor that determines disease manifestation as demonstrated by the second mother who had secondary dengue infection but her disease manifested as DF. It has been reported previously that the exact time between the two dengue infections should be between 1-5 years to enable disease manifestation as DHF(2).

The sequence of dengue virus infections is another important factor that determines disease manifestation. If the second infection is caused by dengue 2, it is more likely that the patient will develop DHF (9). The second baby was infected by dengue 2. If the mother has DF, it is less likely that labor would be complicated by severe bleeding because the natural course of DF has no abnormal hemostasis except about half of the DF cases may have mild thrombocytopenia (platelet count between 50,000-100,000 cells/mm<sup>3</sup>). If the mother has DHF, blood and blood components (fresh whole blood, packed red cell, fresh frozen plasma and platelet concentrate) have to be available in an adequate amount. The first mother was fortunate to deliver her baby just before the critical period when her platelet count was 126,000 cells/mm<sup>3</sup>. After delivery, she entered the critical period when she had abnormal hemostasis and platelet count dropped to 26,000 cells/mm<sup>3</sup>. Since she had a raw surface in the uterus and episiotomy wound, she had massive bleeding until she went into shock. There is increasing incidence of dengue infections in pregnant women, not only at/or around the time delivery, so guidelines in management and for future plans for this special population needs to be established by Pediatricians, Obstetricians and of course the patients' families

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## การติดเชื้อเด็งกีจากมารดาสู่ทารก : รายงานผู้ป่วย 2 ราย

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การติดเชื้อเด็งกี พบมากในประเทศเขตร้อนโดยเฉพาะประเทศไทย การติดเชื้อเด็งกีส่วนใหญ่จะเกิดในเด็กแต่ในผู้ใหญ่ก็สามารถที่จะมีการติดเชื้อได้ การรายงานการติดเชื้อเด็งกีในคนอายุมากกว่า 15 ปี พบถึงร้อยละ 30 คนที่ตั้งครรภ์บางส่วนก็มีโอกาสติดเชื้อนี้ได้และสามารถถ่ายทอดการติดเชื้อไวรัสนี้ไปยังทารกได้

ผู้ศึกษาได้รายงานทารก 2 รายมีอาการเจ็บป่วยจากเชื้อเด็งกีเพียงเล็กน้อยคือเป็น DHF gr II โดยเริ่มมีอาการเมื่ออายุ 6 วัน ทารกทั้ง 2 รายมีไข้ต่ำ ๆ ตับโตและผื่นทั้งตัวแบบจุดเลือดออก ทารกรายแรกมีเลือดขึ้น ตั้งแต่ร้อยละ 40 ถึง 46 และมีน้ำในช่องปอดด้านขวาเพียงเล็กน้อย เกร็ดเลือดต่ำสุดที่ 19,000 เซลล์ต่อลูกบาศก์เมตร มารดามีอาการ DSS ร่วมกับมีเลือดออกหลังการคลอด ทารกรายที่ 2 มีการติดเชื้อเด็งกีชนิดที่ 2 ขณะที่มารดามีการติดเชื้อเพียงไข้เด็งกี ทารกมีเลือดขึ้นระหว่างร้อยละ 52 ถึง 61 ร่วมกับมีน้ำในช่องปอดด้านขวาเพียงเล็กน้อย เกร็ดเลือดต่ำสุดที่ 7,000 เซลล์ต่อลูกบาศก์เมตร มารดาและทารกและมารดาทุกรายหายเป็นปกติแม้ว่าทารกแรกจะมีภาวะเกร็ดเลือดต่ำนานถึง 2 เดือน

**คำสำคัญ :** การถ่ายทอดเชื้อจากมารดาสู่ทารก, การติดเชื้อเด็งกี

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