

Case report of dengue shock syndrome with decrease of consciousness, sepsis, and clinical tuberculosis

Jane Rosaline Sutanto¹, Zuriah Hidajati²

^{1,2}Profesi Dokter, Universitas Tarumanagara, D.K.I Jakarta, Indonesia

ARTICLE INFO

Article history:

Received 29 Nov, 2022

Revised 15 Des, 2022

Accepted 28 Des, 2022

Keywords:

Dengue Shock Syndrome

Sepsis

T.B. Clinic

ABSTRACT

Dengue is a disease caused by the dengue virus, which is a classification of the Flavivirus group. The Aedes mosquito group transmits this virus. Dengue infection can provide a diverse clinical spectrum. This is a type of qualitative research with a case study approach. The case was conducted at the K.R.M.T. Wongsonegoro Regional Hospital, Semarang. Retrieval of data used primary data and secondary data. Case management was done following the Standard Operating Procedures set by the hospital. Data analysis was conducted by comparing cases with review literature sourced from articles or other scientific sources. The case study results pointed out that a girl was brought by her parents to the emergency room at R.S.D. K.R.M.T. Wongsonegoro on April 18, 2022, at 13.30 WIB as a referral patient from the Public Health Center with complaints of seizures and shortness of breath. The child's condition was monitored by experiencing changes on the eleventh day in the PICU Room.

This is an open access article under the [CC BY-NC](#) license.



Corresponding Author:

Jane Rosaline Sutanto,
Profesi Dokter,
Universitas Tarumanegara,
Jln. Letjen S. Parman No. 1, Jakarta Barat 11440, Indonesia.
Email: janerosalinesutanto@gmail.com

INTRODUCTION

Dengue is a disease caused by the dengue virus, which is a classification of the Flavivirus group. The Aedes mosquito group transmits this dengue virus (Ahmad & Poh, 2019; Hidari & Suzuki, 2011; Muller et al., 2017). Dengue infection can provide a diverse clinical spectrum. Dengue virus infection can occur without symptoms (asymptomatic) and cause symptoms such as atypical fever, dengue fever (D.D.) with or without bleeding, and dengue hemorrhagic fever (D.H.F.) with or without shock. Based on data released by WHO, 50 million cases of dengue infection have occurred in all tropical and subtropical regions worldwide. The incidence of dengue virus infection worldwide has increased 30-fold in the last 50 years. It is recorded that around 50–100 million infections occur each year in more than 100 endemic countries, including Indonesia. Based on data from WHO, cases of dengue fever throughout the Americas, Southeast Asia, and the Western Pacific reached 1.2 million in 2008 and more than 3 million in 2013. In 2016, America reported more than 2.38 million cases, the Philippines reported 176,411 cases, and Malaysia 100,028 cases. Indonesia is one of the endemic countries with the highest number of cases in Southeast Asia, with a total of 112,954 cases in 2019.⁶ It is estimated that every year around 50 million people are infected with the dengue virus, of which 500,000 require hospitalization. Nearly 90% of hospitalized patients are children (Ali et al., 2019).

The dengue virus causes dengue from the Flavivirus group. This virus has four serotypes, namely DEN-1, DEN-2, DEN-3, and DEN-4. All of these serotypes can cause dengue fever or dengue hemorrhagic fever. DEN-3 is the most common serotype found in Indonesia. Infection with one of these serotypes confers lifelong immunity against that serotype but does not confer long-term immunity against other serotypes. Thus, a person could be infected with this virus four times. Dengue virus infection can be transmitted through the bite of the *Aedes aegypti* and *Aedes albopictus* mosquito vectors. These two mosquitoes are also vectors of the chikungunya, zika, and yellow fever viruses (Bhatt et al., 2021).

The dengue virus can be transmitted through several methods, such as transmission from mosquitoes to humans, human-to-mosquito transmission, and maternal transmission. In the human-to-mosquito transmission method, mosquitoes can be infected by a viremic person with the dengue virus (Amarasinghe et al., 2011). These infected people may have symptomatic dengue infection for someone who does not yet have symptoms (pre-symptomatic) and does not show any symptoms (asymptomatic). Transmission from humans to mosquitoes can occur two days before the person develops symptoms and up to 2 days after the fever has resolved. The risk of infection in mosquitoes is related to the person's high viremia and high fever. In most people, viraemia lasts 4-5 days, but viremia can last up to 12 days. In mosquito-to-human transmission, the virus is transmitted to humans through the bite of infected female mosquitoes, primarily *Aedes aegypti*. After sucking blood from a person infected with the dengue virus, the virus replicates in the mosquito's midgut and then spreads to the secondary tissue and salivary glands. The time taken from the entry of the virus into the mosquito until the actual transmission to a new host is called the extrinsic incubation period. This period takes 8-12 days if the ambient temperature is between 25-28 °C (Lee et al., 2020; Ranasinghe et al., 2020). Variations in this period depend not only on the surrounding temperature but on several factors, such as daily temperature fluctuations, virus genotype, and initial virus concentration, affecting how long it takes mosquitoes to transmit the virus. After a mosquito is infected, it can transmit the virus. The primary human-to-human transmission method involves the mosquito vector, but there is evidence of maternal transmission from pregnant women to their babies which is possible (Olivera-Botello et al., 2016).

Dengue Shock Syndrome is a hypovolemic shock that occurs due to increased capillary permeability and plasma leakage. Dengue shock usually occurs in the critical phase (3-7 days) and is often preceded by a warning sign. Patients who do not receive adequate fluid therapy will experience shock. Then, the presence of hypovolemia causes the body to carry out a compensation phase through the neurohumoral pathway so that hypoperfusion does not occur in vital organs (Ahmad & Poh, 2019; Lee et al., 2020; Sudulagunta et al., 2016).

RESEARCH METHOD

This type of research is qualitative with a case study approach. The case was taken at the K.R.M.T. Wongsonegoro Regional Hospital, Semarang. Retrieval of data used primary data and secondary data. Case management was done following the Standard Operating Procedures set by the hospital. Data analysis was done by comparing cases with review literature sourced from articles or other scientific sources (Sugiyono, 2017, 2018, 2019).

RESULTS AND DISCUSSIONS

A girl was brought by her parents to the emergency room at R.S.D. K.R.M.T. Wongsonegoro on April 18, 2022, at 13.30 WIB as a referral patient from the Public Health Centre with complaints of seizures and shortness of breath. Previously, the child had shortness of breath and then had a seizure at 11.00 WIB accompanied by a decrease in consciousness. The patient's parents informed that she had a fever since Saturday, April 16, 2022, and had started to get fussy from Thursday, April 14, 2022. She had pointed at his gums, so the patient's parents thought their child would grow teeth. The patient

often coughs but recovers on her own. Then, treatment was carried out for eleven days in the PICU room.

The results of blood laboratory investigations showed an increase in the number of platelets from each blood examination and a decrease in the number of leukocytes. Hb and Ht tend to be below normal values. Electrolyte balance is improving, but there is an increase in S.G.O.T. and S.G.P.T. accompanied by total protein and globulin levels below normal values. X-ray examination of the chest showed bronchopneumonia, and an MSCT scan of the head with contrast showed meningoencephalitis without signs of increased intracranial pressure. Ultrasound examination of the abdomen revealed a duplex pleural effusion. The T.B. scoring examination resulted in 6. On the first day of treatment at the PICU on April 18, 2022, the patient was admitted to the PICU at 15.30 from the E.R. with the condition that the ETT had been removed.

On examination, the general condition was seriously ill, sopor conscious, and cold aral. On the second day, the child looks pale, tightness + decreases, diarrhea +, vomiting -, and nausea +. The child was still sleepy all the time and experienced diarrhea once. On examination, she was still somnolent, with signs of dehydration -, diuresis 5.5, and signs of bleeding -. In the lungs, there was conduction and crackles +/+. Lab results showed Hb 7.4 g/dL; HT 24.2%; Neutrophils 49.4%; platelets 15/ μ L; erythrocytes 2.79/uL; lymphocytes 47.4%; pH 7.186; PCO₂ 16.2 mm Hg; PO₂ 257.7mmHg; HCO₃- 6.2 mmol/L; sodium 130 mmol/L; SGPT 93 U/L; SGOT 424 U/L. The results of the urine examination found P.O.S. bacteria (+1) and positive feces protein. On the third day of treatment, it was noted that the shortness of breath had decreased, fever +, seizures -, and the child was still sleepy. On examination, the child was apathetic with signs of dehydration and signs of bleeding -and diuresis 5.5. On examination of the lungs, there was conduction and rhonchi +/+. Then, on the fourth day, the shortness of breath decreased, fever -, and seizures -the child was still sleepy. On examination, the child was found to be apathetic with signs of dehydration and signs of bleeding -, and diuresis 5.5. The results of the C.T. scan showed that there was a picture of a meningoencephalitis. From the next day until the tenth day, she still experienced the same conditions. Finally, on the eleventh day, the tightness decreased, the heat started to go down, and she began to wake up. On examination, she was aware of compos mentis. Although she was still not active, there were no signs of dehydration and signs of bleeding, and her general condition began to improve. The patient's father looked thin and coughing. The patient had brief contact with her mother's relative, who was confirmed to have T.B.

Non-medical management was carried out for treatment, namely bed rest, O₂ nasal cannula two lpm, and monitoring the patient so that there is sufficient fluid by infusion, having a diet, namely 8 x 75 cc entrakid and nebula/12 hours. The medical action was carried out by injection of meropenem 2x500 mg, amikacin 1x135 mg, ranitidine 2x1/4 ampoules, fluconazole 1x30 mg, methylprednisolone 2x25 mg, citicoline 2x25 mg, mecobalamin 1x25 mg, P.O. zinc 1x20 mg, and P.O. curvit syr 1x1 cth. Follow-up plan and evaluation were done by monitoring the child's awareness and vital signs, monitoring improvement or worsening of complaints and patient's condition, re-monitoring the patient's blood lab by checking D.R., S.G.O.T., and S.G.P.T. again, doing Mantoux test and starting F.D.C. treatment if LFT < 5x normal values and physiotherapy plans for children. Education related to her condition was also delivered to her parents about the conditions experienced by her daughter. It regards management up to the possibility of what could happen while undergoing treatment at the hospital, educating parents about signs that need attention, and if occur to report immediately to the health worker who stays in the room, educating the patient's parents about prevention in the coming days so that the conditions experienced by their daughter do not recur, and advise the patient's parents to screen for T.B. immediately and educate them so that their daughter T.B. treatment does not end later and encourage patients to control routinely.

It is known that the patient's history of growth and development was delayed from her age. The patient was still unable to walk. The patient could only stand by herself for under one minute. In addition, patients also experienced speech delays. The patient could only speak limited words.

From this case, it was known that the child was diagnosed with Dengue Shock Syndrome, which resulted in sepsis and loss of consciousness. The patient also had Clinical T.B. Primary infection with dengue fever, and dengue-like fever was usually self-limited and benign. Loss of fluids and electrolytes, hyperpyrexia, and febrile seizures are the most common complications in infants and young children. Epistaxis, petechial, and purpuric lesions are rare but can occur at any stage. Blood from epistaxis swallowed, vomited, or expelled through the rectum can be confused with gastrointestinal bleeding. Seizures may occur due to high fever.

There are two hypothetical theories regarding the pathogenesis of D.H.F.: the immunopathological mechanism and the theory of secondary heterologous infection. The immune response that plays a role in the pathogenesis of D.H.F. is the humoral response in the form of antibody formation, which is in virus neutralization, complement-mediated cytotoxicity, and antibody-mediated cytotoxicity. In addition, T lymphocytes (CD4 and CD8) have a role in the cellular immune response against the dengue virus. T helper differentiation, namely Th1, will produce interferon gamma, IL-2 and lymphokines, while Th2 will produce IL-4, IL-5, IL-6, IL-10. Meanwhile, monocytes and macrophages also have an essential role in viral phagocytosis. Complement activation by immune complexes also occurs and causes the formation of C3a and C5a. Halstead (1973) stated the hypothesis of secondary heterologous infection. For patients who experience repeated infections with different dengue virus serotypes, re-infection will cause amnestic antibody reactions resulting in high concentrations of immune complexes. Summarizing the opinion of Halstead and other researchers, Kurane and Ennis (1994) stated that dengue virus infection will result in macrophage activation, which will phagocytize the virus-antibody complex, so that the virus will replicate in macrophages and the virus exits the cell, resulting in viremia. Activation of the virus-antibody complex will cause an increase in C3a and C5a, which causes an increase in the permeability of the blood vessel walls resulting in plasma leakage. Infection with dengue virus macrophages, T-helper (CD4), and T-cytotoxic (CD8) can cause lysis of dengue-infected target cells. T-helper cells (CD4) will be activated and produce lymphokines and interferon-gamma, while T-cytotoxic (CD8) plays a greater role in target cell lysis. Gamma interferon will activate monocytes, releasing inflammatory mediators (TNF- α , IL-1, Platelet-activating factor, IL-6, histamine). This release will cause endothelial dysfunction, and plasma leakage occurs.

Among the dengue virus's protein components that have a role in the formation of specific antibodies are proteins E, prM, and NS1 (Sikesa et al., 2022; Villamor et al., 2018). The protein that plays an essential role in the autoimmune mechanism in the pathogenesis of dengue virus infection is NS1. Antibodies against dengue NS1 show cross-reaction with endothelial cells and platelets. Activated endothelial cells can express cytokines, chemokines, and adhesion molecules. Besides the antibodies to the NS1 protein, antibodies to prM can also cause autoimmune reactions because it is suspected that there is a similarity between the NS1 and prM proteins with specific components found in endothelial cells and platelets, which is called molecular mimicry. As a result, cells containing molecules resulting from the bond between the two will be destroyed by macrophages or damaged so that destruction occurs in platelets which causes thrombocytopenia. In endothelial cells, there is increased permeability which results in plasma seepage. Thrombopoietin levels in the blood when thrombocytopenia occurs will increase as compensation for thrombocytopenia. The interaction of the virus with the endothelium causes endothelial dysfunction causing coagulopathy. Dengue virus immune complexes and antibodies in secondary infections can activate the complement system via the classical pathway. NS1 protein can activate the complement system directly through alternative pathways and, if excessive, can cause an increase in vascular permeability (Freise et al., 2021; Samarasekara & Munasinghe, 2018).

The heart maintains circulation by increasing stroke volume, heart rate, and peripheral vasoconstriction. In this phase, blood pressure usually has not decreased, but there has been an increase in heart rate (tachycardia). Suppose plasma leakage continues to occur or the treatment is inadequate. In that case, compensation is carried out by maintaining circulation to vital organs and

reducing circulation to peripheral areas (peripheral vasoconstriction), which clinically causes cold and sweating extremities, cyanosis, mottled skin, C.R.T.> 2 sec. Through peripheral vasoconstriction, there is an increase in peripheral resistance, so diastolic pressure increases. In contrast, systolic pressure remains constant so that the difference between systolic and diastolic will narrow to less than 20 mmHg. In compensated shock, the respiratory system compensates in the form of quite a tachypnea without increased work of the respiratory muscles. If the heart has failed to maintain compensation, this is called decompensated shock, in which case, systolic and diastolic pressures decrease (hypertensive shock). Furthermore, if adequate treatment or treatment is not received, profound shock can occur, characterized by an unmeasurable pulse and blood pressure and increasingly obvious cyanosis (Freise et al., 2021; Trung et al., 2020).

CONCLUSION

Case management follows the standards set by the Regional Hospital. The patient experienced a recovery of consciousness after the seventh day. Non-medical management, namely bed rest and O₂ nasal cannula 2 lpm, was carried out by monitoring the patient so that there was sufficient fluid by infusion, having a diet, namely 8 x 75 cc entrakid and nebula / 12 hours. The medical action was done by injection of meropenem 2x500 mg, amikacin 1x135 mg, ranitidine 2x1/4 ampoules, fluconazole 1x30 mg, methylprednisolone 2x25 mg, citicoline 2x25 mg, mecobalamin 1x25 mg, P.O. zinc 1x20 mg and P.O. curvit syr 1x1 cth. The actions were a follow-up plan and evaluation by monitoring the child's awareness and vital signs, monitoring improvement or worsening of complaints and the patient's condition, re-monitoring the patient's blood lab by checking D.R., S.G.O.T., and S.G.P.T. again, doing Mantoux test and starting F.D.C. treatment if LFT < 5x normal values and physiotherapy plans for children. Education was also given to the parents about the conditions experienced by their daughter. Its education was regarding management up to the possibility of what could happen while undergoing treatment at the hospital, then about signs that need attention and if they occur, they need to report immediately to the health worker who stays in the room, educating the patient's parents about prevention in the coming days so that the conditions experienced by their daughter do not recur and advise the patient's parents to immediately screen for T.B. so that their child's T.B. treatment does not end later, and encourage patients to control routinely.

References

- Ahmad, Z., & Poh, C. L. (2019). The conserved molecular determinants of virulence in dengue virus. In *International Journal of Medical Sciences* (Vol. 16, Issue 3). <https://doi.org/10.7150/ijms.29938>
- Ali, H., Prana, C., & Nasrul, E. (2019). Upregulation of SCUBE1 in dengue virus infection. *Open Access Macedonian Journal of Medical Sciences*, 7(10). <https://doi.org/10.3889/oamjms.2019.352>
- Amarasinghe, A., Kuritsky, J. N., William Letson, G., & Margolis, H. S. (2011). Dengue virus infection in Africa. *Emerging Infectious Diseases*, 17(8). <https://doi.org/10.3201/eid1708.101515>
- Bhatt, P., Sabeena, S. P., Varma, M., & Arunkumar, G. (2021). Current Understanding of the Pathogenesis of Dengue Virus Infection. In *Current Microbiology* (Vol. 78, Issue 1). <https://doi.org/10.1007/s00284-020-02284-w>
- Freise, N. F., Jensen, B., Keitel, V., & Luedde, T. (2021). Gallbladder Wall Thickening associated with Dengue Shock Syndrome in a German traveller - no indication for surgical therapy - a case report. *Tropical Diseases, Travel Medicine and Vaccines*, 7(1). <https://doi.org/10.1186/s40794-021-00148-0>
- Hidari, K. I. P. J., & Suzuki, T. (2011). Dengue virus receptor. In *Tropical Medicine and Health* (Vol. 39, Issue 4 SUPPL.). <https://doi.org/10.2149/tmh.2011-S03>
- Lee, I. K., Hsieh, C. J., Lee, C. Te, & Liu, J. W. (2020). Diabetic patients suffering dengue are at risk for development of dengue shock syndrome/severe dengue: Emphasizing the impacts of co-existing comorbidity(ies) and glycemic control on dengue severity. *Journal of Microbiology, Immunology and Infection*, 53(1). <https://doi.org/10.1016/j.jmii.2017.12.005>
- Muller, D. A., Depelsenaire, A. C. I., & Young, P. R. (2017). Clinical and laboratory diagnosis of dengue virus

- infection. *Journal of Infectious Diseases*, 215. <https://doi.org/10.1093/infdis/jiw649>
- Olivera-Botello, G., Coudeville, L., Fanouillere, K., Guy, B., Chambonneau, L., Noriega, F., Jackson, N., Arredondo-García, J. L., Bouckenoghe, A., Capeding, M. R., Chotpitayasunondh, T., Chua, M. N., Supelano, M. C., Deseda, C., Dietze, R., Frago, C., Hadinegoro, S. R. S., Luong, C. Q., Muhammad Ismail, H. I. H., ... Zambrano, B. (2016). Tetravalent Dengue Vaccine Reduces Symptomatic and Asymptomatic Dengue Virus Infections in Healthy Children and Adolescents Aged 2-16 Years in Asia and Latin America. *Journal of Infectious Diseases*, 214(7). <https://doi.org/10.1093/infdis/jiw297>
- Ranasinghe, K. M. I. U., Dissanayaka, D., Thirumavalavan, K., & Seneviratne, M. (2020). An unusual case of dengue shock syndrome complicated by ilio-femoral deep vein thrombosis; A case report. *B.M.C. Infectious Diseases*, 20(1). <https://doi.org/10.1186/s12879-020-05062-y>
- Samarasekara, K., & Munasinghe, J. (2018). Dengue shock syndrome complicated with acute liver failure and kidney injury, infective endocarditis, and deep vein thrombosis: A case report. *Journal of Medical Case Reports*, 12(1). <https://doi.org/10.1186/s13256-018-1862-1>
- Sikesa, I. G. P. H., Ayu, N. P., & Loekman, J. S. (2022). Acute Kidney Injury in Patients with Dengue Shock Syndrome. *Gazi Medical Journal*, 33(1). <https://doi.org/10.12996/gmj.2022.16>
- Sudulagunta, S. R., Sodalagunta, M. B., Sepehrar, M., Raja, S. K. B., Nataraju, A. S., Kumbhat, M., Sathyanarayana, D., Gummadi, S., & Burra, H. K. (2016). Dengue shock syndrome. *Oxford Medical Case Reports*, 2016(11). <https://doi.org/10.1093/omcr/omw074>
- Sugiyono. (2017). *Metode Penelitian Pendidikan Pendekatan Kuantitatif, Kualitatif dan R &D*. Alfabeta.
- Sugiyono. (2018). *Metode Penelitian Kuantitatif*.
- Sugiyono. (2019). *Metode Penelitian Kuantitatif, Kualitatif, dan R&D* (1st ed.). Penerbit Alfabeta.
- Trung, D. T., Trieu, H. T., & Wills, B. A. (2020). Microvascular Fluid Exchange: Implications of the Revised Starling Model for Resuscitation of Dengue Shock Syndrome. In *Frontiers in Medicine* (Vol. 7). <https://doi.org/10.3389/fmed.2020.601520>
- Villamor, E., Villar, L. A., Lozano-Parra, A., Herrera, V. M., & Herrán, O. F. (2018). Serum fatty acids and progression from dengue fever to dengue haemorrhagic fever/dengue shock syndrome. *British Journal of Nutrition*, 120(7). <https://doi.org/10.1017/S0007114518002039>