International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

Neonatal Dengue with Clinical Sepsis: A Case Report

I Gusti Ngurah Alit Hendra Wahyudi[1], Gusti Ayu Nyoman Yulia Sitta Dewi[2]

Department of Pediatric, Bali Mandara Hospital, Denpasar, Bali, Indonesia
Email: *yudikalit97[at]gmail.com*

Abstract: ***Background: Dengue fever in late pregnancy puts the fetus at great risk because fewer maternal - specific antibodies cross the placenta, leading to a high probability of neonatal dengue infection. We followed a patient in the pediatric health department of RSUD Bali Mandara. Case Persentation: A 9 - day - old baby boy complained of fever for 3 days up to a temperature of 39℃; the fever fluctuates, but it never went down to normal temperature. On physical examination, the baby was found to be less active, crying enough, suction reflex (+), pulse 135x/minute, breathing: 44 x/minute, temperature: 38.8 (axillary), SpO2: 93%, jaundice (+), lower extremities: warm acral (+), left petechiae (+), CRT <2'', jaundice skin of Kramer 2 - 3. Laboratory test's result showed the platelets (69.000), hematocrit (52.2), positive dengue NS1 antigen, and positive dengue IgG and IgM. The patient was diagnosed with neonatal dengue and admitted to Perinatology. Optimal management is needed to treat neonatal dengue. Conclusion: It is important to emphasize the information on dengue transmission in infants, especially in endemic areas considering the complication that may occur, early recognition of dengue will significantly reduce infant mortality. Careful monitoring and proper lab checks can lead to a speedy recovery.***

Keywords: Neonatal dengue, Platelets, Placenta

1. Introduction

Dengue is one of the fastest emerging and developing viral diseases, especially in low - income urban and rural areas. *Aedes* mosquito is a vector that can cause dangerous diseases, namely dengue fever by transmitting through the flavivirus *virus* which belongs to the flaviviridae*family*. The *World Health Organization* (WHO) defines dengue as an acute fever disease associated with two or more of the following signs or symptoms: severe headache, retro - orbital pain, myalgia, arthralgia, skin rash, leukopenia, and hemorrhagic manifestations. In the Philippines as well as Thailand severe dengue fever was first identified circa 1950. Since then the incidence of dengue fever has increased up to 30 - fold.1

Recent estimates indicate 390 million more dengue infections occur per year and only about 90 million more experience clinical manifestations. Who estimates that 3.9 billion people worldwide are at risk of dengue infection. Although preliminary reports describes that dengue fevers primarily infect children, current epidemiological data suggest that infection attacks older age groups rapidly, including pregnant women. The method of dengue virus transmission is obtained through mosquito bites, blood, mucocutaneous and maternal - fetal pathways. Dengue fever during pregnancy is associated with several neonatal complications such as death, miscarriage, low birth weight and premature birth. The majority of reported cases showed dengue fever in neonates whose mothers were infected at the end of pregnancy.1, 2

In 2010 at RS Dr. Soetomo Surabaya there were cases of dengue virus in infants 4.7% - 7.2%, with these results showing that dengue virus infection is evenly distributed from various regions conducted by the study.3 In addition to Indonesia, in Thailand to be exact, there is a category of babies who contracted dengue with an average age of 7.2 months, with the youngest age of 3 months and the most cases at the age of 5 - 9 months at Chonburi. Several studies in Vietnam found the most age of 4 - 10 monthswith a comparison of men: women 115: 86, with 9% of them cases of dengue shock syndrome (SSD). Another study from Vietnam also mentioned that out of 245 infants with dengue fever, 63 infants (25.7%) experienced SSD, with the youngest case from a 1 month old infant and the average infant age was 6.8 months.3

Background: hemorrhagic fever infection in pregnant women in the final trimester of pregnancy can increase the risk of the fetus developing dengue neonates infection due to fewer maternal - specific antibodies passing through the placenta. Currently fetal or umbilical cord blood samples are considered to be a better source for the qualification of intrauterine dengue infection.4 In neonates, transmission of vertical dengue produces varying symptoms, from fever with thrombocytopenia to cerebral hemorrhage.5 Due to the lack of resources and capacity to survey hemorrhagic fevers effectively and also the rare reporting of vertical transmission of the virus, very little is known about neonatal hemorrhagic fevers. Considering that Indonesia is a tropical country that is an endemic area of dengue fever with complications that can increase mortality in neonates, it is important that we understand more about neonatal dengue infection, especially in the case of prevention and transmission.

2. Case Report

Infants, aged 9 days, weighed 3.1 kg have one of the complaints, namely high fever for a period of 3 days before being admitted to RSUD Bali Mandara. High fever post BCG and Polio immunization. The fever fluctuates, but it never went down to normal temperature. Fever with no seizures, shortness of breath and discharge of fluid in the body (vomiting), prior to urination and defecation are

normal. There is no history of family or neighbors suffering from symptoms such as this prior to the incident. The patient was the fifth child, with a birth weight of 3.2 kg, a body length of 48 cm, was born normal and cried immediatley. During pregnancy, the patient routinely checks her pregnancy with midwives and obstetric specialists 4 times and ultrasound twice. History of BCG immunization 1 time, Hepatitis 1 time, and polio 1 time

On physical examination it was found that the baby is less active, sufficient crying, suction reflexes (+). On examination of vital signs, a pulse of 135x/min was obtained, respiratory rate: 44 x/min, temperature: 38.8 ℃ (axilla), SpO2: 93%. On examination the conjunctiva is not anemic, the sclera is not icteric, the thorax is within normal limits, and there is no ronkhi and *wheezing*. In the abdomen, there is icterus (+), there were no ascites or hepatomegaly. Examination of superior extremities: Warm acral (+), cyanosis (-), CRT<2 seconds, inferior extremities: warm acral (+), petechiae sinistra (+), cyanosis (-), CRT<2". Skin examination found jaundice skin of Kramer 2 - 3.

Complete blood laboratory examination showed Leukocytes 6.0, Hemoglobin 17.7%, platelets 69, 000/mm, hematocrit 52.2%, direct bilirubin 0.36, indirect bilirubin 3.52, total bilirubin 3.58 and dengue NS1 Antigen positive. The patient was diagnosed with Neonatal Dengue. During the ER, the patient was given the initial treatment of intravenous fluid D10% 2ml/hour, paracetamol drop 10mg/kgBB, Ampicillin 50 mg/kgBB every 12 hours, Gentamicin 7.5 mg/kgBB every 24 hours, then the patient was subsequently treated in Perinatology and it iscrucial to monitor TTV, routine blood examination, and signs of bleeding.

Table I: Complete Blood examination, blood chemistry and serology

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8
Leukocytes	6.0	5.46	5.70	7.59	6.63	5.89	4.64	8.50
Hemoglobin	17.7	18.0	18.8	16.9	16.3	15.6	15.1	- 14~ - 5
Hematocrit	52.2	48.4	51.9	46.9	44.6	43.2	41.5	40.1
Platelet	69.000	61.000	9.000	8.000	26.000	46.000	69.000	124.000
Procalcitonin			0, 57					
Bilirubin Total	3.58							
Direct bilirubin	0.36							
Indirect bilirubin	3.52							
NS 1			Positive					
IgG Dengue							Positive	
IgM Dengue							Positive	
Blood Culture							No Growth	

On day 3 of treatment or day 4 on the onset of the fever it has been found that thrombocytopenia (platelet 8, 000/mm) is present, so that 30cc TC (Platelet Concentrate) transfusion was given every 12 hours for 3 days and CPAP was installed with FiO2 30% PEEP 7 Flow 8 and monitoring the risk of intracranial bleeding. On day 4, the treatment was carried out to switch Antibiotics to line 2 cefoperazone sulbactam 150 mg every 12 hours, then 40 mg amikacin every 12 hours. Examinations of igM and igG dengue were done on day 7 of treatment or day 8 of fever onset with positive results. The patient experienced an increase in platelets on day 5 of treatment to 26, 000/^{mm3} with the administration of TC transfusions and a decrease in hematocrit (44.6%). The patient's mother exercised igM and igG dengue on the last day of the patient's treatment, it showed a positive results but during the pregnancy the patient never experienced the same fever or complaints. The patient was discharged on day 9 after meeting the Dengue patient return criteria.

3. Discussion

Dengue fever is a disease that can attack anyone indiscriminately through the transmission of very dangerous mosquito, aedes which is also accompanied by the flavivirus.6 Aedes aegypti mosquitoes usually bite between 10 - 12 noon attacking people of all ages. Dengue virus infection affects human populations of all age groups around the world. In some parts of the world, hemorrhagic fever is a child health problem. This case of dengue fever is very indiscriminate with age, but most of those who contract hemorrhagic fever <15 years old are still categorized as children with infant cases made up of 5% of cases of hemorrhagic fever. This case of dengue fever if associated with dengue endemic areas reaches 10% of cases in 2 - 15 months infants infected.1

Antibodies are natural defences possessed by every human being, at stable babies at about 1 year of age receive antibodies from his mother who is susceptible to dengue/DSS.7 This dengue virus infection is related to the loss of the baby's antibodies since, after birth, the anti - body antibodies given by the mother can still prevent various viruses from entering the body, but when the IgG is metabolized, the level will continue to decrease which causes the risk of contracting dengue/DDS. Infants who are 4 - 6 months old are more prone to experiencing dengue/DDS with factors caused by the double effect of receiving antibodies passively. The relationship between *infection - enhancing activities*of maternal serum in primary monocytes with the age of a child infected with the initial virus infection has been described in Kliks et al 1988 study. There are several countries that are trying to prove the relationship of antibodies to the age of newborn babies, one of which is the Philippines which proves that the anti - DEN 3 neutralization ability monitored at birth correlates with the age of symptomatic dengue infants. The next factor is a strong immune response that can compensate for the high virus count in the blood.3 In this case, the patient's mother had positive igM and igG but was asymptomatic at the time of conception. At the age of 3, 4, 6, and 9 months, the following parameter 3%, 19%, 72%, and 99% are the antibodies of the infants respectively, these antibodies are

given from a mother to her child and will slowly disappear until the child is one year of age, at that point it will be completely destroyed. Another study related to this problem is the 2008 tahub study at Queen Sirikit Hospital in Bangkok where 450 infants were found aged 9, 12, and 18 months have, 23%, 9%, and 17% of infants had neutralizing antibodies against 1 or more dengue serotypes, respectively.3

Antibody - dependent enhancement (ADE) is a viral replication mechanism that can alter the multiplying system to be more easy and extensive. Which will certainly increase the number of viruses. A mother will transmit immunoglobulin G to the baby through the placenta that directly binds to different dengue virus serotypes and in addition will mediate viral endocytosis into dendritic cells. When the virus enters the dendritic cells, it interacts with *Ig - like receptor* B1 which has an inhibitory effect on FcR signaling to produce specific antibodies that are more competent to decriminalize the virus. In the end, it facilitates the virus to be able to replicate freely and subsequently infect other cells. Through the ADE system, it will certainly make more viruses that it produces. Apart from the number of viruses, the number of infected cells will also increase. The manifestation of plasma leakage is caused by cell resistance reactions that produce inflammatory mediators. This factor is the cause of the higher severity of disease in primary or secondary dengue infections in infants compared to the children or adults with different types of virus serotypes.8

Non - dengue acute fever is similar to symptoms and signs of infant dengue. It was found that in the Philippines the majority of patients in both groups presented upper respiratory tract symptoms, which is somewhat different from the results of hospital - based studies in Nicaragua and Vietnam, based on community research conducted by Capeding et al.3 The fever lasting for 2 - 7 days was one of the consequences of hemorrhagic fever in infants; it was the same in older children. Upper respiratory tract symptoms (cough, nasal congestion, runny nose, shortness of breath), gastrointestinal symptoms (vomiting, diarrhea), and febrile seizures often occur in infants. The difference between hemorrhagic fever and other common infections in infants (such as pneumonia, bacterial sepsis, meningoencephalitis, oral and nail diseases, measles, rotavirus infection, etc.) is often indistinguishable. The presence of febrile seizures, macular rash, petechiae and lower platelet counts at the onset of the disease is significantly associated with hemorrhagic fever in infants and, acute indistinguishable febrile disease. In[10] of these cases, manifestations of fever would go up to 39℃. the fever fluctuates, but it never went down to normal temperature. In general, less active babies have warm acral and petechiae inferior extremities of the sinistra.

In most neonatal dengue, increased capillary permeability, along with increased hematocrit levels becomes more evident (which usually occurs on days 3 - 6 of illness). In a period of 4 - 48 hours, in this moment there is a period of clinical plasma leakage. During this critical phase, the clinical picture and laboratory findings of neonatal dengue became more prominent. Skin bleeding such as petechiae, mucosal membrane bleeding (e. g. nose and gums), and gastrointestinal bleeding may occur. in most cases, hepatomegaly. Splenomegaly is found in almost 10% of neonatal dengues, seven times more often than in older children.1[0]clinically patients correspond to symptoms that can be found in the critical phase. The laboratory findings in this case are platelets that have decreased on day 3 on the onset of fever, this indicates that the patient has entered the critical phase.

Reports from several studies related to this topic define it in many different ways. A study in Vietnam by Hung et alfound that high fever, petechiae, and hepatomegaly were the most frequent clinical findings in infants with dengue. Findings of symptoms of fever, liver enlargement, and rash were found in 100, 93.1 and 55.2% of infants with dengue fever originated in Chennai, and most likely all infants with dengue virus infection developed thrombocytopenia, with the average number of infant platelets was lower than that of the older children. In Nicaragua, external bleeding and rashes are found in more than 50% of babies with dengue fever. In contrast, in the Philippines, 1 in 41 convalescent rash cases with primary dengue virus infection were found (2%).4

Diagnosis can be ensured by laboratory examinations such as dengue virus isolation, dengue virus nucleic acid detection, NS1 antigen detection and by other serological test examinations.9 In this case NS1 dengue antigens in infants were positive and anti dengue IgM and IgG positive in mothers and infants. When a pregnant or childbearing woman develops signs consistent with hemorrhagic fever, the diagnosis of hemorrhagic fever should take account of her neonates even if the neonate appears healthy at the beginning of the birth. Pain felt in some neonates will be experienced from 11 days after birth. The diagnosis of neonate dengue may eventually be suspected based on clinical experience and then confirmed in the laboratory, but the initial presentation may be compromised by bacterial sepsis, birth trauma, and associated neonate disease. Symptomatic treatment, then supportive treatment under close supervision is the right treatment.9

Inadequate care will produce highly ineffective results, therefore appropriate clinical considerations, including the decision to correct severe thrombocytopenia, should be made. Prophylactic platelet transfusion is a transfusion without any bleeding. A survey by Whitehorn et al., 18 of 306 physicians from approximately 20 countries who regularly handle hemorrhagic fever cases showed that 112 (37.9%) physicians performed platelet transfusions in the absence of bleeding with different platelet levels.1[1 - 12] Macro et al.1[3] It is to be noted that most platelet transfusions are not based on medical reasons, but rather in response to social pressures from patients and their families.

The UK Commission's Standardized Guidelines for Platelet Transfusions recommend that prophylactic platelet transfusions should not be administered to patients with stable thrombocytopenia without bleeding risk factors with a platelet value of 10, 000/mm3. *The Directorate of National Vector Borne Diseases Control Program, India*, stated that prophylactic platelet transfusions were not required in stable

patients even when platelets were < 20, 000/mm. Singapore clinical practice guidelines also recommend administering prophylactic platelet transfusions only in platelets of < 10, 000/mm3 in patients with bone marrow function failure without additional bleeding risk factors, and < 20, 000/mm3 in patients with additional bleeding risk factors or in the event of rapid platelet decline. According to the research of Assir et al.1[4], that, platelet transfusion cannot stop bleeding or shorten the time of bleeding and it has a strong correlation to the side effects of transfusion. Recent studies have shown that stable patients are not recommended for prophylactic platelet transfusion, although platelets at 10, 000/mm3 cannot be used as a benchmark for transfusion. In patients, there was a rapid decrease in platelets from 61, 000/^{mm3} on day 2 of treatment to 9, 000/mm3 on day 3 of treatment in accordance with the indication of concentrated platelet transfusion administration.

What the patient is waiting for is his return. But prior to this stage, there are conditions that must be passed by the patient regarding their body's condition and healing. An example would be the absence of fever for 24 hours without antipyretic administration, then a stable hematocrit, platelet count > 50, 000/ml, smooth breathing, and of course, improved physical condition.9

On day 8 the patient was in good condition without any symptoms or complications. This is supported by maximum care, adequate rest, and of course appropriate therapy. Before being allowed to go home, the prognosis of stage 3 dengue fever hat has a dubian prognosis, is already in a good state and is allowed to go home.

4. Conclusion

It is important to emphasize the importance of dengue transmission in infants, especially in endemic areas. Considering the complication that may occur, early recognition of dengue will significantly reduce infant mortality. Careful monitoring and proper lab checks can lead to a speedy recovery.

References

[1] Thomas, Jessy. Thomas, Priya. George, CR. Case Report: Neonatal Dengue. *International Journal of Contemporary Pediatrics*.2017. Department of Pediatrics, Lisie Hospital, Kochi. India: 2017.
[2] Nguyen, Mr. Minh. Huan, VT. Reda, A. Morsy, S. That's it, HTN. Tri, VD. mau, NK. Elfalturi, MK. Hieu, TH. Hung NT, Hirayama, Kenji. Huy, NT. Clinical Features and Outcomes of Neonatal Dengue at the Children's Hospital 1. Hochi Minh, *Vietnam. Journal of Clinical Virology. Vietnam*.2021. URL: https: //doi. org/10.1016/j. jcv.2021.104758
[3] Husada, Dominicus. Rani, Catarina. Puspitasari, Dwiyanti. Darmowandowo, Widodo. Basuki, PS. Ismoedijanto. ProfilKlinikInfeksi Virus Dengue Pada Bayi di Surabaya. Vol 13, No.6. April 2012. *Sari Pediatri*: RSU DR. Soetomo, Surabaya.
[4] Perret C, Chanthavanich P, Pengsaa K, Limkittikul K, Hutajaroen P, Bunn JE, et al. Dengue infection during pregnancy and transplacental antibody transfer in Thai mothers. *J Infect*.2005; 51: 287 - 93.
[5] Basurko C, Carles G, Youssef M, Guindi WE. Maternal and fetal consequences of dengue fever during pregnancy. *Eur J ObstetGynecolReprod Biol*.2009; 147: 29 – 32.
[6] Maroun, SLC. Marliere, RCC. Barcelus, RC. Barbosa, CN. Ramos, JRM. Moreira MEL. Case Report: Vertical Dengue Infection. *Journal de Pediatria* vol.84, No.6. SociadeBrasileira de Pediatria: 2008.
[7] Lei HY, Huang KJ, Lin YS. Immunopathogenesis of dengue hemorrhagic fever. *Am J Infect Dis* 2008; 4: 1 - 9.
[8] Handayani, Indri. Indrati, AR. Nature, Anggraini. ProfilManifestasiKlinis dan LaboratorisPasien Dengue Bayi yang Menjalani Rawat Inap di RSUP DR. Hasan Sadikin Bandung. *Sari Pediatri*, Vol 19. No.3. October, 2017 DepartemenIlmu Kesehatan Anak, DepartemenPatologiKlinik RSUP DR. Hasan SadikinFakultasKedokteran Universitas Padjajaran, Bandung.
[9] WHO. Handbook For Critical Management of Dengue. Who 2012
[10] Petdachai, Witaya. Sila'an, Jirapan. Nimmannitya, Suchitra. Nisalak, Ananda. Case Report: neonatal Dengue Infection, Report Of Dengue Fever in A 1 – Day – Old Infant. Vol 35 No 2 Juni. Departement of Pediatrics, Prachomklao Hospital, Petchbusi. Thailand 2004.
[11] Makroo RN, Raina V, Kumar P, Kanth RK. Role of platelet transfusion in the management of dengue patients in a tertiary care hospital. *Asian J Transfus Sci*.2007; 1 (1): 4 - 7.
[12] Suhendro, Nainggolan L, Chen K, Pohan HT. Demamberdarah dengue. In: Sudoyo AW, Setiyohadi B, Alwi I, Simadibrata M, Setiati S, editors. *Buku ajar ilmupenyakitdalam*. Jakarta: Pusat PenerbitanIlmuPenyakitDalam FKUI; 2006. p.1709 - 13
[13] Health Sciences Authority–Ministry of Health of Singapore. *Clinical practice guidelines–clinical blood transfusion. Singapore*; 2011
[14] Assir MZK, Kamran U, Ahmad HI, Bashir S, Mansoor H, Anees SB, et al. Eff ectiveness of platelet transfusion in dengue fever: A randomized controlled trial. *Transfus Med Hemother*.2013; 40: 362 - 8. doi: 10.1159/000354837.