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CASE REPORT

ENCEPHALITIS MANIFESTATION IN A PATIENT WITH EXPANDED DENGUE SYNDROME

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Abstract

The expansion of dengue symptoms to other organs has been known as expanded dengue syndrome. One form of this is encephalitis. An 18-year-old male was reported to have communication disruption for one day, high fever for 4 days, headache, retroorbital pain, and myalgia. Thrombocytopenia, hemoconcentration, NS1, and IgG-IgM dengue were positive in laboratory testing. Brain CT results gyral enhancement on the right and left side fronto-temporoparieto-occipital lobe, hypodense area with unclear border on occipital lobe, effacement of sulci and gyri. Dengue hemorrhagic fever and encephalitis were the patient's diagnoses. After five days of therapy, the condition improved. Febrile seizures, intracranial thrombosis/ hemorrhages, encephalopathy, aseptic meningitis/ encephalitis, transverse myelitis, polyneuropathies/ mononeuropathies/ Guillain-Barre Syndrome, and subdural effusions are the neurological signs of expanded dengue infection. CNS involvement reflects severe disease with poorer recovery. A case of encephalitis in a patient with dengue hemorrhagic fever has been reported. Supportive management improves

Keywords: Expanded Dengue Syndrome; Dengue Encephalitis; Neurological Manifestations; Supportive Management.

INTRODUCTION

Dengue is a self-limiting, systemic arboviral infection. The incidence rate of Dengue Hemorrhagic Fever (DHF) in Indonesia has increased significantly over the last 50 years, rising from 0.05 cases per 100,000 person-years in 1968 to 77.96 cases per 100,000 person-years in 2016. In Indonesia, there are 22.55 DHF cases and DHF-related deaths for every 100,000 person-years[1].

Clinical manifestations of dengue virus infection range widely, from dengue fever (DF) to potentially fatal DHF and dengue shock syndrome (DSS). EDS is a rare form of dengue that causes serious damage to the brain, liver, bone marrow, kidneys or heart. Prolonged shock, co-infections, or underlying comorbidities could be the cause. EDS is likely to develop in some high-risk categories, including pregnant women, young children, the elderly, coronary artery disease, hemoglobinopathies, and immunocompromised people (World Health Organization, 2009).

Neurological manifestations of EDS are encephalopathy, febrile seizures, intracranial thrombosis/ hemorrhages, Guillain-Barre Syndrome/ polyneuropathies/ mononeuropathies, aseptic meningitis/ encephalitis, transverse myelitis and subdural effusions (Anam et al., 2017). About 4–21% of dengue patients, meningoencephalitis and encephalitis have been found. CNS involvement reflects severe disease with poorer recovery. The mortality rate from dengue encephalitis may increase to 3.7% (Araújo et al., 2012). We will present a case of encephalitis patient with probable expanded dengue syndrome.

CASE REPORT

Mr. S, a 20-year-old man, unmarried, arrived at the Soetomo Teaching Hospital emergency room with a communication disruption for 1 day. There was altered mentation. There was no hemiparesis, seizures, dysarthria, or asymmetric face. There was a history of moderate-grade, intermittent fever of four days' duration, headache, retroorbital pain, myalgia, nausea, loss of appetite, and lethargy of three days' duration. There were no rash or hemorrhagic manifestations. There was no abdominal pain, vomiting, or abdominal enlargement. There was no cold, cough or shortness of breath, diarrhea, constipation, or weight loss. His previous medical history included a dengue fever at 10 years old. There was no history of traveling or mouse contact. There were no comorbidities.

Based on physical examination, GCS 425, blood pressure 117/76 mmHg, pulse 117 times per minute,

breathing 20 times per minute, axillary body temperature 38.9° C, SpO2 98% with free air. The weight was 50 kg, height was 165 cm (BMI 18.36 kg/m^2). Examination of the head: no anemic conjunctivae, no sclera jaundice, cyanosis, or shortness of breath. No lymph node enlargement or elevated jugular vein pressure. On chest inspection was symmetric. Symmetrical lung areas, no wheezing or rales, and neither murmurs nor gallops in lung examination. Abdominal examination revealed no organomegaly and normal sounds of bowel. Neurology examination: there were no meningeal signs or Kernig sign, Brudzinski 1-4 sign. Lingual palsy and facial palsy were difficult to evaluate. Sensory examination was difficult to evaluate. Motoric evaluation BPR +2/+2, TPR +2/+2, APR +2/+2. There was no Chaddock sign. The cerebellum examination was difficult to evaluate.

Laboratory tests when the patient was admitted to hospital: Hb 15.3 g/dL, Leukocytes 3320/mm3, Platelets 93000/mm3, HCT 43.8%, Neutrophile 70.8%, Lymphocyte 1.3%, Aspartate Aminotransferase (AST) 264 U/L, Alanine Aminotransferase (ALT) 141 U/L, Blood Urea Nitrogen 12 mg/dL, Serum Creatinine (SC) 1.01 mg/dL, Albumin 4.4 gr/dL, Potassium 4.1 mmol/L, Sodium 132 mmol/L, Chloride 93 mmol/L, CRP 0.74 mg/dL, APTT 29.4, PPT 10.8, HBsAg negative, Anti HCV negative, HIV rapid test negative. Blood gas analysis with pH 7.49; pCO2 26; pO2 122; HCO3 19.8; Be -3.5; O^2 saturation 99%. The NS-1 test revealed positive results.

Chest X-ray examination results: heart and lungs within normal limits. Brain CT scan examination: Gyral enhancement on the right and left side frontotemporoparietooccipital lobe, a hypodense area with unclear border on the occipital lobe, effacement of sulci, and gyri. Normal ventricle, cisterna, pons, cerebellum, orbita, mastoid, right and left side paranasal sinus and calvaria. There was no calcification or midline deviation. DHF grade I (4th day) and encephalitis were the patient's diagnoses based on the history, physical examination, laboratory, and radiological examination. Diagnostic plans for this patient are serial complete blood count, NS1, IgG, IgM Dengue, ALT and AST evaluation, and lumbal puncture for cerebrospinal fluid analysis (patient family refused). Treatment plans for the patient were bed rest, head trunk up 30^o, the nasogastric diet starting from 50 ml every 4 hours, infusion of NaCl 0.9% 2000 ml, Metamizole 1 gram every 8 hours intravenously, and Omeprazole 40 mg every 12 hours intravenously.

On the 2nd day of treatment, the patient was still having altered mentation. There was a communication disruption, nausea and fever began to decrease. Based on physical examination, GCS 425, blood pressure 120/70 mmHg, pulse 103 times per minute, breathing 20 times per minute, axillary body temperature 38.6°C. Laboratory tests: Hb 16.7g/dL, Leukocytes 4870/µL, Platelets 42000/µL, HCT 49%, SGOT 255 U/L, SGPT 153 U/L, IgM Dengue positive and IgG Dengue positive. Peripheral blood smear showed erythrocyte normochromic normocytic, polychromasia (-), normoblast (-), leukocyte normal count, dominated with neutrophil segment, immature granulocyte (-), atypical lymphocyte (plasmacytoid), blast (-). Fewer thrombocytes, giant platelets (+), leukocytes with atypical lymphocytes, and thrombocytopenia. Patient diagnosed with DHF grade I (5th day), encephalitis, and elevation of nonspecific transaminase enzymes. The patient's previous therapy is continued.

On the 3rd day of treatment, the patient communicated with a few words. Reduced fever and nausea complaints. GCS 446, 130/70 mmHg blood pressure, 102 regular pulses, breathing 20 times per minute, axillary body temperature 38.0°C, SpO2 98%. Laboratory tests: Hb 15.7g/dL, Leukocytes 5420/µL, Platelets 35000/µL, HCT 46.3, Neutrophile 35.9%, Lymphocyte 53.9%. The patient's previous therapy is continued.

On the 4th day of treatment, altered mentation was better. Fever decreased. GCS 446, blood pressure 117/71 mmHg, pulse 71 times per minute, breathing 20 times per minute, axillary body temperature 36.3°C, SpO2 98%. Laboratory tests: Hb 14.8 g/dL, Leukocytes 6930/µL, Platelets 42000/µL, HCT 44.4%, SGOT 84.4, SGPT 68.1. The patient's previous therapy is continued.

On the 5th day of treatment, there was no altered mentation and communication disruption. Nausea and appetite are getting better. No complaints anymore. GCS 456, 73 pulses per minute, 20 breathings per minute, blood pressure of 120/70 mmHg, axillary body temperature 36.6°C, SpO2 98%. Hb 13 g/dL, Leukocytes 7400/µL, Platelets 93000/µL, HCT 38.3%. Patient diagnosed with DHF grade I (8th day) and encephalitis recovered. The patient was then discharged and given three 500 mg paracetamol tablets. Three days after leaving the hospital, the patient is scheduled to come to the policlinic.

DISCUSSION

Dengue is a self-limiting, systemic arboviral infection. Organ failure, AST or ALT ≥ 1000 units/L, severe bleeding, decreased consciousness, fluid accumulation with respiratory distress, and severe plasma leakage are the signs of severe dengue infection. The rare condition known as EDS involves important organs such as the heart, lungs, kidneys, nervous system, and liver, either with or without fluid leaking (World Health Organization, 2009).

Neurological manifestations of EDS are encephalopathy, febrile seizures, intracranial thrombosis/ hemorrhages, Guillain-Barre Syndrome/

polyneuropathies/ mononeuropathies, aseptic meningitis/ encephalitis, transverse myelitis and subdural effusions (Anam et al., 2017). Dengue encephalitis can be found in DF, DHF, and DSS (Vincent et al., 2022). Headache, convulsions, and altered consciousness are the primary signs of dengue encephalitis (Varatharaj, 2010). In less than 50% of cases of encephalitis, the typical symptoms of dengue fever, such as bleeding, myalgias, and rash are seen. (Solomon & Mallewa, 2001). The following are dengue encephalitis criteria: acute cerebral involvement signs, fever, serum and/or cerebrospinal fluid with dengue genomic material or anti-dengue IgM antibodies, excluding out alternative causes of encephalopathy and viral encephalitis (Soares et al., 2011).

Either direct viral toxicity or dysregulated immunologic response induced on by the virus causes hepatic symptoms. The main targets of DENV infection are hepatocytes and Kupffer cells. Cellular apoptosis is the result of DENV infection of the hepatocytes (Giri et al., 2008). Anorexia, nausea/ vomiting, jaundice, hyperbilirubinemia, liver enlargement, and elevated transaminases are all clinical signs of hepatic involvement in patients (Karoli et al., 2012). There is no special therapy required to treat dengue infections with liver involvement. The key to preventing liver failure is maintaining tissue perfusion and hydration (Dissanayake & Seneviratne, 2018).

Reverse-transcriptase polymerase chain reaction (RT-PCR) technique is used to detect viral nucleic acid in serum during the first week of sickness, Dengue virus infection can be diagnosed (usually positive during the first five days of illness). Widely used and cost-effective, NS1 antigen detection may identify NS1 from days 1–8 of fever begin, independent of primary or secondary dengue infection (Arifijanto et al., 2018). For the early diagnosis of dengue infection, *RT-PCR* and the NS1 antigen are both useful (Aryati et al., 2018). The possibility of a positive NS1 test increases with lowering platelet levels. As early as four days following the beginning of the disease, IgM can be found (Sunari et al., 2023).

A slow and low titer antibody response is a hallmark of primary dengue infection. IgG is found at low titer starting seven days after the disease begins and progressively rises. Four days following the start of the disease, a sharp increase in antibody titer with widespread cross-reactivity indicated a secondary dengue infection (Simmons et al., 2012).

The definition of dengue encephalitis is comprehensive and involves radiological, serological, clinical, and CSF criteria (Carod-Artal et al., 2013). Magnetic resonance imaging (MRI) of the brain, with or without thalamic, cerebellar, and pons bleeding, is frequently normal. While the overall examination of cerebrospinal fluid (CSF) is often normal, elevated white blood cell counts may be detected. Serum and CSF may reveal positive IgM and IgG antibodies to the dengue virus, and IgG affinity tests can be useful in differentiating between primary and secondary dengue. PCR has identified dengue RNA in CSF samples from dengue encephalitis patients. The limited sensitivity of the CSF PCR may be caused by the low virus load in CSF (Domingues et al., 2008).

The dengue virus does not currently have a direct antiviral treatment. Supportive management is preserving adequate intravascular volume. Patients with severe dengue infection, dengue with warning signs of serious infection, or dengue infection with coexisting diseases (diabetes, renal failure, infancy, pregnancy, old age, and poor social status) should be treated inpatiently. Management of fever, plasma leakage, shock, and bleeding (World Health Organization, 2009). Without the use of antivirals, the primary treatments for dengue encephalitis are preserving the airway open, maintaining adequate fluids and nutrition, and monitoring the patient's level of consciousness (Varatharaj, 2010b). Head elevation, mannitol, and steroids can be used to treat elevated intracranial pressure while the patient's level of consciousness is regularly monitored. (Gupta et al., 2022).

The dengue fever mortality rate is less than 1%. Recovery is usually without sequelae. The mortality rate for severe dengue cases or DSS with medically treated is 2−5 %. When severe dengue is not treated, the mortality rate increases by 20%. The death rate from dengue encephalitis may rise by 3.7% (Araújo et al., 2012).

CONCLUSION

We report the case of an expanded dengue syndrome patient with encephalitis manifestations. Diagnosis determination using CSF analysis, radiological, and serological (IgM and IgG Dengue) features. Maintaining the airway, providing sufficient nutrition and fluids, and monitoring the patient's level of consciousness are the primary therapies for dengue encephalitis, without the use of antiviral treatments.

DECLARATION

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Ethical Approval

Consent for Publication

REFERENCES

1.Hoffman JIE, Kaplan S. The incidence of congenital heart disease. J Am Coll Cardiol. 2002;39:1890-900.
2.Park MK. Pediatric Cardiology for Practitioners E-Book: Expert Consult-Online and Print: Elsevier Health Sciences; 2014.
3.Bailliard F, Anderson RH. Tetralogy of fallot. Orphanet J Rare Dis. 2009;4:1-10.
4.Apitz C, Webb GD, Redington AN. Tetralogy of fallot. Lancet. 2009;374:1462-71.

5.Fujiwara T, Kurtts T, Anderson W, Heinle J, Mayer Jr JE. Myocardial protection in cyanotic neonatal lambs. J Thorac Cardiovasc Surg. 1988;96:700-10.
6.Visner MS, Arentzen CE, Ring WS, Anderson RW. Left ventricular dynamic geometry and diastolic mechanics in a model of chronic cyanosis and right ventricular pressure overload. J Thorac Cardiovasc Surg. 1981;81:347-57.
7.Lupinetti FM, Wareing TH, Huddieston CB, Collins JC, Boucek Jr RJ, Bender Jr HW, et al. Pathophysiology of chronic cyanosis in a canine model: functional and metabolic response to global ischemia. J Thorac Cardiovasc Surg. 1985;90:291-6.
8.Ihnken K, Morita K, Buckberg GD, Sherman MP, Young HH. Studies of hypoxemic/reoxygenation injury: Without aortic clamping: III. Comparison of the magnitude of damage by hypoxemia/reoxygenation versus ischemia/reperfusion. J Thorac Cardiovasc Surg. 1995;110:1182-9.
9.Day J.R.S, Taylor K.M. The systemic inflammatory response syndrome and cardiopulmonary bypass. Int J Surg. 2005;3(2);129-140
10.Li S et al. Systemic inflammatory response during cardiopulmonary bypass and strategies. J Extra Corpor Technol. 2005;37(2):180-8
11.Li S, Zhang Y, Li S, Wang X, Zhang R, Lu Z, Yan J. Risk factors associated with prolonged mechanical ventilation after correctvive surgery for tetralogy of fallot. Congenit Heart Dis. 2015;10(3):254-62
12.Almashrafi A et al. Factors associated with prolonged length of stay following cardiac surgery in a major referral hospital in Oman: a retrospective observational study. BMJ Open. 2016;6(6):e010764
13.Puskas J et al. Off-pump coronary bypass provides reduced mortality and morbidity and equivalent 10-year survival. Ann Thorac Surg. 2008;86:1139-46
14.Lassnigg A et al. Influence of intravenous vitamin E supplementation in cardiac surgery on oxidative stress: a double-blinded, randomized, controlled study. Br J Anaesth. 2003 Feb.
15.Matata B, Galinanes M. Cardiopulmonary bypass exacerbates oxidative stress but does not increase proinflammatory cytokine release in patients with diabetes compared with patients without diabetes: regulatory effects of exogenous nitric oxide. J Thorac Cardiovasc Surg. 2000;120(1):1-11
16.Rio D, Stewart A, Pellegrini N. A review of recent studies on malondialdehyde as toxic molecule and biological marker of oxidative stress. Nutr Metab Cardiovasc Dis. 2005;15(4):316-328.
17.Zammert M, Gelman S. The pathophysiology of aortic cross-clamping. Best Pract Res Clin Anaesthesiol. Volume 30, Issue 3. 2016;257-269
18.Etievent J et al. Use of cardiac troponin I as a marker of perioperative myocardial ischemia. Ann Thorac Surg. 1995;59(5):1192-4.
19.Demir I.E, Ceyhan G.O, Fress H. Beyond lactate: is there a role for serum lactate measurement in diagnosing acute mesentric ischemia?. Dig Surg. 2012;29:226-235
20.Jabbari A, Banihashem N, Alijanpour E, Vafaey H, Alereza H, Rabiee S. Serum lactate as a prognositc factor in coronary artery bypass graft operation by on pump method. Caspian J Intern Med. 2013;4(2):662-666
21.Faymonville ME, Pincemail J, Duchateau J, Paulus J-M, Adam A, Deby-Dupont G, et al. Myeloperoxidase and elastase as markers of leukocyte activation during cardiopulmonary bypass in humans. J Thorac Cardiovasc Surg. 1991;102:309-17.
22.Fallouh HB, Kentish JC, Chambers DJ. Targeting for cardioplegia: arresting agents and their safety. Curr Opin Pharmacol. 2009;9(2):220-6.
23.Wallert M, Ziegler M, Wang X, Maluenda A, Xu X, Yap ML, et al. α-Tocopherol preserves cardiac function by reducing oxidative stress and inflammation in ischemia/reperfusion injury. Redox Biol. 2019;26:101292.
24.Ding W, Ji Q, Shi Y, Ma R. Predictors of low cardiac output syndrome after isolated coronary artery bypass grafting. Int Heart J. 2015;56(2):144-9.
25.Yau TM et al. Vitamin E for coronary bypass operations. J Thorac Cardiovasc Surg. 1994;108:302-Van der Ven JPG, Van den Bosch E, Bogers AJCC Helbing WA. Current outcomes and treatment of tetralogy of Fallot. F1000Re. 2019;8:10-19
26.Jonas R. Comprehensive surgical management of congenital heart disease: CRC press; 2002.Park MK, Salamat M. Park's Pediatric Cardiology for Practitioners E-Book: Elsevier Health Sciences; 2020.
27.Thygesen K, Alpert JS, White HD. Universal definition of myocardial infarction. J Am Coll Cardiol. 2007;50:2173-95.
28.Lopaschuk GD, Spafford MA, Marsh DR. Glycolysis is predominant source of myocardial ATP production immediately after birth. Am J Physiol. 1991;261:H1698-H705.
29.Makinde AO, Gamble J, Lopaschuk GD. Upregulation of 5′-AMP–Activated Protein Kinase Is Responsible for the Increase in Myocardial Fatty Acid Oxidation Rates Following Birth in the Newborn Rabbit. Circ Res. 1997;80:482-9.
30.Ghosh S, Falter F, Perrino AC. Cardiopulmonary Bypass: Cambridge University Press; 2015.
31.Ghorbel MT, Cherif M, Jenkins E, Mokhtari A, Kenny D, Angelini GD, et al. Transcriptomic analysis of patients with tetralogy of Fallot reveals the effect of chronic hypoxia on myocardial gene expression. J Thorac Cardiovasc Surg. 2010;140:337-45.
32.Cherif M, Caputo M, Nakaoka Y, Angelini GD, Ghorbel MT. Gab1 is modulated by chronic hypoxia in children with cyanotic congenital heart defect and its overexpression reduces apoptosis in rat neonatal cardiomyocytes. BioMed Res Int. 2015;2015.
33,Chizzonite RA, Zak R. Calcium-induced cell death:

susceptibility of cardiac myocytes is age- dependent. Science. 1981:1508-11.
34.Nakanishi T, Young HH, Shimizu T, Nishioka K, Jarmakani JM. The relationship between myocardial enzyme release and Ca2+ uptake during hypoxia and reoxygenation in the newborn and adult heart. J Mol Cell Cardiol. 1984;16:519-32.
35,Pridjian AK, Levitsky S, Krukenkamp I, Silverman NA, Feinberg H. Developmental changes in reperfusion injury: a comparison of intracellular cation accumulation in the newborn, neonatal, and adult heart. J Thorac Cardiovasc Surg. 1987;93:428-33.
36.Seguchi M, Harding JA, Jarmakani JM. Developmental change in the function of sarcoplasmic reticulum. J Mol Cell Cardiol. 1986;18:189-95.
37.Frank JS, Rich TL. Ca depletion and repletion in rat heart: age-dependent changes in the sarcolemma. Am J Physiol. 1983;245:H343-H53.
38.Hoerter J. Changes in the sensitivity to hypoxia and glucose deprivation in the isolated perfused rabbit heart during perinatal development. Pflugers Arch. 1976;363(1):1-6.
39.Julia P, Kofsky ER, Buckberg GD, Young HH, Bugyi HI. Studies of myocardial protection in the immature heart: III. Models of ischemic and hypoxic/ischemic injury in the immature puppy heart. J Thorac Cardiovasc Surg. 1991;101:14-22.
40.Julia P, Young HH, Buckberg GD, Kofsky ER, Bugyi HI. Studies of myocardial protection in the immature heart: II. Evidence for importance of amino acid metabolism in tolerance to ischemia. J Thorac Cardiovasc Surg. 1990;100:888-95.
41.Breda MA, Drinkwater DC, Laks H, Bhuta S, Como AF, Davtyan HG, et al. Prevention of reperfusion injury in the neonatal heart with leukocyte-depleted blood. The J Thorac Cardiovasc Surg. 1989;97:654-65.
42.Kouchoukos NT, Blackstone EH, Hanley FL, Kirklin JK. Kirklin/Barratt-Boyes Cardiac Surgery E-Book: Elsevier Health Sciences; 2012.
43.Naik SK, Knight A, Elliott MJ. A successful modification of ultrafiltration for cardiopulmonary bypass in children. Perfusion. 1991;6:41-50.
44.Naik SK, Knight A, Elliott M. A prospective randomized study of a modified technique of ultrafiltration during pediatric open-heart surgery. Circulation. 1991;84:III422-31.
45,Naik SK, Balaji S, Elliott MJ. Modified ultrafiltration improves hemodynamics after cardiopulmonary bypass in children. J Am Coll
Cardiol. 1992;19:37A.
46.Wang M-J, Chiu S, Hsu C-M, Wang C-M, Lin P-L, Chang C-I, et al. Efficacy of ultrafiltration in removing inflammatory mediators during pediatric cardiac operations.Ann Thorac Surg.1996;6:651-6.
47.Niki E, Traber MG. A history of vitamin E. Ann Nutr Metab. 2012;61:207-12.
48.Coombes J, Powers S, Demirel H, Hamilton K, Jessup J, Vincent H, et al. Vitamin E deficiency fails to affect myocardial performance during in vivo ischemia-reperfusion. Int J Vitam Nutr Res. 2000;70:293-300.
49.Engin KN. Alpha-tocopherol: looking beyond an antioxidant. Mol Vis. 2009;15:855.
Huang H-Y, Appel LJ. Supplementation of diets with α-tocopherol reduces serum concentrations of γ-and δ-tocopherol in humans. J Nutr. 2003;133:3137-40.
50.Venditti P, Napolitano G, Di Stefano L, Agnisola C, Di Meo S. Effect of vitamin E administration on response to ischaemia–reperfusion of hearts from cold-exposed rats. J Exp Neurosci. 2011;96:635-46.
51.Janero DR. Malondialdehyde and thiobarbituric acid-reactivity as diagnostic indices of lipid peroxidation and peroxidative tissue injury. Free Radic Biol Med. 1990;9:515-40.
52.Naegelen I, Beaume N, Plançon S, Schenten V, Tschirhart EJ, Bréchard S. Regulation of neutrophil degranulation and cytokine secretion: a novel model approach based on linear fitting. J Immunol Res. 2015;2015.
53.Zaffarin AS, Ng SF, Ng MH, Hassan H, Alias E. Pharmacology and pharmacokinetics of vitamin E: nanoformulations to enhance bioavailability. Int J Nanomedicine. 2020;15:9961-9974.
54.Canbaz S, Duran E, Ege T, Sunar H, Cikirikcioglu M, Acipayam M. The effects of intracoronary administration of vitamin E on myocardial ischemia-reperfusion injury during coronary artery surgery. Thorac Cardiovasc Surg. 2003; 51(2) : 57-61.
55.Dhalla NS, Elmoselhi AB, Hata T, Makino N. Status of myocardial antioxidants in ischemia-reperfusion injury. Cardiovasc Res. 2000; 18;47(3):446-56.
56.Rachmat J, Sastroasmoro S, Suyatna FD, Soejono G. Ischemic preconditioning reduces apoptosis in open heart surgery. Asian Cardiovasc and Thorac Ann. 2015; 22(3); 276-283.
57.Sukardi R, Sastroasmoro S, Siregar NC, Djer MM, Suyatna FD, Sadikin M, Ibrahim N, Rahayuningsih SE, Witarto AB. The role of curcumin as an inhibitor of oxidative stress caused by ischaemia re-perfusion injury in tetralogy of Fallot patients undergoing corrective surgery. Cardiol Young. 2016 Mar;26(3):431-8.
58.Hausenloy DJ, Yellon DM. Myocardial ischemia-reperfusion injury: a neglected therapeutic target. J Clin Invest. 2013 Jan 2; 123(1):92-100.
59.Soares ROS, Losada DM, Jordani MC, Evora P, Silva OC. Ischemia/reperfusion injury revisited: an

overview of the latest pharmacological strategies. Int. J. Mol. Sci. 2019. 20(20);5304.
60.Sherwood L. Human Physiology: From Cells to Systems 9th Edition. Cengage Learning; 2016.
61.Zhao RZ, Jiang S, Zhang L, Yu ZB. Mitochondrial electron transport chain, ROS generation and uncoupling (Review). Int. J. Mol. Med. 2019;44:3-15.
62.Canbaz S, Duran E, Ege T, Sunar H, Cikirikcioglu M, Acipayam M. The effects of intracoronary administration of vitamin E on myocardial ischemia-reperfusion injury during coronary artery surgery. Thorac Cardiovasc Surg. 2003; 51(2): 57-61.
63.Timothy M et al. Prophylactic intravenous use of milrinone after cardiac operation in pediatrics (PRIMACORP) study. 2002; 143(1):0-21.
64.Rachmat FD, Rachmat J, Sastroasmoro S, Wanandi SI. Effect of allopurinol on oxidative stress and hypoxic adaptation response during surgical correction of tetralogy of fallot. Acta Med Indones. 2013 Apr;45(2):94-100.
65.Kocak E, Kocak C, Aksoy A, et al. High-sensitivity cardiac troponin T is more helpful in detecting peri-operative myocardial injury and apoptosis during coronary artery bypass graft surgery. Cardiovasc J Afr. 2015;26(6):234-241.
66.Fishbein MC, Wang T, Matijasevic M, Hong L, Apple FS. Myocardial tissue troponins T and I: an immunohistochemical study in experimental models of myocardial ischemia. Cardiovasc Pathol. 2003;12(2):65-71.
67.Chaisiriwong L, Wanitphakdeedecha R, Sitthinamsuwan P, et al. A case-control study of involvement of oxidative DNA damage and alteration of antioxidant defense system in patients with basal cell carcinoma: modulation by tumor removal. Oxid Med Cell Longev. 2016; 2016:5934024.
68.I Made Adi Parmana A. Universitas Indonesia Library. Fakultas Kedokteran Universitas ndonesia; 2022 [cited 2024 Jul 18]. Peran Glutamin Sebagai Protektor Miokard pada Bedah Pintas Arteri Koroner Elektif dengan Fraksi Ejeksi Rendah yang Menggunakan Mesin Pintas Jantung Paru = Myocardial Protecting Role of Glutamine in Patients with Low Ejection Fraction Undergoing Elective On-pump Coronary Artery Bypass Graft Surgery. Available from: https://lib.ui.ac.id
69.Diaz-Frias J, Horenstein MS, Guillaume M. Tetralogy of Fallot. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [cited 2024 Jul 8]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK513288/
70.Pfitzer C, Helm PC, Ferentzi H, Rosenthal LM, Bauer UMM, Berger F, et al. Changing prevalence of severe congenital heart disease: Results from the National Register for Congenital Heart Defects in Germany. Congenit Heart Dis. 2017 Dec;12(6):787–93.
71.Tennant PWG, Samarasekera SD, Pless-Mulloli T, Rankin J. Sex differences in the prevalence of congenital anomalies: a population-based study. Birth Defects Res A Clin Mol Teratol. 2011 Oct;91(10):894–901.
72. P Francannet C, Harris JA, Robert E. The epidemiology of cardiovascular defects, part I: a study based on data from three large registries of congenital malformations. Pediatr Cardiol. 2003;24(3):195–221.
73.Pugnaloni F, Felici A, Corno AF, Marino B, Versacci P, Putotto C. Gender differences in congenital heart defects: a narrative review. Transl Pediatr. 2023 Sep 18;12(9):1753–64.
74.Ziegler M, Wallert M, Lorkowski S, Peter K. Cardiovascular and Metabolic Protection by Vitamin E: A Matter of Treatment Strategy? Antioxidants (Basel). 2020 Sep 29;9(10):935.
75.Martins JT, Li DJ, Baskin LB, Jialal I, Keffer JH. Comparison of cardiac troponin I and lactate dehydrogenase isoenzymes for the late diagnosis of myocardial injury. Am J Clin Pathol. 1996 Dec;106(6):705–8.
76.Onorati F, Cristodoro L, Caroleo S, Esposito A, Amantea B, Santangelo E, et al. Troponin I and Lactate From Coronary Sinus Predict Cardiac Complications After Myocardial Revascularization. The Annals of thoracic surgery. 2007 Mar 1;83:1016–23.
77.Ni L, Wehrens XHT. Cardiac troponin I—more than a biomarker for myocardial ischemia? Annals of Translational Medicine. 2018 Nov;6(Suppl 1):S17–S17.
78.Babuin L, Jaffe AS. T roponin: the biomarker of choice for the detection of cardiac injury. CMAJ. 2005 Nov 8;173(10):1191–202.
79.Mahajan VS, Jarolim P. How to Interpret Elevated Cardiac Troponin Levels. Circulation. 2011 Nov 22;124(21):2350–4.
80.Basit H, Malik A, Huecker MR. Non–ST-Segment Elevation Myocardial Infarction. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [cited 2024 Jul 9]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK513228/
81.Madsen LH, Christensen G, Lund T, Serebruany VL, Granger CB, Hoen I, et al. Time Course of Degradation of Cardiac Troponin I in Patients With Acute ST-Elevation Myocardial Infarction. Circulation Research. 2006;10;99(10):1141–7.