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DETERMINATION OF DENGUE VIRAL INFECTION SEVERITY IN PEDIATRIC BASED ON PHYSICAL EXAMINATION AND LABORATORY TESTS: A CASE STUDY OF A 7 MONTHS OLD BABY WITH DENGUE HAEMORRHAGIC FEVER

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ABSTRACT

Background: Dengue viral infection can infect people of all ages, including infants less than 1-year-old. The Disease severity of dengue infection consists of asymptomatic infection and symptomatic infection. The symptomatic infection has varying degrees of severity: undifferentiated fever, dengue fever, DHF, and Dengue Shock Syndrome (DSS). **Method:** The data obtained by interviewing the patients' parents for the symptoms and patients' medical records for information on the treatments and examinations. **Case:** A 7 months old baby arrived at the hospital with a continuous abrupt 3 days fever, the condition is accompanied by watery stool two times a day, vomiting once a day. **Discussion:** The patient arrived at the hospital with a continuous abrupt 3-day fever. The results of the physical examination showed a positive tourniquet test and palpable liver. The laboratory test results showed that the patient has thrombocytopenia, and the chest x-ray results showed that the patient has pleural effusion. **Conclusions:** The patient was diagnosed with DHF without shock and sent home after the patient got fluid therapy, supportive, and symptomatic treatments.
Keywords: Dengue Haemorrhagic Fever, thrombocytopenia, pleural effusion.

BACKGROUND

One of the most dangerous viral infection known to humankind is one that is caused by the virus dengue because more than 40% of the human population is in danger of the infection, according to the World Health Organization (WHO), an estimated 100 million dengue viral infection happens yearly and that the dengue virus can infect all ages including infants under the age of 1 year old.[1–3] Three factors contribute to the spread of dengue viral infection: the human, the virus, and the vector.[1] The incubation period of the dengue virus within vectors is 8-10 days, while the incubation period of the dengue virus in humans is 3-14 days before the symptoms start to show.[1] In general, dengue viral infection symptoms consist of high fever, headache, nausea, vomiting, malaise, abdominal pain, and joint pains.4 A study of 118 infants under the age of one in Vietnam concluded that 99% of the infants infected with dengue virus presents petechiae.[3]

Dengue viral infection severity consists of asymptomatic dengue infection and symptomatic dengue infection. There are varying degrees of severity in symptomatic dengue viral infection, which are unspecified fever, dengue fever, which is characterized by headaches, retro-orbital pain, myalgia, arthralgia, and signs of hemorrhage. Dengue Haemorrhagic Fever (DHF) characterized by

signs of plasma leakage that can manifest as haemoconcentration, pleural effusion, and ascites. DHF can also present with hypotension, weak pulse, cold acral, and fidgety behavior, indicating circulatory failure. Furthermore, the most dangerous degree of dengue viral infection is Dengue Shock Syndrome (DSS), which presents with a non-palpable pulse.[3] DHF in infants less than one year of age is a disease with various and interesting morbidities and based on a said statement. The author is interested in making a case report on infant DHF to understand the disease better.

CASE REPORT

A 7 months old infant was taken to Emergency Room (ER) of Diponegoro National Hospital on 22 January 2020 at 21.45 with a fever since 3 days ago. The fever's onset is abrupt, continuous, and lasts all day with the highest temperature reaching 39^{o}C. The patient got paracetamol to alleviate the fever, but the fever returns a few hours after. The fever is accompanied by malaise, decreasing appetite, watery feces twice every day about 50 ccs each defecation, no smell of acid, with food remnants present. The patient also experienced nausea and vomiting once a day, about 50 ccs each vomiting, food remnants present, no blood, and no black color. No presence of gum bleeding, epistaxis, rashes, red or black stool. History of past illness, the patient experienced upper respiratory tract infection at the age of 4 months and had no history of similar symptoms. No family or neighbors that experience similar symptoms. In the ER, the patient seems limp, a pulse of 120x per minute, respiratory rate of 20x per minute, the temperature of 39^{O}C, and a positive tourniquet test. Physical examination was within a normal range. The patient got an infuse of Ringer Lactate (RL) 5cc/Kg/hour and paracetamol, zinc, and domperidone. The patient was diagnosed with DHF. During the 5th to the eighth day, the physical examination showed that the liver was palpable 3 cm under the costal arch and still a positive tourniquet test. The patient's laboratory tests showed thrombocytopenia, and the RLD X-Ray showed a Pleural Effusion Index (PEI) of 38%. The patient went home after the laboratory results are stable and free of fever 4x24 hours without antipyretics.

	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8
Haemoglobin (gr/dL) N: 10,1-13,1	11,8	11,5	11,1	10,8	10,5	10,4
Haematocrit (%) N: 32-44	36	33,4	35	37,4	35,7	34,9
Leukocyte(x10^3/mm^3) N: 6,0-17,5	5,6	6,35	11,18	14,88	10,68	18,54
Thrombocyte(x10^3/mm^3) N: 229-553	33	20	10	12	24	163
Temperature (^{o}C)	38	37	36.9	36	36.9	36.9

Table 1. Haemoglobin, hematocrit, leukocyte, thrombocyte, and temperature values

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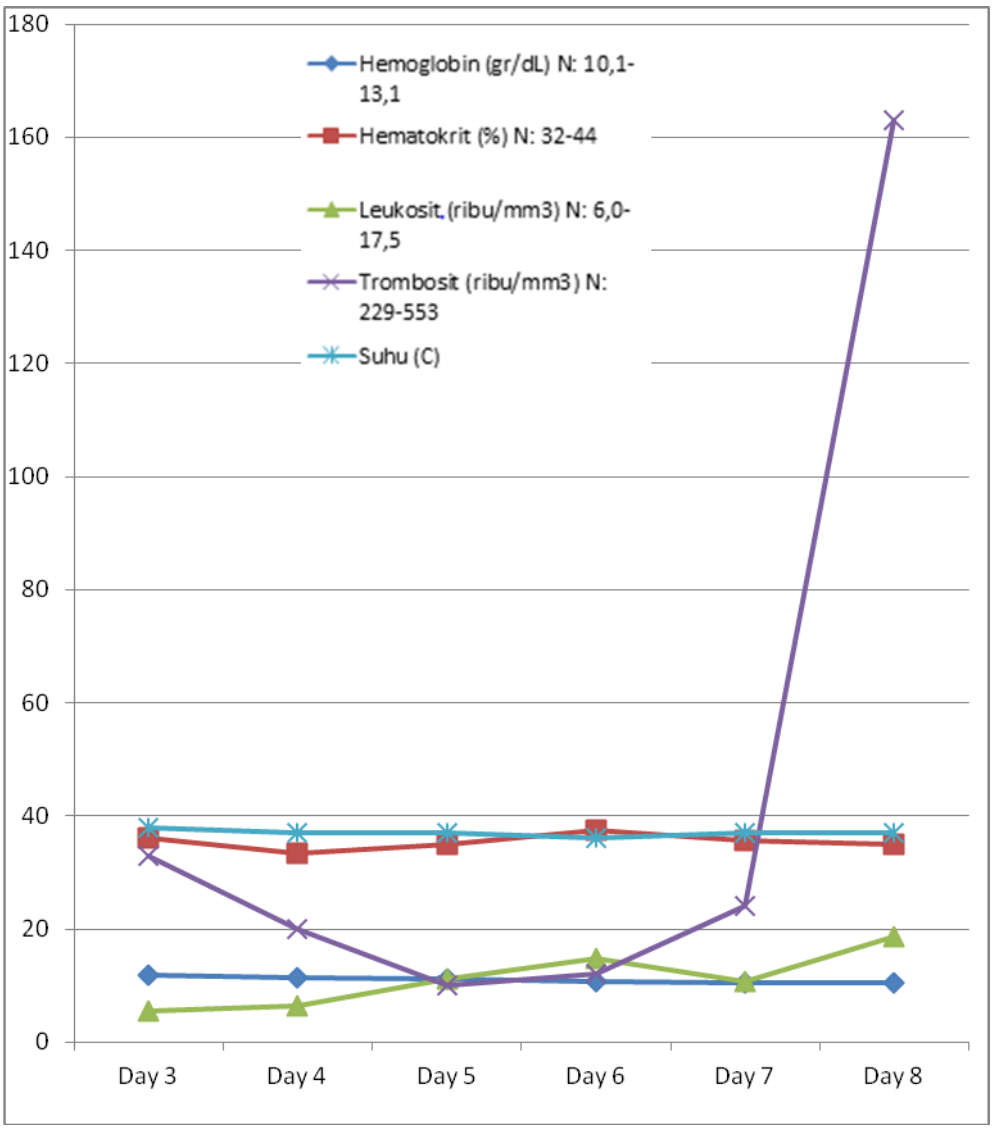

Figure 1. Graph of Haemoglobin, hematocrit, leukocyte, thrombocyte, and temperature values

DISCUSSION

Dengue fever and DHF is an acute fever disease that is caused by the virus dengue.3 The dengue virus is an enveloped positive chain RNA virus from the family *Flaviviridae* and comprised of four main serotypes, DEN-1, DEN-2, DEN-3, and DEN-4, with DEN-2 and DEN-3 is more related to DHF according to past literature.[2,3] Primary infection of one serotype is usually asymptomatic or light symptomatic. However, in secondary infections, DHF or DSS may occur.[5] Lifelong immunity against one of the serotypes obtained after the infection of serotype. However, immunity against other serotypes is only partial immunity. Dengue fever and DHF is a mosquito-borne disease with the primary vector being the mosquito species *Aedes aegypti*, but can also be carried by the mosquito species *Aedes albopticus*.[2] The spread of dengue fever and DHF occurs if the female *Aedes aegypti* suck the infected human blood within the viremia phase which is two days before the

onset of fever dan 4 to 5 days after the onset of fever.[5,6]

In dengue viral infections, IgM antibody against the dengue virus can be found in the blood at around the 4th or fifth day of sickness within the first week. The IgG antibody against the dengue virus in dengue viral infection can be found in the blood at the 7th to the 10th day of sickness in primary infection but can be found quicker in secondary infection.[7]

The serological test of the patient on the 5th day of sickness showed a positive IgM and a negative IgG result, which indicates that the patient is experiencing a primary infection. This condition is in line with the parents' statement that the patient has never experienced similar symptoms. If the patient were to have a secondary infection, the risk of more severe symptoms is higher according to the secondary infection hypothesis.[8]

Clinical manifestations of dengue fever and DHF differs even though the pathogen is the same. Dengue fever is a mild syndrome that presents with a high fever (39^{o}C- 40^{o}C) and is accompanied by several other non-specific symptoms, which are headaches, vomiting, abdominal pain, myalgia or arthralgia, and a positive tourniquet test which indicates a provoked bleeding or petechiae which indicates unprovoked bleeding. The condition may be worsened with thrombocytopenia <100.000/mm3, other more uncommon bleeding signs, i.e., epistaxis, hypermenorrhea, and gastrointestinal bleeding. In general, the symptoms of DHF include high fever, bleeding signs, hepatomegaly, circulatory failure or shock may occur, and signs of plasma leakage, which are haemoconcentration, hematocrit elevation of >20% from previous testing, pleural effusion, and ascites. The liver, kidney, brain, and heart's involvement indicates an expanded dengue syndrome isolated organopathy unusual manifestation that can be caused by co-infection, comorbidities, or complications from prolonged shock.[5]

The three phases of DHF are febrile phase, critical phase, and convalescence phase. The clinical manifestations usually occur 1 to 2 days after the virus has entered the human blood through the vector.[7,9] The febrile phase begins with a presentation of high fever with a temperature of 39-40^{o}C with an abrupt onset, myalgia, headache, nausea, vomiting, and abdominal pain, this phase lasts 2-3 days, in this phase bleeding signs are light such as petechiae which may appear in the axilla, extremities, face, and the palatum.[3,5,8]

The critical phase usually occurs on the 5th day and lasts until the 7th day. In this phase, the fever has declined, but the thrombocyte value decreased as well (<100.000/mm3), hematocrit elevation, which is the sign of plasma leakage that may cause circulatory failure and shock. In this phase, clinical and laboratory patient monitoring is crucial. After the critical phase, the convalescence phase occurs, if the plasma leakage has resolved, the fluid in the pleural cavity and the abdominal cavity will be reabsorbed in the circulation within 12-24 hours after the plasma leakage has resolved, or 36-48 hours aftershock, or 60-72 hours after initial plasma leakage. In this phase the hemodynamics are stabilizing.[5]

In this patient, the patient arrived in the ER with a 3-day fever and limpness, nausea, and vomiting. The physical examination results showed that the liver is palpable 3cm under the costal arch, and a positive tourniquet test. The laboratory tests in the 3rd to the 5th day of sickness showed thrombocytopenia (<100.000/mm3). The RLD X-ray result showed a pleural effusion in the left pleural cavity, which is a sign of plasma leakage. Based on the physical and

laboratory examinations, the patient is experiencing DHF without shock.

Dengue viruses that get into the epidermis layer of the skin will be taken by an Antigen Presenting Cells (APC). Then the virus replicates itself in the APC. The APC will return to a lymph node, which gives the T cells a signal to secrete TNF-alpha, IFN-gamma, IL-6, and IL-8, which are pro-inflammatory molecules that have a role in viral elimination and plasma leakage. The increased vascular permeability mechanism is still unclear, but it is believed that Reactive Oxygen Species (ROS) and pro-inflammatory molecules can increase vascular permeability by breaking down the glycocalyx which is the layer of the endothelium that maintains the integrity of the vessel.[9]

One of the manifestations of plasma leakage is pleural effusion that visible by performing a chest X-ray with the RLD position to determine the PEI value.3 The presence of pleural effusion increases the risk of hypoxemia and increased work of breathing, and it also increases the risk of death by respiratory failure. A past study on the correlation between PEI values and the mortality of children with DSS concluded that>15% of PEI values are a risk factor for respiratory failure in DSS.[10]

In this patient, the chest RLD X-ray resulted in the presence of pleural effusion with a PEI value of 38% which according to a previously stated research, the patient is in the risk of respiratory failure and must be strictly monitored for blood pressure, respiratory rate, heart rate, bleeding signs and hemodynamics.

The three principals in DHF treatments are fluid therapy, supportive therapy, and symptomatic therapy. Patients that are not able to be fed orally is an indication of intravenous fluid therapy. Hematocrit that keeps rising or presence of shock signs is also an indication of intravenous fluid therapy. In the febrile phase, DHF patients are given maintenance infuse consisting of dextrose and electrolytes, and in the critical phase, patients are given crystalloid fluid infuses such as Ringer Lactate (RL), Ringer Acetate (RA), or NaCl 0.9%. The initial dose of fluid therapy is 7cc/Kg/hour for 1-2 hours if the patient's condition improves, then decreased to 5cc/Kg/hour for 4 hours, and then 3cc/Kg/hour. In the convalescence phase, patients are given the same infuse of dextrose and electrolytes. During fluid therapy, it is crucial to monitor the patient's condition for general state and vital signs every 2-4 hours for patients without shock and every 1-2 hours for patients with shock.[5]

This patient was given fluid therapy of RL infuse, and paracetamol drops 1ml if fever is present >38^{o}C, domperidone syrup 15ml every 8 hours, zinc syrup 2.5ml every 24 hours. The patient was monitored for the general state, vital signs, diuresis, and warning signs. The parents should continue breastfeeding.

In general, the prognosis of DHF is good as long as fluid therapy is right and adequate. Clinical parameters for good prognosis are stable hemodynamics, fever-free, no abdominal pain, an increase in appetite, no signs of bleeding, vomiting free, and adequate urine output. It is essential to stop fluid therapy to prevent over-hydration and its complications if the clinical parameters stated are present.

CONCLUSION AND SUGGESTION

A 7 months old child arrived in the ER with three days fever that is accompanied by limpness, decrease in appetite, nausea, vomiting once a day, watery stool twice a day, and a laboratory results of thrombocytopenia (10.000/uL), leukopenia (5600/uL), and a positive

tourniquet test. The patient got fluid, supportive, and symptomatic treatments.

DHF is a relatively common case that happens numerous times with a relatively simple treatment, and the author would like to state that early and accurate diagnosis is crucial so that the treatment may start immediately to prevent severe complications. Family education is vital for the prevention of shock.

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